ASSSESSMENT OF RADIOACTIVITY IN MAN

VOL. II

INTERNATIONAL ATOMIC ENERGY AGENCY, VIENNA, 1964
ASSESSMENT OF RADIOACTIVITY IN MAN

VOL. II

CORRIGENDA

In the paper "PHYSICAL MEASUREMENTS AND CLINICAL FINDINGS OF PERSONS WITH RADIUM BURDENS" by H. Muth and E. Oberhausen the following values should be corrected:

Page 218, line 5 should read: 11 µc Ra\(^{226}\)

Page 218, lines 18 and 19 should read: .... the coefficient of the daily Ra\(^{226}\) excretion is \(2.3 \times 10^{-6}\). This value is smaller by the factor 3 than those given by ....

Page 218, last paragraph, first line should read: This equation applied to case 14 leads to a value of \(t = 62\) yr.

Page 218, last paragraph, third line should read: .... this value is at least 1.5 times too high.

Page 219, Table IV, case 14 should read:
11 \times 10^{-6} in the second column and
2.3 \times 10^{-6} in the fourth column.

Page 637: The Chairmen of Sessions 9 to 16 are as follows:

Session 9  C. POLVANI  CNEN, Via Belisario 15, Rome, Italy
Session 10  B. RAJEWSKY  Max-Planck-Institut für Biophysik, Frankfurt/Main, Federal Republic of Germany
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Session 15  P. R. KAMATH  Atomic Energy Establishment, Trombay, Bombay, India

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Page 649: The following author should be inserted after K. Lidén:

Lister, B. A. J.: I, 329
ASSESSMENT
OF RADIOACTIVITY IN MAN
ASSESSMENT
OF RADIOACTIVITY IN MAN

PROCEEDINGS OF THE SYMPOSIUM ON THE
ASSESSMENT OF RADIOACTIVE BODY BURDENS
IN MAN
HELD BY THE
INTERNATIONAL ATOMIC ENERGY AGENCY
INTERNATIONAL LABOUR ORGANISATION
AND
WORLD HEALTH ORGANIZATION
AT HEIDELBERG, 11 - 16 MAY 1964

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FOREWORD

This Symposium on the Assessment of Radioactive Body Burdens in Man was organized jointly by the International Atomic Energy Agency, the International Labour Organisation and the World Health Organization and was held in Heidelberg from 11 - 15 May 1964. It was attended by 181 participants from 28 countries and 6 international organizations.

It was the objective of the Symposium to bring together experts from the various scientific disciplines of physics, chemistry, biology, medicine and mathematics, and to survey their experience in the assessment of radioactive body burdens in man and the resultant radiation doses. In most investigations of internal contamination the errors in the physical measurements are smaller than the errors associated with the interpretation of measurements. For this reason special emphasis was laid in this meeting on the interpretation of measured data.

The 67 papers and the discussions which they stimulated are published in these Proceedings produced in two volumes. Volume I includes all papers which deal with problems generally common to many isotopes: in-vivo counting, bioassay techniques, sample counting and analysis of data. Volume II includes those papers concerned with radioisotopes of specific elements: caesium, radium, radon, strontium, tritium, thorium, uranium, plutonium and rare earth elements.

These Proceedings should prove invaluable to all radiation protection services entrusted with the physical surveillance of internal radiation exposure of man. They should complement the studies of the International Commission on Radiological Protection (ICRP) and assist the work of the Organizations that jointly organized the meeting.

The three Organizations wish to express their appreciation to the Government of the Federal Republic of Germany for its generous invitation and to the scientists who contributed the valuable new information.
EDITORIAL NOTE

The papers and discussions incorporated in the proceedings published by the International Atomic Energy Agency are edited by the Agency's editorial staff to the extent considered necessary for the reader's assistance. The views expressed and the general style adopted remain, however, the responsibility of the named authors or participants.

For the sake of speed of publication the present Proceedings have been printed by composition typing and photo-offset lithography. Within the limitations imposed by this method, every effort has been made to maintain a high editorial standard; in particular, the units and symbols employed are to the fullest practicable extent those standardized or recommended by the competent international scientific bodies.

The affiliations of authors are those given at the time of nomination.

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CAESIUM
(Sessions 8 and 9)
THE ASSESSMENT OF RADIOACTIVE CAESIUM
IN MAN

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Abstract — Résumé — Аннотация — Resumen

THE ASSESSMENT OF RADIOACTIVE CAESIUM IN MAN. The content of radiocaesium (caesium-134, caesium-137) in the human body may be estimated either by body radioactivity measurement or by excretion analysis. This paper discusses some of the difficulties of these two methods.

The use of a whole-body counter poses a problem of calibration; this may be done by means of a solution-filled phantom or (for caesium-137) by the administration of caesium-132. Comparison of these two methods shows that use of an average calibration factor derived from a phantom gives results which are not in error by more than ± 12% for subjects weighing between 50 kg and 100 kg.

In the estimation of radiocaesium contents by excretion analysis there are several sources of uncertainty. The biological half-life varies among individuals from about 50 d to 150 d or more, with a mean of about 110 d. Use of the mean value to calculate a body content from the daily excretion rate can therefore give a result in error by a factor of as much as two. Experimental evidence will be presented to show that in many cases an estimate of the biological half-life can be obtained from the ratio of the urinary to faecal excretions.

The effect of the short-lived component in the retention of caesium on the estimation of a body content is much more important. Use of the correct urinary excretion rate based on the long-lived component can overestimate the content by as much as eight times when applied to the caesium content of urine voided in the first 24 h after intake. The over-estimate from the contents of individual 24-h urine samples does not fall below 50% until about one week after intake. Day-to-day variations introduce errors of no more than ± 30%.

There are marked diurnal variations in the urinary excretion rate of caesium; multiplication by three of the caesium content of an 8-h urine sample voided during the day to obtain the 24-h output over-estimates the excretion rate but by not more than about 30%.

An alternative estimate of the body content of caesium-137 (in μc) results from multiplying the caesium-137/potassium ratio (in μc/g) in the urine by 450. The uncertainties in this estimate, and ways of reducing them, are discussed.
Le taux d'élimination du césium par voie urinaire comporte des variations journalières importantes ; en triplant la teneur en césium d'un échantillon d'urine recueilli pendant 8 h durant le jour pour obtenir la quantité éliminée par 24 h, on obtient un taux d'excrétion trop élevé sans que toutefois cette surestimation soit supérieure à environ 30%.

Pour évaluer la charge corporelle de césium 137 (en µCi), une autre méthode consiste à multiplier le rapport $^{137}$Cs/K (en nCi/g) de l'urine par 450. L'auteur examine les incertitudes que peut comporter cette évaluation et les moyens permettant de les minimiser.

ОПРЕДЕЛЕНИЕ СОДЕРЖАНИЯ РАДИОАКТИВНОГО ЦЕЗИЯ У ЧЕЛОВЕКА. Содержание радиоактивного цезия (Cs$^{134}$ и Cs$^{137}$) в организме человека можно определить либо путем измерения радиоактивности организма, либо с помощью анализа выделений. В статье обсуждаются некоторые трудности, встречающиеся при использовании этих методов.

Использование счетчика для измерения активности всего тела выдвигает проблему калибровки; это может быть выполнено с помощью наполненного раствором фантома или (для Cs$^{137}$) путем введения цезия-132. Сравнение этих двух методов показывает, что использование среднего коэффициента калибровки, полученного на фантоме, дает результаты с ошибкой не более ± 12% для обследуемых весом от 50 до 100 кг.

При определении содержания радиоактивного цезия с помощью анализа выделений существуют различные источники неточности. Период полувыведения варьируется у отдельных лиц от 50 до 150 дней или более, при средней величине около 110 дней. Поэтому использование средней величины для подсчета содержания изотопа в организме на основе скорости суточного выделения может привести к ошибочному результату с фактом, зависящим от величины между разными часами периода полувыведения. Экспериментальные данные показывают, что во многих случаях период полувыведения можно определить, вычисляя отношение величин выделений с мочой и экскрементами.

Влияние компонентов с коротким периодом полураспада при задержке цезия на определение содержания этого элемента в организме имеет гораздо больши значение. Использование приведенной величины скорости выделения с мочой, основанной на определении компонентов с длительным периодом полураспада, может привести к переоценке величины содержания почти в 8 раз при применении этой величины к определению содержания цезия в моче, выделенной в первые сутки после поглощения изотопа. Переоценка при исследовании суточных проб мочи у отдельных лиц не снижается ниже 50% в течение недели после поглощения. Ошибки при определении колебаний в разные дни составляют не более ± 30%.

Детерминированное содержание цезия-137 в организме (в микрокюри) получается за счет умножения коэффициента Cs$^{137}$ (калий в нанокюри/г) и мочи на 450. Обсуждаются погрешности при этом определении и способы их уменьшения.

DETERMINACIÓN DEL CESIO RADIACTIVO EN EL HOMBRE. El contenido de cesio radiactivo (cesio 134, cesio 137) en el organismo humano puede evaluarse por antropogammametría o por análisis de las excreciones. En la memoria se examinan algunas de las dificultades inherentes a ambos métodos.

El empleo de un antropogammámetro plantea un problema de calibración, éste puede resolverse recurriendo a un modelo relleno de solución o (en el caso de cesio 137), por administración de cesio-132. La comparación de estos dos métodos muestra que la aplicación de un coeficiente medio de calibración, deducido de un modelo, proporciona resultados cuyo margen de error no es superior a ± 12%, para sujetos de peso comprendidos entre 50 y 100 kg.

En la evaluación del contenido de cesio radiactivo por análisis de las excreciones hay diferentes causas de indeterminación. El periodo biológico varía de unos individuos a otros entre unos 50 d y 150 d o más, con un valor medio de unos 110 d. Por consiguiente, la aplicación de este valor medio para calcular la carga corporal a partir de la velocidad de excreción diaria puede dar lugar a errores de hasta el 200%. El autor presenta pruebas experimentales de que en muchos casos es posible calcular el periodo biológico a partir de la razón existente entre la excreción urinaria y la excreción fecal.

El efecto del componente de periodo corto en la retención de cesio, al calcular la carga corporal, es mucho más importante. La aplicación de la velocidad de excreción urinaria correcta correspondiente al componente de periodo largo puede inducir a atribuir un valor excesivo, incluso 8 veces superior al valor real, a la carga corporal cuando se trata del contenido de cesio de la orina evacuada en las primeras 24 h que siguen
a la absorción: Este error por exceso, resultante del contenido de muestras individuales de orina evacuada durante 24 h, no desciende a menos del 50% hasta una semana después, aproximadamente, de la absorción. Las variaciones cotidianas son causas de errores no superiores a ~30%.

La velocidad de excreción urinaria del cesio acusa considerables variaciones diurnas. La multiplicación por tres del contenido de cesio de una muestra correspondiente a ocho horas, de orina excretada durante el día para evaluar, la cantidad correspondiente a 24 h da lugar a una sobreestimación de la velocidad de excreción, aunque dicha sobreestimación no es superior a 30%, aproximadamente.

Otro procedimiento para calcular la carga corporal de cesio-137 (en µc) consiste en multiplicar por 450 la razón $^{137}$Cs/potasio (en ng/g) de la orina. El autor examina las causas de indeterminación de este procedimiento y la manera de aminorarlas.

### 1. INTRODUCTION

1.1. Caesium-137 (half-life 30.4 yr) is produced in high yield in the fission of uranium and plutonium, and it is currently present in all persons as a result of contamination of man's food-chain by fall-out from nuclear test explosions [1-3]. With the expanding use of nuclear power stations, the number of persons potentially exposed to large amounts of caesium-137 is likely to increase, and it is important to be able to assess the content of the radionuclide in workers occupationally exposed to it, or in persons resident in the environment of nuclear establishments. This paper describes and discusses the methods of measuring radio-caesium in man.

1.2. The maximum permissible body burden of caesium-137 for occupational exposure is 30 µc, but for members of the general population it is 10 µc, while it is still smaller for children [4]. In considering the sensitivity of any method, it should be borne in mind that it may be necessary to detect and measure one-tenth or one-hundredth of the quantities mentioned.

1.3. Another radioisotope, caesium-134 (half-life 2.1 yr), may be present in man's environment, but as it is produced only by neutron irradiation of stable caesium, it is much less important than caesium-137. The maximum permissible body burden of caesium-134 is 20 µc for occupational exposure. Except where they refer specifically to the maximum permissible levels, the radiations from, or half-life of caesium-137, all the remarks in this paper apply equally to both isotopes.

1.4. There are two principal methods of measuring radio-caesium in the human body, radioactivity measurement or excretion analysis. In the former, advantage may be taken of the gamma-radiation emitted by the short-lived daughter barium-137 m (half-life 2.6 min, 0.66 MeV quanta) of caesium-137 or by caesium-134 (principally 0.6 MeV and 0.8 MeV quanta) to assay the body's content of either radionuclide in a whole-body counter [5]. In excretion analysis the radio-caesium may be measured in the untreated excreta (usually urine) by gamma-ray spectrometry [6] or by chemical separation and beta-counting [7]. In this paper we are less concerned with techniques than with the interpretation of the results.
2. BODY RADIOACTIVITY MEASUREMENT

2.1. The use of scintillation counters in an adequate shield provides a very sensitive method for the measurement of radio-caesium (and other gamma-ray-emitting nuclides) in the human body. The detector size need not be particularly large; thus measurements of fall-out caesium-137 levels were reported in 1957 with statistical standard errors of ± 1 nc with the use of four crystals of thallium-activated sodium iodide only 4.5 cm diam. by 5.1 cm thick[8]. The use of larger crystals, especially those having the excellent energy resolution currently possible, has the advantage of making the photo-peak much more prominent in the gamma-ray spectrum, and this makes possible the unambiguous measurement of caesium-137 in the presence of gamma-ray emitters with quanta of energies close to 0.66 MeV (e.g. RaC - 0.61 MeV, Zr95-Nb95 - 0.76 MeV).

2.2. Some methods of calibration of whole-body counters for caesium-137 have been discussed elsewhere [9]; briefly, the methods available were measurement in the "arc position" (for levels >0.1 μc), use of a phantom filled with a solution of caesium-137, or calculation from the known gamma-ray activity of the subject's potassium content. Inter-laboratory comparisons of the results of measurements on the same individuals suggest that the absolute errors by the different methods are less than ± 1 nc at levels below 10 nc, and less than ± 10% for levels above 10 nc. These errors are acceptable for all purposes.

2.3. The availability in recent years of the 6.2-d isotope caesium-132 has made possible a more direct method of calibration. This radionuclide emits gamma-rays principally of energy 0.669 MeV and because of its short half-life it can be safely administered to humans at levels of about 1 μc. Measurement of the response from a known amount in vivo enables a calibration factor to be determined readily. We have calibrated our four-crystal spectrometer [10] for caesium-137 using caesium-132, and we have studied the variation of the calibration factor with body build for ten volunteer subjects weighing from 50 to 99 kg.

2.4. The caesium-132 was administered orally in a solution containing 1 mg of stable caesium as the chloride. All the excreta were collected for at least 8 d and their contents of caesium-132 were determined by gamma-ray spectrometry and comparison with suitable standards, so that the body retention could be determined at any time. To study changes in distribution of the caesium-132 in vivo, "profile curves" were determined for two of the subjects, using a slit-collimated crystal [11]. The results showed that there was a change in the distribution during the first few days but there was no detectable change between the sixth and twelfth days [12]. For each subject values of the calibration factor (counts/minute in the photo-peak from 1 nc caesium-132) were calculated and plotted as a function of time. Despite the changing distribution, the calibration factor was essentially constant after the first day, although in most cases there was a marked decrease in the first 24 h. We therefore took the mean value of all measurements (4 to 11 in number) for each subject, and the results are set out in Table I.
TABLE I

CAESIUM-132 CALIBRATION FACTORS FOR TEN SUBJECTS

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Calibration factor (cpm/nc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F. T.</td>
<td>F</td>
<td>49</td>
<td>50.5</td>
<td>156</td>
<td>10.63</td>
</tr>
<tr>
<td>D. N.</td>
<td>M</td>
<td>26</td>
<td>58.4</td>
<td>170</td>
<td>10.64</td>
</tr>
<tr>
<td>D. B.</td>
<td>M</td>
<td>41</td>
<td>62.0</td>
<td>184</td>
<td>10.68</td>
</tr>
<tr>
<td>A. C.</td>
<td>M</td>
<td>42</td>
<td>62.5</td>
<td>152</td>
<td>9.58</td>
</tr>
<tr>
<td>B. J.</td>
<td>M</td>
<td>30</td>
<td>66.4</td>
<td>163</td>
<td>9.55</td>
</tr>
<tr>
<td>B. T.</td>
<td>M</td>
<td>41</td>
<td>73.4</td>
<td>173</td>
<td>10.00</td>
</tr>
<tr>
<td>J. R.</td>
<td>M</td>
<td>37</td>
<td>77.9</td>
<td>178</td>
<td>9.32</td>
</tr>
<tr>
<td>L. S.</td>
<td>M</td>
<td>33</td>
<td>80.7</td>
<td>186</td>
<td>9.39</td>
</tr>
<tr>
<td>A. M.</td>
<td>M</td>
<td>35</td>
<td>86.8</td>
<td>190</td>
<td>9.46</td>
</tr>
<tr>
<td>R. M.</td>
<td>M</td>
<td>49</td>
<td>96.8</td>
<td>177</td>
<td>8.33</td>
</tr>
</tbody>
</table>

2.5. A correlation of these data with a parameter related to body build would permit a prediction of the calibration factor for a subject of any weight or height. The quantity

\[ \sqrt{W/H}, \]

where \( W \) is the body weight in grams and \( H \) is the height in cm, may be taken as a measure of the radius of a cylindrical body. In Fig. 1 the calibration factors are plotted as a function of this parameter (open circles), and there seems to be a good correlation. Also plotted are the values of the caesium-137 calibration factors (corrected to 100% gamma-ray abundance) obtained with eight different phantom shapes (solid circles). The point shown as a cross represents the average calibration factor for the five phantom shapes for which

\[ \sqrt{W/H} > 19 \text{ g}^2 \text{ cm}^{-2}; \]

this factor has been used to calculate the caesium-137 contents of all persons regardless of their build. From the scale at the right of Fig. 1 it is apparent that this has not introduced an error of more than 12% for any individual for whom

\[ 18 < \sqrt{W/H} < 23.5. \]

2.6. It is interesting to compare the spread of values measured for our ten subjects with the spread predicted for them by a quasi-theoretical calibration factor reported by MENEELY and his colleagues [13] for a single
8 in X 4 in crystal and subjects reclining in a "tilting chair". Meneely's expression can be re-arranged in the form

\[
\frac{\text{cpm/nc}}{W} = 0.0134 \sqrt{\frac{W}{H}} e^{-0.119 \sqrt{\frac{W}{H}}},
\]

where \( W \) and \( H \) are in grams and cm respectively. The values of this factor for the ten subjects listed in Table I show a much bigger spread (from +18% to -20%) about the mean value, than do our results. This suggests that the independence of efficiency on body build, which has been repeatedly claimed for this crystal-subject geometry is no better than for our arrangement of four crystals and stretcher.

2.7. It is clear that the body content of caesium-137 can be estimated with reasonably good accuracy by external counting at levels down to 1 nc, and use of a phantom filled with a solution of caesium-134 would enable this isotope to be estimated with similar precision. These remarks apply to radio-caesium which has been metabolized and is distributed throughout the soft tissues. Because all the simple compounds of caesium are very soluble in body fluids, this situation will be reached quite rapidly after entry into the body (two or three days), whether by ingestion or by inhalation, but the possibility must also be considered of retention (even if only temporary) in the lung of an "insoluble" complex compound of caesium (the cobaltinitrite, the bismuth iodide complex, etc.). This may require a different calibration factor, although with our four-crystal spectrometer we do not believe it would differ by more than about 30%. For other crystal-subject geometries (particularly that using a "tilting chair") there might be a much larger difference.

2.8. The possible need to measure caesium-137 in children raises somewhat different problems. Our own experience suggests that there is little
difficulty in making the measurements in infants less than 6 months old and in children over 5-6 yr old. Calibration must probably be by measurements of a suitably small phantom, as it is most undesirable to administer caesium-132. It may well be that excretion analysis may be considered more satisfactory provided that adequate accuracy can be assured. We shall consider next the problems of the assessment of radio-caesium in man by excretion analysis.

3. CAESIUM EXCRETION RATES

3.1. The quantitative determination of a toxin in the human body from measurements of the excretion rate requires that the excretion pattern be known with some precision. In the case of caesium it is now well established that the whole-body retention can be expressed as the sum of two exponential functions of time. The half-life of the small (~10%) shorter-lived component is about 1 d, but the half-life of the principal component is very variable among individuals; values reported lie in the range 50-200 d (for a recent review see [12]). The average seems to be between 100 and 110 d. To calculate the body content, the mean daily excretion rate is multiplied by the mean life in the body, which is simply

\[
\text{biological half-life} = \frac{0.693}{\text{half-life}}
\]

Clearly use of the average value for the biological half-life to calculate a body content from the daily excretion rate can give a result in error by as much as a factor of two, for a subject with a biological half-life at either extreme. This may be immaterial if the calculated content is many times less than the maximum permissible, but it may be an embarrassingly high error if the estimated content approaches or exceeds the maximum permissible. In such cases an estimate of the biological half-life is needed urgently unless the content can be determined unambiguously by body radioactivity measurement. In fact, the distribution of values for the biological half-life appears, on the basis of limited data, to be normal with a standard deviation of about 35% of the mean value of 105 d. The standard error on an assumed half-life of 105 d for any individual is therefore ±35%. We shall show later how a better estimate may be obtained.

3.2. The caesium-132 dose administered to each of the ten subjects discussed above, contained in addition about 100 nc caesium-134, and we have used this nuclide to measure the retention of caesium in the subjects and to study the excretion [12, 14]. We have carried out several investigations of the excretion especially by the two subjects with the shortest and longest biological half-lives, intended to throw light on the uncertainties in estimating body contents of caesium by excretion analysis. It so happened that the authors of this paper showed the shortest and longest biological half-lives in the group.
3.3. A striking observation in our results was the remarkable similarity between the faecal excretion rates for most of the subjects of the study, despite the fact that the urinary excretion rates differed among individuals by more than a factor of two. The data in Table II illustrate this point; they show the cumulative urinary and faecal excretions at various times by subjects J.R. and B.T. (The exact values of the half-lives in these two subjects have not been established yet; for the purposes of this paper they may be taken as 60 and 130 d respectively.) In the first 20 d after ingestion both subjects excreted in the faeces 3.1% of the ingested dose, yet J.R. had excreted 27% in the urine, while B.T. had only excreted 12.5% by this route. The urinary excretion of all the other subjects fell between these limiting values; on the other hand their faecal excretions showed little variation. Complete collections of the excreta from all subjects were only continued for eight days; for seven of the subjects the cumulative faecal excretion in this period was between 1.61 and 1.98% of the dose and the other three excreted 1.30% (subject L.S.), 2.56% (subject A.C.) and 2.55% (Mrs. F.T.). We shall refer below to these observations.

3.4. The low excretion of caesium in the faeces, especially in the first few days after ingestion, demonstrates that entry into the blood is essentially complete. The mean faecal excretion found by ROSOFF and her colleagues [15] for seven hospital patients in the first seven days after oral administration of caesium-137 was 1.83% of the dose administered (range 1.5-2.1%).

### Table II

<table>
<thead>
<tr>
<th>Days from ingestion</th>
<th>Cumulative urinary excretion (% of dose)</th>
<th>Cumulative faecal excretion (% of dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>J.R.</td>
<td>B.T.</td>
</tr>
<tr>
<td>1</td>
<td>5.92</td>
<td>3.34</td>
</tr>
<tr>
<td>3</td>
<td>11.37</td>
<td>5.07</td>
</tr>
<tr>
<td>4</td>
<td>12.86</td>
<td>5.82</td>
</tr>
<tr>
<td>5</td>
<td>14.20</td>
<td>6.41</td>
</tr>
<tr>
<td>6</td>
<td>15.40</td>
<td>6.98</td>
</tr>
<tr>
<td>7</td>
<td>16.55</td>
<td>7.56</td>
</tr>
<tr>
<td>8</td>
<td>17.56</td>
<td>8.01</td>
</tr>
<tr>
<td>11</td>
<td>19.95</td>
<td>9.14</td>
</tr>
<tr>
<td>15</td>
<td>23.31</td>
<td>10.53</td>
</tr>
<tr>
<td>20</td>
<td>26.97</td>
<td>12.48</td>
</tr>
</tbody>
</table>
This is in close agreement with our value for the first seven days of 1.78%, although the spread of our results is a little bigger (1.20-2.54%).

3.5. The similarity in the faecal excretion rates among our subjects and those of Rosoff et al. led us to consider the possibility of predicting the biological half-life from the urinary/faecal excretion ratio. If the daily faecal excretion rate is F% of the body content, it can easily be shown that the biological half-life is given by the equation

$$T = \frac{69.3}{(U/F + 1)^F}$$

where $U$ is the daily urinary excretion rate as a percentage of the body content. In Fig. 2 we have plotted as a function of $(U/F + 1)^{-1}$, our values for the biological half-life in the ten subjects and in two others for whom excretion data were available; we have also included such other data as are recorded in the literature [15-17]. Of 17 subjects only two give results which lie significantly outside the limits corresponding to $0.15 > F > 0.10$.
and it would seem that in most cases a rapid assessment of the biological half-life can be made with an error of ±20% or less by assuming that

$$ F = 0.12. $$

This would reduce substantially the error inherent in the assumption of an average value for the biological half-life. It is perhaps worth noting that the two subjects who give values which lie outside the limits drawn in Fig. 2 were not completely "normal". The one subject of our series was developing a pleural effusion of tuberculous origin and the other subject had inactive chronic tuberculosis [15]. It is not clear whether these conditions affected the caesium excretion pattern.

3.6. The situation with regard to the excretion rate of radio-caesium by children is by no means as clear as in the case of adults. There is some evidence that the biological half-life is lower; thus MIETTINEN et al. [22] estimated a mean value of 44 d for a group of 17 boys aged between 10 and 14 yr. We have made an approximate estimate of the biological half-life of caesium in two girls from measurements of the body content and mean daily excretion of fall-out caesium-137 [14]. The results indicated values of 34 d for a 6 yr old and 39 d for an 8 yr old, but these may have been underestimated because environmental levels were increasing at the time. If there is a change of half-life with age then it presumably starts at birth and increases steadily until adulthood is reached.

4. VARIATIONS IN CAESIUM EXCRETION RATES

4.1. The discussion so far has ignored the effect of the short-lived component on the excretion rate. Figure 3 shows the retention and excretion rates (urinary plus faecal) of caesium-132 and -134 by subjects J.R. and B.T. in the first three weeks after ingestion. The retention at time \( t \) was estimated by subtracting from 100% the cumulative excretion in urine and faeces up to time \( t \), and it may be slightly over-estimated by any continuing loss in the sweat [12]. The retention equations shown were fitted by eye and it will be appreciated that the values for the half-lives are not particularly accurate. The equations for the curves drawn through the excretion data were obtained by differentiating the retention equations with respect to time and applying a negative sign, and they fit the data well. The important point to be noted from these results is the large decrease in the excretion rate in the first few days. The data in Table III show the effect of this on the assessment of the body content from individual daily urinary excretions, with application of the excretion rate corresponding to the correct biological half-life of the long-lived component for each individual, and with the adoption of 0.11%/d excreted in the faeces. The contents calculated from urine voided in the first 24 h were six and eight times the true contents, and the over-estimates were still up to 50% after five to seven days. Following accidental intake, the urine voided in the first 24 h is usually collected and analysed. Our results show that the body content cannot be estimated with any precision from such an analysis, and that further collections will be needed.
### TABLE III

**ESTIMATES OF BODY CONTENT OF RADIO-CAESIUM FROM INDIVIDUAL 24-h URINE SAMPLES FROM TWO SUBJECTS**

<table>
<thead>
<tr>
<th>Days after Ingestion</th>
<th>Subject J. R. (Half-life 60 d)</th>
<th>Subject B. T. (Half-life 130 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated content</td>
<td>True content</td>
</tr>
<tr>
<td>0-1</td>
<td>6.0</td>
<td>8.2</td>
</tr>
<tr>
<td>1-2</td>
<td>4.0</td>
<td>*</td>
</tr>
<tr>
<td>2-3</td>
<td>1.9</td>
<td>*</td>
</tr>
<tr>
<td>3-4</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>4-5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>5-6</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>6-7</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>7-8</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>8-21 mean:</td>
<td>1.00</td>
<td>1.03</td>
</tr>
<tr>
<td>range:</td>
<td>0.76-1.30</td>
<td>0.90-1.26</td>
</tr>
</tbody>
</table>

*Urine voided between 1 and 3 days was inadvertently bulked.*

4.2. After the clearance of the short-lived component (i.e. about seven to ten days) no individual urine sample voided in the next 13 d gave a result which was in error by more than 30%. Although this may well be acceptable for many purposes, it should be borne in mind that the two men were volunteer subjects, and that all the urine collections were true 24-h samples. In practice it may be difficult to ensure that samples collected for bioassay do represent the total for 24 h. It is therefore of interest to investigate the possibility of determining the 24-h urinary excretion rate from the urine voided during the working day. Subjects J. R. and B. T. collected urine voided at 2-h intervals during the day, bulking the night's output; in order to get enough activity to measure the caesium-134 and potassium contents with good statistical precision it was necessary to bulk the urine voided in five days, but this had the advantage of reducing the fluctuations noted in individual 24-h samples (Table III). The results are plotted in Fig. 4 together with the urine flow rates and the caesium-134/potassium ratios (in arbitrary units). Marked diurnal variations in the excretion rate of the caesium-134 were observed, and these corresponded quite well with the variations in the urine flow. It is interesting to note that there were three peaks in the caesium-134 excretion by subject J. R., all of about the same magnitude, while there were only two prominent peaks in the case of subject B. T.

4.3. The effects of the diurnal variations on the estimation of the 24-h output from the output during eight hours of the working day may be seen from
the data in Table IV. In each case, multiplication by three of the 8-h output gives a result which is greater than the 24-h output, although not by more than about 30% (subject B. T.). Because the results in Fig. 4 and Table IV were based on the mean excretion rates over five days, we are not able to say whether the diurnal variations would show quite the same pattern when the total 24-h output rises or falls to the extreme values about the mean, as indicated in the last entries in Table III.

4.4. The 8-h output can be used to estimate the 24-h output more accurately by multiplying by the ratio of the urine volumes, as shown in the last line of Table IV. The creatinine content of the 8-h output might conceivably be used to estimate the 24-h urine volume, although there are considerable uncertainties in this procedure [18]. It is interesting to note that the factor of 2.68 found by OAKLEY [18] to give the best estimate of the 24-h creatinine excretion from the 8-h output, gives quite reasonable results when applied to the 8-h excretion of caesium-134. Thus using this factor, we obtain estimated 24-h outputs of 1.04% and 0.46% for subjects J. R. and B. T. respectively, while the true values were 1.00% and 0.39%. There is still an error of 18% in the case of subject B. T.
Fig. 4

Histograms showing the diurnal variations in caesium excretion in the urine (solid lines), and in urine flow (broken lines) for the same subjects as in Fig. 3.

The points represent the values of the caesium-134/potassium ratios (in arbitrary units).

4.5. An alternative approach to the problem of estimating the radio-caesium content of the body has been considered. This is based on the observation that the average value for the fall-out caesium-137/potassium ratio in the body is just three times that in the urine [19], although in individuals there is a variation from 1.9 - 4.6, which arises as a result of variability in the biological half-life of caesium [12], and in the dietary intake of potassium. Since caesium-137 (or caesium-134) and potassium can be determined simultaneously in a urine sample by gamma-ray spectrometry, in principle the caesium body content (in nc) can be derived by multiplying the urinary caesium, potassium ratio (in nc/g) by a factor which incorporates the body potassium content (0.21% of the gross body weight for a young adult man). Thus for a potassium content of 150 g, we have the average relation
<table>
<thead>
<tr>
<th></th>
<th>Subject J. R.</th>
<th>Subject B. T.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Half-life 60 d)</td>
<td>(Half-life 130 d)</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>Cs(^{134}) excretion (%) of body content</td>
<td>Volume (ml)</td>
</tr>
<tr>
<td>24-h sample</td>
<td>1632</td>
<td>1697</td>
</tr>
<tr>
<td>8-h sample</td>
<td>536</td>
<td>750</td>
</tr>
<tr>
<td>(8-h sample) x 3</td>
<td>(1788)</td>
<td>(2250)</td>
</tr>
<tr>
<td>(8-h sample) x 24-h volume</td>
<td>(2252)</td>
<td>(2252)</td>
</tr>
</tbody>
</table>

Table IV

Estimation of the 24-h urinary excretion of caesium-134 from the 8-h output, for two subjects.

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\[ C = 450 \left( \frac{C_\text{S}}{K} \right)_{\text{urine}} \]

where \( C \) is the caesium content of the body. For females with their lower average potassium content, the factor 450 should be replaced by 300.

4.6. An estimate obtained in this way is sensitive to almost all of the sources of variability already discussed, with the additional ones of uncertainty in potassium body content and daily urinary excretion. The potassium body content can be estimated by allowing for age, sex and weight, but certainly not to better than \( \pm \) 15\% for any individual. From the points plotted in Fig. 4 we note that there were diurnal variations in the caesium-134/potassium ratio in both subjects. The magnitude of these variations and their influence on the assessment of the body content may be gauged from the data in Table V. In the case of subject B.T. the ratio for the 8-h period during the day was only 4% different from the 24-h mean, whereas the ratio for subject J.R. was nearly 16% lower for the 8-h sample than the mean for the 24 h. This merely reflects the fact that the ratio was higher during the night than the day for J.R. but about the same for B.T. We believe that measurement of the caesium-137/potassium ratio in the urine affords a convenient means of monitoring the average level of fallout caesium-137 in the body, as suggested by MORGAN and ARKELL [19], but the factor of 3 in the relation between the ratio in vivo and in urine only applies to diets for which the average daily potassium intake is about 3.5 g [19, 20]. For Japanese diets the average is only 1.4 g [21], and the factor is reduced accordingly.

5. RECOMMENDED PROCEDURE

5.1. As a result of our investigations it is possible to recommend a procedure for the estimation of radio-caesium in the human body by excretion analysis, which will minimize the possible sources of error which have been discussed. If the content arises as the result of a known accident, the presence
of the radionuclide in the body may be confirmed by analysis of a urine sample collected some hours after the probable time of intake. It can be estimated that the body content is definitely less than the maximum permissible for occupational exposure, if the urine concentration is less than 0.1 \( \mu \text{c}/\text{l} \) for caesium-137 or 0.07 \( \mu \text{c}/\text{l} \) for caesium-134. Even if these limits are reached or exceeded in the first few samples there is no undue cause for alarm because as has been shown the excretion rate drops very considerably in the first few days.

5.2. Once the fact is established that the maximum permissible body burden has not been exceeded it is suggested that no attempt be made to estimate the actual content for five to seven days. In this time the effects of the short-lived component of the excretion rate become small compared with the other uncertainties (see Table III). We believe that the following method for determining the daily urinary excretion rate offers the best chance of accuracy combined with simplicity. Samples of urine voided during eight hours of the working day are collected on each of three successive days and the average radio-caesium output is determined. This is then multiplied by 2.7 to give an estimate of the 24-h output. The choice of three days is based on a study of the individual daily outputs summarized in the last entries in Table III. While the scatter of the results decreases as the number of consecutive days' samples increases, the improvement beyond three days is not such as to warrant the extra inconvenience of collecting and analysing more samples. The error on the estimated 24-h output is probably no greater than \( \pm 20\% \) if the results of our study are typical.

5.3. An estimate of the biological half-life must now be obtained; we have already seen that there is an inherent standard error of \( \pm 35\% \) in the assumption of an average value of about 105 d, with the possibility of a factor of two in the actual error. If all faecal samples voided during the three days of urine sampling are also collected, we believe that an estimate of the biological half-life can be obtained from the urinary/faecal excretion ratio (Fig. 2), with a standard error of about \( \pm 20\% \). If 24-h sampling of urine and faeces could be managed (instead of the 8-h urine sampling suggested) for three days the error on the half-life could be reduced to perhaps \( \pm 12\% \). The improvement over the inherent error of \( \pm 35\% \) in the assumption of an average half-life must be weighed against the inconvenience of collecting and analysing faeces. In any event is should be possible to estimate the radio-caesium body content with a standard error of between \( \pm 25\% \) and \( \pm 40\% \).

5.4. Assessment of the caesium content of children by excretion analysis is not possible with similar accuracy until more is known about the biological half-life, its variation with age and its variation between individuals. For children under the age of 16, use of a biological half-life of 50 d would probably not give an under-estimate of the body content, but we cannot say to what extent it might give an over-estimate.

ACKNOWLEDGEMENTS

We wish to thank Mr. D. Newton and Miss J. I. Mason who gave much assistance in the early stages of the excretion and retention study; we are
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also grateful to the ten volunteer subjects for their whole-hearted co-operation in collecting urine and faeces for up to three weeks.

REFERENCES

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DISCUSSION

R.G. THOMAS: Dr. C.R. Richmond at the Los Alamos Scientific Laboratory gave caesium-132 to humans who had previously been studied with caesium-137. He found a much shorter half-life in the body with caesium-132. With your data the range in half-life for the ten people was from about 60 to 150 d. Have you also conducted caesium-137 studies on these persons in order to establish whether the variations observed are individualistic or due to the isotopic contribution of the material used?

J. RUNDO: I find Dr. Richmond's findings very difficult to understand. Our estimates of biological half-life for these ten cases were based on caesium-134 rather than caesium-132. I know that a suggestion has been made that the shorter half-life obtained with caesium-132 is a consequence of the relatively large amount of stable caesium with which it is administered.

I should like to make one or two points which I was not able to make in my oral presentation. The ten subjects were chosen with two requirements in mind. One was that they should cover a large range in weight so as to permit calibration of the equipment for such a range. The other was that they should cover a large range in fallout caesium content, because we
suspected that this range in caesium content was a consequence of differences in biological half-life and not of dietary habits. In fact, we already had at that time fairly good evidence that that was the case. In two subjects we found contents differing by a factor of three, while their daily excretion rates differed by only 10 or 15%. We had previously estimated the biological half-life for the ten subjects using the fallout caesium-137 (that is to say, we measured the body contents and the mean daily excretion) and we got values which were in substantial agreement with those obtained by administering a single acute dose of the caesium-132/134 mixture.

In other experiments we have in a sense done what Dr. Richmond has done: we have administered a caesium isotope with a large amount of caesium carrier, and we derived a half-life which is essentially the same as that deduced from the half-life under conditions of chronic exposure.

R. C. THOMAS: I should like to point out the resemblance of data which we have obtained for the excretion by rats of caesium-137 to your data for humans. The amount of caesium-137 appearing in faeces is practically a constant and bears little relationship to body burden. Why then do you feel that faecal analysis is a reasonable bioassay procedure?

J. RUNDO: I would not like to go too deeply into the question of the activity in the faeces of rats because I am, for obvious reasons, more interested in metabolism in humans. But I would say that, in determining the biological half-life from chronic exposures at fallout levels in the two subjects from our group of ten volunteers, we obtained the same urinary/faecal excretion ratio within experimental error as we obtained with the caesium-132/134 mixture.

C. E. MILLER: Have you measured the distribution of caesium-137 along the length of the body? If so, how does the distribution of caesium-137 from fallout differ from that of administered caesium-132 or caesium-134 and how does any difference in distribution affect the accuracy of your calibration?

J. RUNDO: We have only crude information on the comparative distributions of caesium-132 and caesium-134 and of fallout caesium-137. Scans along the body with uncollimated counters gave qualitatively very similar results for normal subjects (i.e., caesium-137) and subjects accidentally contaminated with caesium-134. In any case, after the first 24 h there was no change in the calibration factor despite the fact that "profile" curves showed that changes in distribution were certainly taking place for 4-5 d.
MATERNAL AND INFANTILE METABOLISM OF CAESIUM

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RADIATION PHYSICS DEPARTMENT, UNIVERSITY OF LUND, SWEDEN

Abstract — Résumé — Аннотация — Resumen

MATERNAL AND INFANTILE METABOLISM OF CAESIUM. Investigations concerning the caesium metabolism of three women from late pregnancy to some months after partus are reported. In two cases, biological half-times of about 30 d are found, in contrast to the half-times usually found of about 70 d. The transfer of activity from mother to child via placenta and later via breast milk has been investigated in the three cases. The specific activity of the infant was, at partus, close to that of its mother. A biological half-time for caesium in children of only 25 d was obtained in two cases. Both caesium-137 and caesium-132 were used for the investigations. The radiation doses to the subjects from these isotopes were very small and comparable with the monthly doses from body potassium. Some conclusions on the possibilities of future work are presented.

METABOLISME DU CÉSIUM CHEZ LA MÈRE ET CHEZ LE NOUVEAU-NÉ. Les auteurs présentent les résultats des études qu’ils ont faites pour déterminer le métabolisme du césium chez trois femmes en état de grossesse avancée et pendant les trois mois qui ont suivi l’accouchement. Chez deux sujets, ils ont constaté des périodes biologiques de 30 j environ contre des périodes habituelles de 70 j environ.

Ils ont étudié, chez les trois sujets, le transfert d’activité de la mère au fœtus par l’intermédiaire du placenta et, plus tard, au nouveau-né par le lait maternel. À l’accouchement, l’activité spécifique du nouveau-né était voisine de celle de la mère. Chez deux enfants, les auteurs ont constaté que la période biologique n’était que de 25 j. Ils ont utilisé pour ces études le césium 137 et le césium 132. Les doses d’exposition dues à ces radioisotopes étaient très faibles et comparables aux doses mensuelles dues au potassium contenu dans le corps humain. Les auteurs présentent des conclusions sur l’orientation possible des travaux futurs.

ОБМЕН ЦЕЗИЯ У МАТЕРИ И РЕБЕНКА. Изучался обмен цезия у трех женщин в позднем сроке беременности и в течение нескольких месяцев после родов. В двух случаях период полувыведения составлял около 30 дней, в противоположность обычному сроку около 70 дней. Перенос активности от матери к ребенку через плаценту и грудное молоко изучался в трех случаях. Специфическая активность у ребенка во время родов была такой же, как у матери. В двух случаях период полувыведения для цезия у детей составлял 25 дней. Для исследований использовались Cs137 и Cs132. Доза облучения, получаемая пациентами за счет этих изотопов была очень мала и сравнима с месячными дозами, создаваемыми в организме калием. Представлены некоторые соображения относительно исследований в будущем.

METABOLISMO DEL CESIO EN LA MADRE Y EN EL NIÑO LACTANTE. Se describen las investigaciones relativas al metabolismo del cesio en tres mujeres, investigaciones que abarcaron desde las últimas fases del embarazo a algunos meses después del parto. En dos casos, se registraron períodos biológicos de unos 30 d, que contrastan con el valor normalmente observado (alrededor de 70 d). En los tres casos se investigó la transferencia de actividad de la madre al niño por conducto de la placenta y, más tarde, por intermedio de la leche materna. La actividad específica de los niños fue, en el momento del parto, aproximadamente igual a la de sus respectivas madres. En dos casos se observó para el cesio un período biológico de sólo 25 d. Para las investigaciones se utilizó tanto cesio 137 como cesio 132. Las reducidas dosis de irradiación procedentes de estos isótopos fueron comparables con las dosis mensuales debidas a la carga corporal de potasio. Se exponen algunas conclusiones acerca de las posibilidades de trabajos futuros.

1. INTRODUCTION

Caesium-137 from nuclear weapon tests has proved to be definitely present in certain groups of people, such as Lapps and Eskimos [1, 2, 3]. Dif-
ferent aspects of the metabolism of caesium in man have consequently great interest for the complete evaluation of the radiation hazards to which these groups are exposed. This investigation gives some results concerning the caesium excretion rate in women and children and transfer of activity from mother to child.

The results of an investigation concerning the secretion of caesium in breast milk have recently been reported by AARKROG [4]. A study of placental transfer of strontium in a human subject has also recently been published by RIVERA [5].

2. METHODS OF INVESTIGATION

2.1. Material

Two pregnant women (IS, I-gravida 22 yr old and EN, II-gravida 26 yr old) voluntarily consumed reindeer meat. The meat was naturally contaminated with Cs$^{137}$ to a specific activity of 25-40 nc per kg fresh weight. One of the women (IS) was also studied after an oral intake of Cs$^{132}$ 10 months after partus. A third pregnant woman (EB, I-gravida 23 yr old) was orally given a solution of Cs$^{132}$. All of them were healthy subjects with no known metabolic disturbances.

All three subjects and their infants were measured using whole-body counting on different occasions before and after partus. Samples of the food ingested, excreta, placenta, amniotic fluid, blood from the delivery and breast milk were assayed gammaspectrometrically. The energy interval used for determination of Cs$^{137}$ and K$^{40}$ was 600-720 keV and 1360-1560 keV respectively. However, it was not possible to collect all kinds of samples from all subjects. All three infants were breast-fed during the period of investigation.

2.2. Whole-body counting

The body activity determinations were performed with a low-background whole-body monitor. The adults were measured in a chair geometry of the Argonne type with a 5 inX4 in or 8 inX4 in NaI (Tl) crystal. The geometry has proved to be rather sensitive to a redistribution of activities in the body [6]. In order to be able to make corrections for such redistribution a special study was undertaken.

At regular intervals a male subject voluntarily ate reindeer meat containing 25.5 nc Cs$^{137}$ per kg fresh weight. He was investigated by means of frequent measurements with the 5 inX4 in crystal in the 42 cm chair geometry and excreta were assayed.

The varying sensitivity of the counter due to redistribution could be calculated.

The results, which are shown in Table I, were then used to evaluate the chair measurements on the women. From an earlier thorough calibration an equilibrium sensitivity of the counter of 2.9 cpm per nc was found.

The children were measured lying on a bed with the 8 inX4 in crystal 28 cm above the bed. Calibration was made with a cylindrical plastic bottle filled with solutions of Cs$^{137}$ and K$^{40}$. 
TABLE I

VARIATION OF SENSITIVITY OF THE 42-cm CHAIR GEOMETRY WITH A 5 in X 4 in NaI (Tl) CRYSTAL

<table>
<thead>
<tr>
<th>Time of measurement after activity intake (h)</th>
<th>Sensitivity of the counter (cpm/nc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.8 ± 0.1</td>
</tr>
<tr>
<td>3</td>
<td>3.4 ± 0.1</td>
</tr>
<tr>
<td>28</td>
<td>3.0 ± 0.1</td>
</tr>
<tr>
<td>earlier calibration</td>
<td>2.9 ± 0.1</td>
</tr>
</tbody>
</table>

3. RESULTS

3.1. Caesium metabolism of the mothers

Figures 1, 2 and 3 show the times of reindeer meat intake before partus and retention patterns before and after partus for IS and EN. For evaluation of the retention data a one-exponential excretion curve is assumed for periods beginning more than three days after activity intake. Owing to differences in the body shape before and after partus, the sensitivity of the counter may have changed, so the curve before partus is treated separately from the curve after partus.

The build-up curve for IS is shown in Fig. 1. After 29 d the total activity intake is 77 nc Cs\textsuperscript{137}, while the body burden is only about 33 nc. This indicates a very short half-time (17 d for the later part of the build-up curve) if we assume that 13% of the activity intake is excreted with a half-time of 1.5 d. The retention curve between the end of the intake period and partus indicates a half-time of 33 d (least squares fit). This is shown in Fig. 2.

The discrepancy between the two values illustrates the difficulties in the derivation of metabolic data from the build-up curve in experiments with chronic feeding.

If a two-exponential retention curve is assumed, and if we assume that 40% of the activity intake goes to the compartment with the fast excretion rate, we get a half-time of the slow component of roughly 30 d. No excreta measurements exist that could confirm these whole-body counting results. The interpretation of the retention curve after the end of the intake period but before partus (Fig. 2) is simpler, and probably gives more reliable results.

After partus the excretion rate for this woman was considerably slower, corresponding to a half-time of 69 ± 4 d (Fig. 2). When she was orally given a Cs\textsuperscript{132} solution ten months later, the biological half-time was 65 ± 5 d, in good agreement with the value obtained for the three months period beginning immediately after partus.
Intake of Cs\textsuperscript{137} by food and the corresponding body burdens for IS.
The double SD in each body activity measurement is less than 3%.
Mostly IS ate reindeer meat at about 12.0 p.m. and the body activity was measured about 4 h later.
\( t = 0 \) on the 29th day corresponds to the 100% day in the retention curve for IS (Fig. 2).

The other woman (EN) consumed reindeer meat containing 25.5 nc Cs\textsuperscript{137} per kg fresh weight. During a period of 10 d beginning 22 d before partus she ate about the same amount every day. She consumed a total of 21.8 nc. The seventh and the sixth day before partus she again ate meat containing a total of 5.1 nc. She was measured in the whole-body counter before the beginning of the investigation and rather frequently up to the day before partus and again three times after partus.

The last time was 176 d after the beginning of the meat intake. Figure 3 shows the measured retention due to the above mentioned intake. It is normalized to 100% at partus. Since the fast excretion component at 6 d after the last activity intake is of minor importance [7] a one-exponential decrease is assumed from the time of partus. A most probable half-time
Fig. 3

The net retention of Cs\(^{137}\) in EN after oral intake of contaminated meat.

The bars indicate ±2 SD.

This woman had meals of meat on 11 initial consecutive days and on the 18th and 19th day.

The retention at partus has arbitrarily been chosen as 100%.

The measured body content at this time was 26.5 nc.

Partus was on the 25th day.

The results of the whole-body counting after partus indicate a biological half-time of about 73 d.

of 73 ± 10 d is obtained after partus. The retention is calculated on the assumption that the woman had the same Cs\(^{137}\) intake through her normal food during the whole investigation. That is to say, the measured retention is corrected for the body activity obtained at the beginning of the investigation.

When calculating the slope of the regression line the point at 176 d (in June, 1962) was given less importance since the woman probably got extra Cs\(^{137}\) through her food in the beginning of the summer of 1962. The half-time obtained agrees well with the results of measurements on IS. Contrary to these cases, a much shorter half-time was obtained for EB, who was given Cs\(^{32}\). Figure 4 shows a retention curve corresponding to a biological half-time of 32 ± 2 d. It should be emphasized that this woman was only followed 17 d after partus. For the last two women, EN and EB, the excretion rate before partus could not be studied in detail.

For EB, the amount of caesium secreted in breast milk was followed. Figure 5 shows the specific activity of the breast milk relative to the average specific activity of the mother. The milk production is also shown. The sampling was by necessity incomplete. Activity data shown are scattered more than justified by errors in the measurement of the activity. Samples were taken at different times of the day and at different times of a meal and this might to some extent account for the spread in the data. There also seems to be some tendency for the specific caesium content of the milk relative to that of the mother to decrease with time after partus. The secretion in mother's milk is roughly 5% of the total excretion. It should be noticed that the total excretion rate for this woman was twice as fast as that for the other two women.
Retention of Cs\textsuperscript{137} after oral administration of 100 g solution to EB.

The standard deviation in each measurement is less than the size of the crosses.

The retention at partus is arbitrarily chosen as 100%.

The curve indicates a biological half-time of 32 d.

Specific activities of milk samples from the two other women showed for IS 70% of the mother's specific activity 100 d after partus and for EN less than 3.3% 45 d after partus. The fraction of the total excretion the actual days would be about 80% and less than 3%, respectively. Great individual variations, superimposed on the indicated variations of milk activity at different sampling occasions, probably account to a great extent for the spread of the figures. The 70% value was obtained in September, 1962, so this high value may also to some extent be due to uncontrolled Cs\textsuperscript{137} intake through food.
3.2. Metabolism of the children

The most accurate data on infant metabolism were obtained from the Cs$^{132}$ case, since the activities allowed relatively accurate assays of the child as well as of the breast milk, and of the excreta of the child. A retention curve for this child, corrected for activity intake through breast milk is shown in Fig. 6. Again the period over which the measurements extended was short. In this period a very small excretion during the first two days,

![Retention curve for Cs$^{132}$ child](image)

confirmed by excreta measurements, is followed by an exponential decrease with a half-time of 25 ± 3 d. In the calculation of the given error it is assumed that the errors in the correction for activity intake through breast milk are negligible. The direct measurements show that the total body retention decreases although activity is administered through breast milk.

Retention curves for the two other infants are shown in Fig. 7. For these children, too, the body burden of Cs$^{137}$ decreases. After correction for activity intake, assuming that the specific activity of the breast milk was 20% of that of the mother, the figures from the child born by IS indicate a biological half-time of 21 ± 5 d in agreement with the Cs$^{132}$ child.

3.3. Discrimination between mother and child

Placenta, placental blood, amniotic fluid and umbilical cord blood were collected. The specific activities of the placenta and the child, normalized to the average specific body activity of the mother, immediately after partus, are shown in Table II. For comparison the activity is also given in relation to the potassium content. The amniotic fluid showed about one-fifth of the mother's specific activity, the blood between one-third and one-half.

The specific activity of the child is slightly less than that of its mother. If reference to potassium is made, the relative activity of the child born by EN becomes higher than that of the other two children. The reason is that this child had a lower potassium content than the other two. The placental
Per cent retention

Fig. 7

Retention of Cs\textsuperscript{137} in the children born by IS and EN.

- ••• Measured values for the child born by IS.
- +++ Measured values for the child born by EN.
- •••• Calculated retention curve for the child born by IS.

Corrections have been made for activity intake through breast milk.
The bars indicate ±2 SD. The indicated biological half-time is 21 d.

TABLE II

RADIO-CAESIUM ACTIVITY DATA FOR VARIOUS OBJECTS IMMEDIATELY AFTER PARTUS *

<table>
<thead>
<tr>
<th>Subject</th>
<th>IS</th>
<th>EN</th>
<th>EB</th>
<th>IS</th>
<th>EN</th>
<th>EB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotope</td>
<td>Cs\textsuperscript{137}</td>
<td>Cs\textsuperscript{137}</td>
<td>Cs\textsuperscript{137}</td>
<td>Cs\textsuperscript{137}</td>
<td>Cs\textsuperscript{137}</td>
<td>Cs\textsuperscript{137}</td>
</tr>
<tr>
<td>A</td>
<td>2 SD</td>
<td>A</td>
<td>2 SD</td>
<td>A</td>
<td>2 SD</td>
<td>B</td>
</tr>
<tr>
<td>Mother</td>
<td>100</td>
<td>2</td>
<td>100</td>
<td>3</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>Placenta</td>
<td>59</td>
<td>2</td>
<td>78</td>
<td>5</td>
<td>139</td>
<td>5</td>
</tr>
<tr>
<td>Child</td>
<td>85</td>
<td>6</td>
<td>96</td>
<td>8</td>
<td>95</td>
<td>4</td>
</tr>
</tbody>
</table>

* Normalization to mother as indicated in the Table. The double standard deviation (SD) of the figures is also given.

Activities vary considerably. Reference to potassium does not change the relation between the placental activities significantly.

3.4. Other results

From the whole-body counting of the children their potassium content could be estimated. For the children born by IS, EN and EB, respectively,
the potassium contents were \(2.1 \pm 0.3\), \(1.5 \pm 0.3\) and \(2.2 \pm 0.4\) g potassium per kg body weight.

When the cotton diapers from the Cs\(^{132}\) baby were measured, small amounts of an unexpected nuclide were found. The peak in the gamma spectrum was around 750 keV. From other studies \(\cite{8}\) it is known that clothes sent to the laundry have become contaminated with Zr\(^{95}\)-Nb\(^{95}\). The same thing had probably happened here. In some diapers the contamination amounted to about 1 nc/kg dry diapers.

4. DISCUSSION

4.1. Metabolic data

The availability of meat with a suitable natural Cs\(^{137}\) contamination gave us an opportunity to make these special metabolic studies using low-level whole-body counting techniques. The results from the metabolic studies on pregnant women around partus show that excretion rates corresponding to biological half-times of about 30 d may occur. For the women half-times from 30 to 70 d were found, which should be compared with often found half-times from 80 to 150 d \(\cite{7, 9}\). RUNDO \(\cite{10}\) and ROSOFF et al. \(\cite{11}\) also found excretion rates corresponding to half-times of about 50 d. The different women exhibit different retention patterns. The investigations also show that pregnancy can cause a changed excretion rate. Further investigations in this field are suggested, since the subject has bearing on the estimation of radiation doses to children born by contaminated mothers.

The observed ratio, specific activity of child relative to specific activity of mother, is close to unity. The observed ratio, specific activity of placenta relative to specific activity of mother, shows substantial variations. Although these may have been caused by individual biological differences between the women, it should not be disregarded that activity intake closer to partus coincides with higher relative placental specific activity. Only further investigations can show if this is a case of mere chance.

From the data published by AARKROG \(\cite{4}\) one can derive that in the case reported the secretion in breast milk at chronic feeding was about 40\% of ingested activity (and thereby of the total excretion) at the beginning of the lactation period and about 20\% at the end of it. Aarkrog's data from a single administration of Cs\(^{137}\) show that a high initial secretion in breast milk is followed by a lower secretion. The high initial secretion and the fact that the woman investigated by him secreted about three times as much milk as EB may explain why only 5\% of the total excretion was via breast milk in EB's case.

A very fast excretion for the infants has been revealed. The biological half-time is about 25 d. This is quite in line with the findings by MIETTINEN et al. \(\cite{3}\) that boys of average age 12 yr had a biological half-time of about 44 d while the half-time for related adult men was about 64 d.

Generally, the obtained results show that great care must be taken in the interpretation of obtained data, since these may be strongly influenced by uncontrolled, small dietary intakes.
In Table III are shown radiation doses for the two isotopes used. The advantage with respect to radiation dose of using Cs\(^{132}\) is slightly greater than the figures show since this isotope gives almost 1.00 useful gammas per decay, whereas Cs\(^{137}\) gives only 0.85. The radiation doses to the investigated women and children are shown in Table IV. The radiation doses are of the same order of magnitude as the monthly doses from the body content of potassium.

**TABLE III**

RADIATION DOSES FROM Cs\(^{137}\) AND Cs\(^{132}\) *

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Length (cm)</th>
<th>Total radiation dose (mrad)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>T(_B) = 70 d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cs(^{137})</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>1.46</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>1.51</td>
</tr>
<tr>
<td>40</td>
<td>150</td>
<td>2.01</td>
</tr>
<tr>
<td>70</td>
<td>170</td>
<td>2.14</td>
</tr>
<tr>
<td>100</td>
<td>180</td>
<td>2.26</td>
</tr>
<tr>
<td>Locally absorbed</td>
<td></td>
<td>1.18</td>
</tr>
</tbody>
</table>

* The two isotopes are assumed to be uniformly distributed in human subjects having an initial specific activity of 1 nC/kg body weight. Doses are calculated for two different biological half-times T\(_B\) according to HINE and BROWNELL [12]. The contribution to the total dose from locally absorbed radiation is also given. These have been calculated from betas, conversion electrons, characteristic X-rays and Auger electrons for Cs\(^{137}\) (gross average energy 0.23 MeV) and from the characteristic X-rays and Auger electrons for Cs\(^{132}\) (gross average energy 0.03 MeV).

4.3. Conclusions

Primarily, the aim of this investigation has been to find results applicable to radiation protection calculations. Some results have been obtained that directly permit calculation of the radiation doses for children born by mothers who have ingested radio-caesium before partus. The results also confirm that the biological half-time for caesium increases with age.
TABLE IV

RADIATION DOSES TO THE INVESTIGATED MOTHERS AND CHILDREN *

<table>
<thead>
<tr>
<th>Subject</th>
<th>Isotope</th>
<th>Total administered activity (nc)</th>
<th>Total radiation dose from the activity administered (mrad)</th>
<th>Monthly dose from body potassium (mrad)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS</td>
<td>Cs(^{137})</td>
<td>77</td>
<td>1.5</td>
<td>1.4</td>
</tr>
<tr>
<td>IS</td>
<td>Cs(^{137})</td>
<td>700</td>
<td>1.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Child</td>
<td>Cs(^{137})</td>
<td>4</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>EN</td>
<td>Cs(^{137})</td>
<td>27</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Child</td>
<td>Cs(^{137})</td>
<td>2</td>
<td>0.6</td>
<td>1.2</td>
</tr>
<tr>
<td>EB</td>
<td>Cs(^{137})</td>
<td>1280</td>
<td>1.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Child</td>
<td>Cs(^{137})</td>
<td>55</td>
<td>0.7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

* The additional radiation dose from the administered radio-caesium is compared with the monthly dose from the natural body burden of potassium.

However, the results indicate that many doubtful points exist. Only more extensive investigations can give definite answers. For instance this is the case for the metabolism of the mother before and after partus, placental transfer of activity to the child and retention of caesium in the breast-fed child when caesium is chronically administered to the mother.

We have found that investigations of this kind are possible without severe disturbances in the normal life of the mother and the child, and that the radiation dose to the investigated subjects can be kept small compared with the dose from natural background radiation and even compared with the dose from the natural content of potassium in the subjects.

ACKNOWLEDGEMENTS

The authors wish to express their sincere gratitude to Dr. Kurt Lidén for aid and advice during the course of the investigation. Grants from the Swedish Atomic Research Council are gratefully acknowledged.

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THE METABOLISM OF CAESIUM IN MAN

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Abstract — Résumé — Аннотация — Resumen

THE METABOLISM OF CAESIUM IN MAN. This review is a synthesis of results obtained by authors who submitted papers on the metabolism of caesium in man and was prepared at the request of the scientific secretariat of this Symposium.

MÉTABOLISME DU CESIUM CHEZ L'HOMME. Cette étude fait la synthèse des résultats obtenus par des auteurs qui ont présenté des mémoires sur le métabolisme du césium chez l'homme; elle a été établie à la demande du secrétariat scientifique du Colloque.

МЕТАБОЛИЗМ ЦЕЗИЯ В ОРГАНИЗМЕ ЧЕЛОВЕКА. Этот обзор представляет собой обобщение результатов, полученных авторами, которые представили доклады по вопросу метаболизма цезия в организме человека, и был подготовлен по просьбе научного секретариата симпозиума.

METABOLISMO DEL CESIO EN EL HOMBRE. El presente estudio constituye una síntesis de los resultados obtenidos por autores que han presentado memorias sobre el metabolismo del cesio en el hombre, y se ha preparado a petición de la Secretaría científica de este Simposio.

1. INTRODUCTION

Before the beginning of our present atomic age the element No. 55 caesium had no known importance in biologic systems. The presence of caesium in animal tissue was reported for the first time in 1939 [1]. But only recently the presence in man of its single stable isotope, Cs133, has been proved with sufficient reliability [2, 3]. Its long-lived radioactive isotope, Cs137 (half-life 29.7 yr [4]) was detected in humans for the first time in 1956 [5] and it is now present in all inhabitants of the globe.

Until recently the physiology and metabolism of caesium were entirely unknown. Now radioisotopes of caesium have become pronounced potential radiation hazards. Thus we need detailed knowledge about the behaviour of this element in the body and in the biosphere, which should enable us to establish methods for preventing its entrance in the body or for enhancing its elimination from the body.

In this symposium 17 papers have been submitted on caesium. In addition to the nine papers scheduled for this review a few of the papers to be reviewed by Dr. Miettinen will be referred to as they contain metabolic data.

2. DISTRIBUTION OF CAESIUM IN THE HUMAN BODY

2.1. The caesium-potassium relationship

As an alkali metal the chemistry of caesium resembles closely that of potassium. The distribution and metabolism of caesium in the body, there-
fore was thought to be closely related to potassium. This is only partly true. Hence the caesium-potassium ratio should not be used as a metabolic parameter.

2.2. Bone

At present it is well known that caesium mainly concentrates in soft tissue, particularly in muscles. But for bone widely different and contradictory results have been reported. According to ANDERSON and GUSTAFSON [6] ribs from 1961 showed the same Cs$_{137}$ concentration as muscle tissue. They also found a pronounced age effect with a minimum concentration at age 15 to 20. HARRISON et al. [3] report a stable caesium muscle/femoral bone ratio of 3 to 1 for samples from 1960. However, in [13] the authors describe careful investigation of the Cs$_{137}$ content of samples of femoral bone, bone marrow and muscle tissue from subjects of two age groups, 20 to 30 and 55 to 65. These authors do not find any significant age difference in the caesium concentration of the compact bone tissue of the femur. They report also a muscle/bone ratio of about 20 to 1 for femur in both groups and of 10 to 1 for ribs in the older group. These values disagree entirely with those for ribs reported in [6] for Cs$_{137}$ and in [2] for stable Cs.

2.3. Blood

Blood is a body tissue which offers certain difficulties in caesium distribution studies owing to the fast transfer to and elimination from the blood. In [22] YAMAGATA proposes a method to estimate the average body content of Cs$_{137}$ in a large population based on measurements of blood from blood banks. From total body activity and blood measurements of seven men and two women the author obtained a body/blood concentration ratio given in Table I, where also recently published values [7] are given for comparison. In view of the even larger spread in the latter case it is not surprising that the author's total body activity determinations with muscle samples and with blood analysis differ within the range -20% to +110%. Table I introduces a question of whether there is a real difference in the body/blood concentration ratio of various population groups.

2.4. Microscopic distribution

The microscopic distribution and molecular binding of caesium in human tissue is not known. Investigations in this field should introduce a third phase in the caesium research of biological systems. In [14] this problem is touched upon. The authors have studied the in vitro incubation of Cs$_{137}$ in whole blood from rats at temperatures from 0 to 37°C. They have found an increase of the uptake in the red blood cells with temperature even after washing, supporting their theory that a biochemical process should be involved in binding the caesium ions on the inside of the blood cells, rather than a physical adsorption process on the outside of the cells.
THE Cs\textsuperscript{137} CONCENTRATION RATIO FOR BODY TO BLOOD

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>YAMAGATA [22]</td>
<td>3.5 (2.2 - 5.3)</td>
<td>1.1 (0.8 - 1.3)</td>
</tr>
<tr>
<td>SALO et al.,</td>
<td>6.3 (3.4 - 19.2)</td>
<td>4.4 (1.6 - 8.5)</td>
</tr>
</tbody>
</table>

3. THE GROSS METABOLISM OF CAESIUM IN THE HUMAN BODY

Promoted by the recently increased availability of whole-body counters the number of investigations on the whole-body retention and excretion of radio-caesium gradually rises. The build-up of the body caesium level from chronic exposure via the food, or the change of body retention after acute exposure have been studied by long-term whole-body measurements. The results can be fitted to a two-component exponential equation.

In several papers on caesium submitted to this symposium there are data presented on the retention and the elimination rates $\lambda$, usually given as a biologic half-time $T_{1/2}$, the relationship of which is simply $T_{1/2} \times \lambda = \ln 2 = 0.693$. These new data contribute substantially to our knowledge in this field. They are presented in Fig. 1. A few useful, recently published data are also included for comparison. The data in [15, 16] are obtained from contaminated persons and are therefore given separately in Table II. All other data originate from single oral or intravenous administration studies or from a food intake analysis.

From [17] five individual values can be identified; for the other five persons in the age group 26 to 49, and with half-times from 78 to 100 d, a mean value at 90 d - 36 yr is plotted.

![Biological half-time of cesium in man](image)

*Fig. 1*

Biological half-times presented as a function of age; and for females and males separately.

Other data are presented in Table II.
In [18] biological half-times of 21 and 25 d for newborns are presented. These interesting data seem to be the only ones of their kind hitherto reported in the literature.

From the literature only a few useful data can be extracted due to lack of information on age and sex. RICHMOND et al. [8] made careful studies of four cases; half-times from 110 to 147 d were obtained. COHN et al. [9] gave interesting values for older persons; however, because they have been obtained from patients, it may be questioned if they are fully comparable with those of the healthy persons presented in Fig. 1.

The general pattern of Fig. 1 indicates that the elimination rate of caesium is rather high in children, with a short biologic half-time; the latter increases to a certain extent with age but probably levels off or even decreases at a higher age. A short half-time of 20 d for newborns and 40 d for the average age of 10 are reported. However, the data on children are few and more research is required. Professor SPIERS [10] recently reported that their preliminary results showed half-times for newborns as low as 8 to 10 d in agreement with values of 7 and 10 d given by Rundo in these Proceedings. In the age range 20 to 50 there are substantially more results available scattered in the range, 32 to 155 d. A rather strong concentration around 60 to 80 d is obvious. All female values are smaller than 80 d. However, the average value of 140 d given in [19] and obtained for a large number of persons, cannot easily be attributed to a biologic variability only. Perhaps there is a real difference in the caesium metabolism for people living and working in various regions of the world, which exhibit strong differences in climate, in dietary habits, in manual labour, etc. Half-times reported from Finland, Sweden, and also Russia [11], are concentrated in the range 50 to 80 d. The British data are mostly found in the range 80 to 110 d (even when considering other published data of adults) and the German

### Table II

**BIOLOGIC HALF-TIMES OF RADIOCAESIUM OBTAINED FROM STUDIES OF SUPERFICially CONTAMINATED PERSONS**

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>$T_{1/2}$ (d)</th>
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<tr>
<td>Hesp 1)</td>
<td>25</td>
<td>M</td>
<td>68</td>
</tr>
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<td></td>
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<tr>
<td>Jeanmaire 2)</td>
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<td>Jordan 3)</td>
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<td>M</td>
<td>76</td>
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<tr>
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<td>95</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>M</td>
<td>126</td>
</tr>
</tbody>
</table>

1) "The retention and excretion of caesium-137 by two male subjects";
2) "Note au sujet de deux types de contamination humaine par le $^{137}Cs$";
3) "Caesium-137 chloride retention following accidental ingestion"; these Proceedings.
average value is 140 d. The number of reported Canadian half-times are limited but they point towards a range of 100 to 130 d. From the United States the scattering of half-times is large but the data displayed in Fig. 1, together with those reported in the literature, also indicate a concentration in the range 100 to 130 d.

The future will reveal if the consideration above is more than speculation.

3.1. The enhancement of the caesium elimination rate

Are there any ways of influencing the elimination of caesium from the human body? In [20] two experiments are described dealing with this problem. In one of them the effect of a diuretic compound is studied in two subjects. Two control subjects were also studied. The authors concluded that no substantial difference in urine excretion and in the 20-d Cs$^{137}$ retention was observed in spite of an almost doubled potassium excretion. A more detailed study of such effects is desirable. In the second experiment thyroid extract was administered to one obese person in a weight reduction programme. The therapy had no effect in reducing the person's Cs$^{134}$ activity in spite of the expected increase of the cellular metabolism. Incidentally, his half-time seems to be extraordinarily large, perhaps more than 250 d.

At present there are no known methods of enhancing the caesium excretion from the human body.

3.2. The caesium metabolism in pregnant women

An interesting observation is presented in [18]. The caesium elimination rate for a pregnant woman was found to change abruptly at childbirth, the half-times before and after partus being 33 and 67 d. It is very attractive indeed to consider this phenomenon as a result of the general hormonal and metabolic change which occurs in the female body in such a case. If this is true, it has some relationship to the unsolved problem regarding the caesium metabolism.

3.3. The fast metabolic component

The long-term component of the gross body metabolism of caesium dominates its behaviour in the body but it has been proved that a short-term process contributes also. From data presented in [17, 15, 20, 21] in summary it can be said that this fast fraction constitutes 3 to 22% of the administered activity and that it is characterized by a biologic half-time of 0.5 to 2.5 d. It is further treated in Section 4.2.

4. UPTAKE AND EXCRETION

4.1. Uptake

The dominating uptake of caesium occurs with almost 100% efficiency from the gastrointestinal tract, but inhalation and skin deposition should also
be considered as they are particularly important from a radiation hazard point of view.

Inhalation and lung deposition is reported in [15]. Profile scanning of one case revealed that the lung region contained about 15% of the total body activity. This depot was eliminated with a biologic half-time of 23 d. However, the chemical form of the contaminant could not be determined.

Deposition on the skin is another important route of accidental exposure. In [16], three superficially contaminated persons were investigated. Cs\textsuperscript{137} found in excreta accounted for only a small fraction of the observed decrease in activity between the fifth and eleventh day, probably due to removal of skin contamination. A quantitative analysis of this process can be made by means of the data given in Table 1 of [16] for subject A. With proper extrapolation it can be shown (Fig. 2) that 18% of subject A's body content at the fifth day was eliminated with a half-time of 3.5 d. Only very few data on the elimination rate of skin contamination of caesium are available in the literature. RUNDO [12] reports a half-time of 3.7 d.

![Analysis of the Cs\textsuperscript{137} retention data of case A in [16] indicating a possible skin contamination component](image)

4.2. Excretion

The elimination of caesium from the human body mainly follows the urinary route but a non-negligible fraction also appears in the faeces.

The rapidly-excreted fraction results in rather high urine levels during the first 24 h after administration, from 3 to 8% according to the data given in [17, 21]. Information on the rate and size of the rapid fraction is presented in [17, 15, 20, 21]. Thus half-times are found in the range 0.6 to 2.3 d. The fraction of the administered activity being excreted with this rate is rather widely scattered, ranging from 3 to 22%.

In [21] the new observation is made that a large part of the rapid fraction appears in the urine voided during the first few hours after administration. Figure 1 and Table 1 of [21] show that this fraction can be represented by a sum of two exponential functions, the first one with a half-time of about 2 h and the second one with the previously-known half-time of 1 to 2 d.

In metabolic studies, the 100% collection of all excreta and treatment of faeces samples always constitute difficulties. Until recently the faecal
caesium excretion was poorly known. Recent studies by RUNDO, reported by himself in [17] preceding this review have added substantial data to our knowledge. These data, supported by results on faeces excretion reported in [21] indicate that for the first week after administration a daily faecal excretion of 0.20 to 0.44% of the given activity occurs. Later, after the initial phase has cleared, the rate decreases to less than half, ranging from 0.09 to 0.14%/d. The results in the same papers show that 10 to 20% of the total excretion appears in faeces. However, for the above-mentioned lung-contaminated case in [15] after the 15th day following intake 30% of the excreted caesium was observed in the faeces. In Fig. 9 of this paper an interesting result is shown, namely that for the first 6 days more Cs$^{137}$ was excreted per day in faeces than in urine. No explanation is given for this rather surprising result; probably the solubility of the contaminant, being partly deposited in the lungs, plays a role.

In the papers reviewed no information is available on the importance of sweat as a caesium excretion route. Furthermore, data on the saliva content of caesium is completely lacking in the literature.

5. THE TRANSFER OF CAESIUM FROM MOTHER TO FOETUS AND BREAST MILK

In several experiments with animals the transfer of caesium to foetus and milk has been studied but very few data are available for human females. An interesting contribution in this field is given in [18]. At partus the caesium concentration of mother, placenta and foetus was found to be approximately the same for the three cases studied. Thus, during the last part of the pregnancy, no significant discrimination of caesium between mother and foetus occurs.

The secretion rate of caesium into milk varies considerably. In a carefully studied subject the milk concentration was 20% of the average body concentration. The elimination of caesium via this route constituted 5% of the total excretion. However, a large biologic variability is anticipated and further studies are needed in this field.

6. CONCLUSIONS

The general pattern of the human caesium metabolism gradually improves. Important contributions to this field have been presented in the papers reviewed. As usual, in the case of human beings, the biologic variability complicates research work.

However, many details are lacking. A particularly controversial problem deals with the caesium concentration in bone tissue. Extended investigations are needed in this field.

There is a complete lack of knowledge on the biochemical behaviour of caesium in man. Our possibilities to elucidate the question of enhancing the excretion rate will not improve very much until certain information on the biochemistry of caesium is available.
REFERENCES

[22] YAMAGATA, N., "Assessment of the total body burden of caesium-137 in people by the analysis of blood", these Proceedings.
ASSESSMENT OF THE TOTAL BODY BURDEN OF CAESIUM-137 IN HUMANS BY THE ANALYSIS OF BLOOD

N. YAMAGATA
INSTITUTE OF PUBLIC HEALTH, TOKYO, JAPAN

Abstract — Résumé — Аннотация — Resumen

ASSESSMENT OF THE TOTAL BODY BURDEN OF CAESIUM-137 IN HUMANS BY THE ANALYSIS OF BLOOD

Analysis of post-mortem samples for caesium-137 has been carried on in Japan because whole-body counters are limited in number and not mobile, making the assessment of the population mean levels inconvenient. However, the collection of muscles from autopsies throughout the country is complicated and inconvenient in that a sample should be taken immediately after death.

Considering that only such data as are useful for the assessment of the mean levels of caesium-137 in people are required and it is unnecessary to know individual values, the composite samples of as many individuals as possible would be enough for the analysis. For this purpose, whole blood samples were considered as the best substitute for muscles, as the blood collection system covers the whole country, including 47 licensed blood banks and about 100 hospitals.

Sampling inspection is made continuously of citrated whole blood at the National Institute of Health, Tokyo, where about 500 ampoules are checked, representing more than three million donors throughout the country per year. Less than half the blood in an ampoule was consumed for inspection and the remaining half was stocked to make a composite for the determination of caesium-137 level.

Blood ashes were analysed for the stable caesium content by a neutron activation method. The results afforded the relation between the concentration in the whole blood and the total body amount (1.4 mg for 70 kg man) and this relation would be identical to that for caesium-137 in an equilibrium condition. The results of blood analysis for caesium-137 obtained since June 1963 were compared with those of muscle analyses made during the same period. Good agreement was observed and the blood analysis was found to be the best means for assessing the total body burden of caesium-137 in a population.
constaté une bonne concordance. On peut en conclure que l'analyse du sang constitue le meilleur moyen d'évaluer la charge corporelle de césium 137 pour une population donnée.

ОПРЕДЕЛЕНИЕ ОБЩЕГО СОДЕРЖАНИЯ ЦЕЗИЯ-137 В ОРГАНИЗМЕ ЧЕЛОВЕКА С ПОМОЩЬЮ АНАЛИЗА КРОВИ. В Японии производится исследование содержания цезия-137 в образцах, полученных у умерших людей, так как количество счетчиков для измерения радиоактивности всего организма ограничено, а имеющиеся аппараты немобильны, что затрудняет определение средних уровней заражения населения. Однако получение мышечной ткани после аутопсии со всех концов страны является сложным и неудобным процессом, так как образцы необходимо брать сразу же после смерти.

Учитывая ценность лишь таких данных для определения средних величин содержания цезия-137 у людей и необходимость знания индивидуальных величин, следует добиваться получения комбинированных образцов для анализа от возможно большего числа лиц. Для этой цели наиболее подходящими были признаны образцы цельной крови, поскольку система сбора крови распространена по всей стране и охватывает 47 имеющих лицензию банков переливания крови и около 100 госпиталей.

Проверка образцов цитратной цельной крови производится постоянно в Национальном институте здравоохранения, Токио, где проверяется около 500 ампул крови, полученной от более чем 3 млн. доноров в стране за год. Менее половины крови из ампулы использовалось для проверки, а оставшаяся половина сохранялась для приготовления смеси для определения уровня цезия-137.

Для определения содержания стабильного цезия золу крови исследовали с помощью нейтронного активационного анализа. Полученные данные указывают на наличие связи между концентрацией цезия в цельной крови и его общим содержанием в организме (1,4 мг для человека весом 70 кг); это соотношение является идентичным для цезия-137 в равновесном состоянии. Результаты анализов крови на содержание цезия-137, полученные начиная с июня 1963 года, сравнивались с данными исследования мышц за тот же период. Обнаружено хорошее соответствие данных, и использование анализа крови было признано наилучшим способом для определения в организме общего содержания цезия-137 у населения.

EVALUACIÓN DE LA CARGA CORPORAL TOTAL DE CESIO-137 EN EL HOMBRE POR ANÁLISIS DE SANGRE. En el Japón se efectúan análisis de muestras procedentes de autopsias para determinar su contenido de cesio-137, pues se dispone de pocos antropogammámetros; estos aparatos adolecen además del inconveniente de no ser móviles, lo que dificulta la determinación de la carga corporal media de la población. Ahora bien, el acopio de tejidos musculares convenientes de autopsias practicadas en todo el país es complicado y presenta inconvenientes, pues las muestras deben tomarse en el instante preciso de la muerte.

Teniendo en cuenta que sólo se requieren los datos útiles para evaluar la carga corporal media de cesio-137 en la población y que es innecesario conocer los valores individuales, deberán bastar para el análisis muestras colectivas que representen el mayor número posible de sujetos. Para este fin, se considera que el mejor sustitutivo de los tejidos musculares son las muestras de sangre entera, dado que el sistema de acopio de sangre se extiende a todo el país y abarca 47 bancos de sangre autorizados y unos 100 hospitales.

La sangre entera tratada con ácido cítrico se inspecciona continuamente por muestreo en el Instituto Nacional de Salud de Tokio, donde se comprueban al año unas 500 ampollas que representan más de 3 millones de donadores de sangre de todo el país. Para la inspección se consume menos de la mitad de la sangre de cada ampolla, en tanto que el resto se guarda para constituir una muestra colectiva con el fin de determinar el contenido de cesio-137.

La sangre calcinada se analizó para determinar su contenido de cesio estable por activación neutónica, los resultados permitieron establecer una relación entre la concentración en la sangre entera y el peso total del cuerpo (1,4 mg para una persona de 70 kg) y esta relación sería idéntica a la correspondiente al cesio-137 en estado de equilibrio. Los resultados referentes al cesio-137 reunidos desde junio de 1963 mediante los análisis de sangre se han comparado con los obtenidos por análisis de tejidos musculares, efectuados durante el mismo periodo. Se ha observado una concordancia satisfactoria y se estima que los análisis de sangre constituyen el mejor medio para evaluar la carga corporal total de cesio-137 en la población.

1. INTRODUCTION

Measurements of the total body burden of caesium-137 can be made conveniently using whole-body counters. However, large numbers of indi-
individuals have been counted only in North American and Western Europe. In countries where whole-body counters are not available or are quite limited in number, it may be feasible to obtain population mean levels of caesium-137. In Japan, analysis of post-mortem samples has been carried on since August 1958 at the Institute of Public Health. However, collection of post-mortem muscle samples throughout the country is complicated and inconvenient. Samples should be collected immediately after death.

Since only data for the assessment of mean levels of caesium-137 in people are required, it is not necessary to know individual values, a composite sample of many individuals is satisfactory for analysis. For this purpose, whole blood samples were considered the best substitute for muscles. A system of blood banks covers the whole country, making the collection of samples simple and convenient.

For estimation of total body burden, the relation between the concentration of caesium-137 in blood and in the total body must be known. This paper presents the results of basic determinations of both the concentration of caesium-137 in blood and in the total body for individual human subjects. Estimates of total body burden in Japanese people are given, based on blood and muscle analyses.

2. SAMPLING OF WHOLE BLOOD

The blood collection system covers the whole country including 47 licensed blood banks and about 100 hospitals. Sampling inspection of the citrated whole blood is made continuously at the National Institute of Health, Tokyo. About 500 ampoules are checked yearly, representing more than three million donors. Less than half of the blood in an ampoule is consumed for routine inspection; the remaining half or an aliquot is stocked to make a composite for the determination of caesium-137.

Since July 1963 composite samples have been made and the caesium-137 levels measured by low-background beta counting technique after radiochemical separation, as described in section 3. The results are shown in Table I.

3. SAMPLE PROCESSING AND ANALYSIS.

An attempt was made to find a simple treatment, such as centrifuging or deproteinizing, to concentrate caesium-137 into a small fraction of blood. However, as expected from knowledge of the distribution of alkali elements in blood fractions, centrifugation and treatment with a deproteinizing agent (Trichloroacetic acid) failed, although a concentration of caesium-137 with regard to potassium by a factor of about two was observed in the sediments (Fig.1). Therefore, evaporation and dry ashing were adopted to process the sample of blood.

A composite sample of blood (usually one litre) is homogenized by vigorous mechanical agitation and an aliquot of 150 g is taken into a fused silica basin. This is evaporated to dryness on a hot plate, put into an electric furnace and ashed at 450–500°C. The ash is dissolved by adding hydrochloric acid to the basin after the addition of carrier caesium (20 mg).
TABLE I

Cs$^{137}$ IN THE WHOLE BLOOD SAMPLES OBTAINED FROM BLOOD BANKS THROUGHOUT JAPAN IN 1963

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Time of collection</th>
<th>No. of individuals</th>
<th>Cs$^{137}$ in blood (pc/kg)</th>
<th>Weighted av. for month</th>
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</thead>
<tbody>
<tr>
<td>5-6</td>
<td>July 17</td>
<td>18</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>12</td>
<td>Aug. 14</td>
<td>4</td>
<td>37</td>
<td>32</td>
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<td>13-15</td>
<td>Aug. 28</td>
<td>17</td>
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<td>16-17</td>
<td>Sept. 4</td>
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</tbody>
</table>

Radiochemical separation is by the dipicrylaminate-chloroplatinate method as described elsewhere [1]. The overall error in the determination is considered as ±10% or less.

4. BASIC DETERMINATIONS ON LABORATORY PERSONNEL

Total body burdens of nine laboratory personnel were measured with a whole-body counter at the Japan Atomic Energy Research Institute, using the method developed by SUGURI [2]. On the day before or after the whole-body
TOTAL BODY BURDEN OF CAESIUM-137

BLOOD
(1020 g)

CENTRIFUGE

SEDIMENT
9.5 pc. Cs$^{137}$
C. U. 108

SUPERNATANT
16% TCA

SEDIMENT
49.7 mg K
4.5 pc. Cs$^{137}$
C. U. 91

Fig. 1
Distribution of caesium-137 in blood fractions.

measurement, approximately 100 ml of blood was taken from each of the subjects, processed as described in section 3, and the caesium-137 content measured by $\beta$-counting. The results are shown in Table II.

- 5. ESTIMATING METHOD OF THE TOTAL BODY BURDEN

Table II indicates a fairly large fluctuation of the correlation factor between levels in blood and in the total body. The data for females is ex-

<table>
<thead>
<tr>
<th>Date of measurement</th>
<th>Subject personnel</th>
<th>Sex</th>
<th>Age</th>
<th>Body weight (kg)</th>
<th>Cs$^{137}$ in blood (pc/kg)</th>
<th>Total body burden (nc)</th>
<th>Factor f*</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 Nov. '63</td>
<td>Jw</td>
<td>m</td>
<td>32</td>
<td>57.5</td>
<td>40</td>
<td>10.8</td>
<td>4.7</td>
</tr>
<tr>
<td>&quot;</td>
<td>K</td>
<td>m</td>
<td>22</td>
<td>61.2</td>
<td>37</td>
<td>10.0</td>
<td>4.4</td>
</tr>
<tr>
<td>&quot;</td>
<td>Ob</td>
<td>m</td>
<td>22</td>
<td>53.0</td>
<td>34</td>
<td>5.1</td>
<td>2.8</td>
</tr>
<tr>
<td>&quot;</td>
<td>Sa</td>
<td>m</td>
<td>29</td>
<td>65.3</td>
<td>40</td>
<td>11.4</td>
<td>4.4</td>
</tr>
<tr>
<td>&quot;</td>
<td>Su</td>
<td>m</td>
<td>24</td>
<td>55.7</td>
<td>32</td>
<td>9.5</td>
<td>5.3</td>
</tr>
<tr>
<td>8 Jan. '64</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>56.0</td>
<td>86</td>
<td>8.4</td>
<td>2.3</td>
</tr>
<tr>
<td>&quot;</td>
<td>N</td>
<td>m</td>
<td>37</td>
<td>56.0</td>
<td>91</td>
<td>11.0</td>
<td>2.2</td>
</tr>
<tr>
<td>&quot;</td>
<td>Is</td>
<td>m</td>
<td>43</td>
<td>52.0</td>
<td>92</td>
<td>10.4</td>
<td>2.2</td>
</tr>
<tr>
<td>&quot;</td>
<td>On</td>
<td>f</td>
<td>23</td>
<td>47.5</td>
<td>100</td>
<td>3.8</td>
<td>0.8</td>
</tr>
<tr>
<td>&quot;</td>
<td>So</td>
<td>f</td>
<td>22</td>
<td>43.0</td>
<td>69</td>
<td>3.9</td>
<td>1.3</td>
</tr>
</tbody>
</table>

$* f = \frac{\text{Total body burden of Cs}^{137}}{\text{Body weight (kg) \times Cs}^{137} \text{ in blood (pc/kg)}}$
cluded from further discussion, because the amount of caesium-137 per kilogram of body weight is known to be sex-dependent [3].

The mean value of eight determinations of the factor \( f \) is 3.5, with a standard deviation of \( \pm 1.3 \). Therefore, if these determinations were made on subjects in which equilibrium conditions between blood and the whole-body tissues were obtained with respect to caesium-137, the total body burden of a man could be calculated by the equation: \( \text{Cs}^{137} \) in blood \( (\text{pc/kg}) \times \) body weight \( (\text{kg}) \times 3.5 \). In Table III, the estimate calculated on this basis is compared with the estimate from muscle analysis. In both cases a body weight of 56 kg is assumed as the average for Japanese adults.

Muscle samples have been collected from autopsies. The method of estimation is based on knowledge of the distribution of stable caesium in the human body; concentration of caesium-137 in \( \text{pc/g} \) of fresh muscle multiplied by 38 gives the total body burden in nc [4].

**TABLE III**

COMPARISON OF THE TOTAL BODY BURDENS OF \( \text{Cs}^{137} \) IN JAPANESE PEOPLE ESTIMATED FROM BLOOD AND MUSCLE ANALYSES (1963)

<table>
<thead>
<tr>
<th>Month of collection</th>
<th>From muscle analysis (nc)</th>
<th>From blood* analysis (nc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>April</td>
<td>4.6 (18)**</td>
<td>-</td>
</tr>
<tr>
<td>May</td>
<td>3.8 (34)</td>
<td>-</td>
</tr>
<tr>
<td>June</td>
<td>3.6 (16)</td>
<td>-</td>
</tr>
<tr>
<td>July</td>
<td>3.8 (19)</td>
<td>3.1 (18)</td>
</tr>
<tr>
<td>August</td>
<td>4.6 (28)</td>
<td>6.3 (21)</td>
</tr>
<tr>
<td>September</td>
<td>4.2 (27)</td>
<td>8.8 (20)</td>
</tr>
<tr>
<td>October</td>
<td>4.9 (34)</td>
<td>7.1 (50)</td>
</tr>
<tr>
<td>November</td>
<td>4.2 (18)</td>
<td>6.7 (26)</td>
</tr>
<tr>
<td>December</td>
<td>7.2 (13)</td>
<td>5.7 (44)</td>
</tr>
</tbody>
</table>

* Factor of 3.5 was used for calculation.
** Figures in parentheses indicate number of individuals.

6. DISCUSSION

It would not be justified to assume an equilibrium condition with respect to caesium-137 in the blood and the total body at the time of the present determinations. Because of the rapid turnover rate of caesium-137 in blood as compared with muscles, a change in the foodstuff level will be followed by a rapid change in blood relative to muscle. In consideration of the biological half-life of caesium-137, muscle will not reach equilibrium with the
diet until after a few months' delay, whereas blood will reach an equilibrium in a very short time.

Table II shows that higher concentrations of caesium-137 in blood were observed on 8 January 1964 than on 20 November 1963, even in the same subject (personnel Su). This might have been caused by introduction to the diet of newly-harvested crops of higher contamination level or by a change in menus in the Christmas-New Year season. In any case, an increase in the concentration of caesium-137 in blood reduced the factor $f$ because there was no noticeable change in the total body burden. When the foodstuff level is growing, the factor would become small and vice versa. Therefore, a consistent value of the factor does not occur in non-equilibrium conditions.

The discrepancy observed in Table III between estimates of total body burden from blood and muscle analyses could also be attributed to the above-mentioned factors. The peak muscle level observed in December might correspond to the peak value of blood in September-October; however, this should be verified by further data.

Another approach to the estimation from blood analysis will be obtained, knowing the distribution of stable caesium in blood and in the total body. The analysis of stable caesium in blood is now going on.

7. CONCLUSION

In equilibrium or near equilibrium conditions, blood analysis may serve as a good substitute for the whole-body counting in assessing total body burden of caesium-137 in people. This method will be also useful in predicting levels in the near future when continuous monitoring is being performed. Parallel determinations of both blood and the total body levels on several control subjects would be useful as reference for this assessment.

Among the indirect methods of evaluating the mean levels of caesium-137 in people, blood has the advantage of convenience in collection method over other media such as muscle, total diet and urine. However, one of its disadvantages is the uncertainty in finding the multiplicative factor, which is also involved in assessment by diet analysis.

ACKNOWLEDGEMENTS

The author is indebted to Y. Ichikawa, Division of Blood, National Institute of Health, for the collection of blood samples, to Mr. S. Suguri and Mr. S. Ohtani, Japan Atomic Energy Research Institute, for the whole-body measurement and to Mr. K. Iwashima and Mr. S. Tani for their laboratory assistance.

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REFERENCES

DISTRIBUTION OF CAESIUM-137 IN SAMPLES CONSISTING OF SOFT TISSUE, BONE AND BONE-MARROW (PRELIMINARY RESULTS)

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Abstract — Résumé — Аннотация — Resumen

DISTRIBUTION OF CAESIUM-137 IN SAMPLES CONSISTING OF SOFT TISSUE, BONE AND BONE-MARROW.

The investigations which were performed up to now on the distribution of caesium-137 in the human organism could not explain exactly the distribution of the radio-caesium between bone and bone marrow. That is why a reliable estimation of the radiation burden of the skeleton caused by the incorporation of atmospheric caesium-137 is not given in the literature.

Therefore, the concentration of caesium-137 in compact bones as well as in bone marrow was determined. Furthermore, the concentration of caesium-137 in the soft tissue of the same individuals was measured.

INTRODUCTION

The distribution of the fission product caesium-137 within human tissue has been investigated by several authors, determining the caesium-137 content in post-mortem samples [1, 2, 3, 4, 5].
The results have indicated that the concentration of caesium-137 in bone tissue is on the same level or even higher than the content in muscular tissue \([1, 2, 3, 5]\).

Contrary to these investigations there are findings that the content in muscular tissue is 2 - 3 times the value found in bone tissue \([4]\). Besides this, the investigations performed regarding patients in whom caesium-137 was injected revealed that the specific activity of caesium-137 in the skeleton is lower than the activity in soft tissue \([6]\).

The presented paper, therefore, is intended to clarify the discrepancies in literature and to give information on the distribution pattern of caesium-137 in soft tissue, compact bone and bone-marrow.

With reference to the investigations performed by YAMAGATA et al. \([2]\) and ANDERSON et al. \([5]\) determining the content of caesium-137 in rib bones in correlation to the individual's age, we selected soft tissue and bone samples taken from individuals brought ad exitum in the age group 55 - 65 yr. The results of the above-mentioned authors revealed that the specific activity of caesium-137 per gram of bone ash taken from 60 - 70 yr-old individuals was 3 - 4 times the specific activity found in individuals of 15 - 20 yr old.

**DETERMINATION OF CAESIUM-137 BY EMPLOYMENT OF THE GAMMA-RAY SPECTROMETRY**

The content of caesium-137 in animal and human tissue samples was determined by both low-level beta-ray counting technique and gamma-ray spectrometry.

The spectrometer consisted of a well-type NaI(Tl) crystal (3-in diam. \(\times\) 2.5 in) a 3-in photomultiplier tube, type Dumont 6363, and a 512 channel pulse-height analyser (see Fig.1). It was installed in an air-conditioned low-background laboratory with 2-m-thick walls constructed of reinforced concrete. This below the ground laboratory made it possible to reduce the integral counting rate by a factor of \(2.7\) within the range of energy from 0.1-3 MeV— as measured against the outside level.

A further reduction of the background by a factor of 60 was attained by a shielding system consisting of a 1-m-thick wall of mercury being located on the inside wall of a steel cage with 10-cm-thick walls. Within the above mentioned range of energy the resulting background was 125 cpm. It was only 16 cpm, however, within the range of energy covered by the area of the photo-peak of barium-137 (the spectral range was selected to be between 580 and 740 keV).

In order to take account of the different sample heights in the well-type crystal (see Fig.1), the calibration of the spectrometer was performed by the employment of both the calibrated solution of caesium-137 (with an accuracy of \(\pm 3\)% and the bone ash spiked with caesium-137. The calibration factor extrapolated to the sample height zero was 0.425 cpm/pc caesium-137. This means that 21% of the gamma-quanta emitted from barium-137m were counted within the range (from 580 to 740 keV) of the photo-peak's energy.

At a total measuring period of 800 min, a background of 16 cpm and a relative statistical error of \(\pm 20\)% the lower limit of detection is \(5 \times 10^{-11}\) c of caesium-137.
As the energy of caesium-137 beta is low enough for measurable self-absorption to occur, this must be corrected for by preparing a self-absorption curve for various thicknesses of the caesium precipitate. This was done within a range of thickness of from 10 - 100 mg/cm² (see Fig. 2).

With an amount of 50 mg of caesium carrier added to each sample prior to analysis, the amount of caesium hexachloroplatinate recovered at the end of the analysis was 100 mg on an average (corresponding to 40 mg of caesium). The surface of the precipitate on the filter paper was 2.41 cm² on an average; consequently the thickness of the precipitate is 42 mg Cs₂PtCl₆/cm².

The calibrating process was performed by counting precipitates of caesium hexachloroplatinate labelled with caesium-137 employing varying sample thicknesses. With a thickness of 42 mg/cm², only 0.45 cpm/10⁻¹² cm were counted, i.e. the counting efficiency is approximately 20%. The results
are graphed in Fig. 2. This graph also shows the results of calibration measurements obtained by HARLEY [7] which are well in agreement with ours.

At a background of 1 cpm and a counting efficiency of 0.45 cpm/pc caesium-137 (determined for a precipitate thickness of 42 mg/cm²), the lower detection limit is approximately $3 \times 10^{-12}$ c of caesium-137. The relative statistical error is ±20%.

THE CHEMICAL PROCESSING OF TISSUE SAMPLES

The material was wet-ashed, as in soft tissue caesium was found to be volatile at temperatures higher than 450°C [8]. Besides this, caesium is reported to be incorporated into the glaze of porcelain crucibles during dry ashing [9].

The bone marrow and tissue were attacked by a sulphonating process [10] within a few hours, whereas the compact bones were attacked by a more tedious refluxing procedure using fuming nitric acid. After the sulphonating attack the samples were evaporated to a few millilitres and then diluted with
distilled water to a volume of about 50 ml. In this volume caesium was
separated.

After the nitric acid attack the solution was evaporated to dryness and
digested with sufficient hydrochloric acid. Now calcium and phosphorus
were precipitated by vigorous stirring and the drop-wise addition of ammonia,
followed by a solution of ammonium carbonate. The filtrate was evaporated
to dryness, ammonium chloride expelled by heating and the residue digested
with diluted hydrochloric acid.

In the samples thus mineralized caesium was separated from the other
alkalines by means of silicotungstic acid. Silicotungstic acid was employed
instead of phosphomolybdic acid [11] or phosphotungstic acid [12], as the
precipitations with the latter ones were found to be affected by the presence
of not negligible amounts of ammonia [11, 12].

Besides this, our experiments revealed that it was easier to obtain a
good caesium recovery in a sulphuric acid medium containing such amounts
of ammonia which can be expected during the course of analysis, than by
precipitation with silicotungstic acid.

After the separation of caesium with silicotungstic acid it was precipi-
tated and weighed as caesium hexachloroplatinate. Recovery of caesium
in a model sample containing such concentrations of potassium as are to be
expected in tissue was, on the average, 85%. One hundred grams of mus-
cular tissue contain about 350 mg of potassium [13]. In the biological
samples the recovery of caesium was on the same level but often somewhat
lower.

The precipitate of caesium hexachloroplatinate was practically free
from potassium, so that no interference of the low counting-rate was to be
expected due to the beta-ray activity of potassium-40. A cross check as to
the presence of potassium was performed by the employment of a spectro-
graphic determination. The analytical procedure is detailed elsewhere [10].

RESULTS

The specific activities found in the stag are shown in Table I. The fe-
moral compacta were thoroughly cleaned from muscular tissue, grease,
periosteum and bone marrow.

The human tissue samples were taken from autopsies performed in cases
of suicide, accident or short-period diseases.

The compact bones were thoroughly cleaned by brushing and filing from
the bone marrow, spongiosa, periosteum and soft tissue. As mentioned
above there is a correlation between the individual's age and the specific
activity of caesium-137 found in the compacta of ribs [5]. This correlation
is at a minimum at the age of puberty. The content of caesium-137 in the
samples was determined by direct measurement of the ribs cleaned from
marrow under a crystal scintillation counter.

This correlation between caesium-137 content and age is the reason
why our preliminary results cover the decennia following the age of puberty
and the age from 55 to 65 yr. In the decennium from 55 to 65 yr of age maxi-
mum specific activity was to be expected.
TABLE I: FEMORAL ACTIVITY IN THE STAG

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Specific activity¹ of Cs¹³⁷ found in femoral marrow (pc/kg)</th>
<th>compacta (pc/kg)</th>
<th>musc. tissue (pc/kg)</th>
<th>Femoral activity ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>S 1</td>
<td>33.0</td>
<td>124</td>
<td>1000</td>
<td>1</td>
</tr>
<tr>
<td>S 2</td>
<td>35.5</td>
<td>114</td>
<td>1000</td>
<td>1</td>
</tr>
<tr>
<td>S 3</td>
<td>36.5</td>
<td>116</td>
<td>1610</td>
<td>1</td>
</tr>
<tr>
<td>S 4</td>
<td>40.9</td>
<td>102</td>
<td>1000</td>
<td>1</td>
</tr>
<tr>
<td>S 5</td>
<td>51.1</td>
<td>103</td>
<td>970</td>
<td>1</td>
</tr>
<tr>
<td>S 6</td>
<td>68.5</td>
<td>132</td>
<td>1830</td>
<td>1</td>
</tr>
<tr>
<td>S 7</td>
<td>74.4</td>
<td>190</td>
<td>1620</td>
<td>1</td>
</tr>
<tr>
<td>S 8</td>
<td>75.4</td>
<td>176</td>
<td>660</td>
<td>1</td>
</tr>
<tr>
<td>S 9</td>
<td>213.0</td>
<td>744</td>
<td>6070</td>
<td>1</td>
</tr>
<tr>
<td>S 10</td>
<td>234.5</td>
<td>958</td>
<td>7570</td>
<td>1</td>
</tr>
</tbody>
</table>

Average: 1                     2.9    26

¹ The activities are given in pc/kg wet weight.

The results of these investigations are set out in Table II; H 1 - 4 are samples covering the decennium from 20 - 30 yr and H 5 - 8 the decennium from 55 - 65 yr of age. As the bone marrow in the two femurs obtained from each individual did not contain the minimum activity of caesium-137 which was necessary for counting, the femoral bone marrow of six femurs belonging to three individuals were combined prior to analysis.

As to the decennium from 55 - 65 yr of age the content of caesium-137 in liver and spleen was estimated in a few cases. The average activity was 300 pc/kg of wet tissue. With reference to the content of caesium-137 determined by ANDERSON [5] in ribs, we analysed ribs, with marrow discarded, of a few 60-yr-old individuals, and found the specific activity to be as low as 60 pc/kg of wet weight. Up to now no ribs of younger individuals were analysed.

In Table III both measuring methods covering the content of caesium-137 in human and animal muscular tissue and bones are compared. These results were obtained by the employment of both the gamma-spectrometry and the low-background anti-coincidence counting technique of beta-rays. The identity of the measuring methods is within ±4% for the content of caesium-137 in soft tissue and within ±20% in bone tissue. The activity of caesium-137 in bone tissue to be counted is close to the limit of detection, if the gamma-ray counting technique is employed, due to lower specific activity of caesium-137 in bone tissue compared with the activity in soft tissue. This is the reason
TABLE II

FEMORAL ACTIVITY IN MAN

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Specific activity* of Cs$^{137}$ found in femoral marrow (pc/kg) compacta (pc/kg) musc. tissue (pc/kg)</th>
<th>Femoral activity ratio$^\dagger$ marrow compacta musc. tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>HM 1</td>
<td>45</td>
<td>690.</td>
</tr>
<tr>
<td>HM 2</td>
<td>48</td>
<td>780.</td>
</tr>
<tr>
<td>HF 3</td>
<td>61</td>
<td>620.</td>
</tr>
<tr>
<td>HM 4</td>
<td>59</td>
<td>980.</td>
</tr>
<tr>
<td>HM 5</td>
<td>33</td>
<td>580.</td>
</tr>
<tr>
<td>HF 6</td>
<td>32</td>
<td>800.</td>
</tr>
<tr>
<td>HM 7</td>
<td>39</td>
<td>1020.</td>
</tr>
<tr>
<td>HM 8</td>
<td>36</td>
<td>800.</td>
</tr>
</tbody>
</table>

Average 1 1.2 21

* The activities are given in pc/kg wet weight.
$^\dagger$ H = Human; M = Male; F = Female

for a discrepancy in the determined activities in bones as high as ±20% if the results of the two measuring methods are compared with each other.

ESTIMATION OF DOSE-RATES IN HUMAN SKELETON AND SOFT TISSUE

The calculation of the dose-rate of the beta and gamma radiation of caesium-137/barium-137 in muscular and bone tissue is based on the specific activities of caesium-137 scheduled in Table IV.

The dose-rate being produced by the gamma radiation emitted from barium-137 within the human soft tissue was calculated for the axis of a cylinder. Its height was assumed to be infinity and its radius 5 or 20 cm, respectively. The calculations are based on two cylindrical models with different radii in order to estimate separately the absorbed dose for trunk and extremities. The data necessary for the estimation of the factor of geometry are based on the values published in the Reactor Shielding Manual[4].

The coefficient of linear energy transfer is 0.032 cm$^2$ /g if the quantum energy is 0.662 MeV [15]. The probability that gamma-quanta from barium-137 are emitted is 0.92 related to the beta-decay of caesium-137.

If the specific muscular activity is assumed to be 780 pc caesium-137 per kilogram, the annual dose-rate of gamma-radiation is calculated to be 5 mrad, if the radius of the cylinder is 20 cm, and 1.9 mrad if the radius is 5 cm. The annual dose-rate for the muscular tissue due to the beta-radiation
### TABLE III

**COMPARISON OF THE BETA-RAY AND THE GAMMA-RAY COUNTING TECHNIQUE**

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Femoral compacta (shaft)</th>
<th>Femoral muscular tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>beta-ray counting*</td>
<td>gamma-ray technique*</td>
</tr>
<tr>
<td>S 6</td>
<td>135</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>129</td>
<td>112</td>
</tr>
<tr>
<td>S 7</td>
<td>190</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>141</td>
</tr>
<tr>
<td>S 8</td>
<td>177</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>174</td>
<td>122</td>
</tr>
<tr>
<td>S 10</td>
<td>944</td>
<td>880</td>
</tr>
<tr>
<td></td>
<td>972</td>
<td>-</td>
</tr>
<tr>
<td>HM 1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HM 2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HF 3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HM 4</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td>HM 5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HM 7</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* The activities are given in picocuries per kilogram wet weight.

H = Human; M = Male; F = Female; S = Stag

emitted from caesium-137 is 3.4 mrad. In the bone marrow with an average specific activity of caesium-137 as high as 33 pc/kg the annual dose-rate from beta radiation was calculated to be 0.14 mrad. For the compacta having a comparably high activity (44 pc/kg) the annual dose-rate due to beta-radiation is calculated to be 0.19 mrad. This value was divided by the ratio of the mass stopping powers of bone: soft tissue in order to obtain the dose-rate of the cavities of bone. The ratio of mass stopping powers was assumed to be 0.93 according to the values published in literature [15, 16].

With this assumption the annual dose-rate due to beta radiation for the cavities filled with soft tissue is 0.2 mrad. In each case, the total body burden of the tissue is composed of the actual portion of beta- and gamma-
**TABLE IV**

**DISTRIBUTION OF Cs\(^{137}\) IN HUMAN BODY**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Organ weight % of total body</th>
<th>(\text{Cs}^{137}) cont. (pc/kg)</th>
<th>Total organ (\text{Cs}^{137}) cont. (pc)</th>
<th>Organ act. % of total body</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscul. tissue</td>
<td>43</td>
<td>780</td>
<td>23400</td>
<td>71.5</td>
</tr>
<tr>
<td>Compact bone</td>
<td>10</td>
<td>44</td>
<td>300</td>
<td>0.9</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>4.3</td>
<td>33</td>
<td>100</td>
<td>0.3</td>
</tr>
<tr>
<td>Liver</td>
<td>2.4</td>
<td>300</td>
<td>500</td>
<td>1.5</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.21</td>
<td>300</td>
<td>40</td>
<td>0.1</td>
</tr>
<tr>
<td>Other tissues</td>
<td>40</td>
<td>300*</td>
<td>8400</td>
<td>25.7</td>
</tr>
<tr>
<td><strong>Total body (\text{Cs}^{137}) content</strong></td>
<td></td>
<td><strong>32 740</strong></td>
<td></td>
<td><strong>234 pc/kg.K.</strong></td>
</tr>
</tbody>
</table>

* \(\text{Cs}^{137}\) content of other soft tissues assumed to be equal to that of liver and spleen.

Radiation. Assuming the cylindrical radius to be 20 cm, the total dose-rate \(D_t(20)\) is calculated according to the following formula

\[
D_t(20) = D_\beta + D_\gamma(20) = 3.4 + 5 = 9.4 \text{ mrad/yr.}
\]

If the radius is assumed to be 5 cm, the formula is

\[
D_t(5) = D_\beta + D_\gamma(5) = 3.4 + 1.9 = 5.3 \text{ mrad/yr.}
\]

The total mean body burden of the muscular tissue is calculated to be 6.9 mrad/yr. This value is obtained by forming the average from \(D_t(20)\) and \(D_t(5)\).

The total dose-rate in bones is composed of the beta dose-rate — calculated to be 0.2 mrad/yr in the cavities — and the gamma dose-rate in the muscular tissue, being calculated for the axis of a cylinder with its radius to be 5 or 20 cm, respectively.

For calculation of the dose-rate in the skeleton due to gamma radiation, it is necessary to have information on the distribution of the individual parts of the skeleton expressed in percent of weight in the trunk and the extremities. LOWRANCE and LATIMER [17] estimated the portion of the extremities to be 52% and the portion of the trunk to be 28% of the weight of the total skeleton. Therefore, 52% of the total gamma-radiation dose absorbed by the skeleton corresponds to the dose received by the bone of the extremities (approximately a cylinder with a radius of 5 cm) and 28% corresponds to the dose received by the trunk (approximately a cylinder with a radius of 20 cm). According to this estimation the contribution to the gamma dose received by the skull bone (20% of the total skeleton) due to gamma radiation emitted from the soft tissue was neglected.
With the results mentioned in the preceding sections, the mean dose of the skeleton amounts to

\[
D_t = D_B + 0.52 \times D_\gamma(5) + 0.28 \times D_\gamma(20) = 0.2 + 1.0 + 1.4 = 2.6 \text{ mrad/yr.}
\]

The bone marrow is considered to be a column within a cylinder consisting of soft tissue. On the assumption that the portion absorbed by the compacta is negligibly low, the dose-rate in the bone marrow due to gamma radiation is equal to the dose-rate in the bone marrow within a cylinder having a radius of 20 cm, calculated as follows:

\[
D_t(20) = D_B + D_\gamma(20) = 0.14 + 5 = 5.14 \text{ mrad/yr.}
\]

The analogous dose-rate in a cylinder having a radius of 5 cm amounts to

\[
D_t(5) = D_B + D_\gamma(5) = 0.14 + 1.9 = 2.04 \text{ mrad/yr.}
\]

The total average dose rate in the bone marrow — based upon the assumptions given above — amounts to

\[
D_t = D_B + 0.52 \times D_\gamma(5) + 0.28 \times D_\gamma(20) = 0.14 + 1.0 + 1.4 = 2.5 \text{ mrad/yr.}
\]

The average-dose-rates in the skeleton and the muscular tissue are scheduled in Table V.

For comparison, the absorbed dose-rate due to radiation emitted from strontium-90/yttrium-90 (mean beta-ray energy = 1.13 MeV, specific activity = $1 \times 10^{-12}$ c/g calcium = $1.3 \times 10^{-13}$ c/g wet bones) was calculated. The annual dose-rate is calculated to be 2.7 mrad in the compact bones and 2.9 mrad in the Haversian system (0 - 50\(\mu\)m diam.) with the ratio of the mass stopping powers to be 0.93. The dose-rate in the Haversian system is in the same order of magnitude for strontium-90/yttrium-90 and caesium-137.

DISCUSSION OF THE EXPERIMENTAL RESULTS

The investigations performed at the compacta of the femur shaft with its marrow and periosteum eliminated revealed that the specific activity of caesium-137 in human muscular tissue is about twenty times the activity found in the femoral compacta. On the other hand, the specific activities of caesium-137 in the compact bone and in the bone marrow seemed to be comparably high (see Table IV). The specific activity of caesium-137 in marrow-free ribs is about 1.5 times the activity found in the femoral compacta.

In the stag a similar distribution pattern of caesium-137 in femoral compacta, bone marrow and muscular tissue has been observed (see Tables I, II and IV). The average specific activity of caesium-137 in muscular tissue was ten times that found in compacta of the femur. Contrary to the findings
CAESIUM-137 IN TISSUE, BONE AND MARROW

TABLE V

AVERAGE Cs$^{137}$ CONTENT OF HUMAN AND ANIMAL TISSUE SAMPLES

<table>
<thead>
<tr>
<th>Species</th>
<th>Bone marrow (pc/kg)</th>
<th>Comp. bone femur shaft (pc/kg)</th>
<th>Musc. tissue (pc/kg)</th>
<th>Liver/spleen (pc/kg)</th>
<th>Ribs marrow-free (pc/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Man</td>
<td>52</td>
<td>132</td>
<td>1210</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Stag</td>
<td>33</td>
<td>44</td>
<td>780</td>
<td>300</td>
<td>60</td>
</tr>
</tbody>
</table>

In man, the caesium-137 activity determined in the femoral compacta of the stag was three times the activity found in the bone marrow. In other words, the specific activity of caesium-137 in bone marrow correlated to muscular tissue was 26 times lower in the case of the stag. PAAKKOLA and MIETTINEN [18] also found that in the reindeer the specific activity of caesium-137 in bones is remarkably lower than the activity found in muscular tissue.

For the decennia 20–30 and 60–70 yr. of age there seemed to be no correlation between the specific activity and the individual's age. Contrary to the results found by other scientific teams [2, 5] in the femoral compacta there is rather a slight decrease of the content of caesium-137 with age.

An estimation of the total-body content of caesium-137 based on the specific activities in bone marrow, compact bones, muscular tissue, liver and spleen (as scheduled in Table IV) was performed. The values necessary for the calculation and the results are summarized in Table VI.

The specific activity of caesium-137 found in liver and spleen was assumed to be the average specific activity in soft tissue except muscular tissue. The calculated average total body content of caesium-137 in the standard man (calculated for spring, 1964) amounts to 33 nc corresponding to 470 pc/kg body weight or 240 pc/g of potassium, whereas in September 1963, according to measurements of MUTH and OBERHAUSEN [19] the specific activity of caesium-137 was approximately 150 pc/g of potassium.

TABLE VI

TOTAL AVERAGE DOSE-RATES IN HUMAN SKELETON AND MUSCULAR TISSUE

<table>
<thead>
<tr>
<th>Organ</th>
<th>Total average dose-rate (mrad/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>6.9</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>2.5</td>
</tr>
<tr>
<td>Bone (Havers. system)</td>
<td>2.6</td>
</tr>
</tbody>
</table>
It can be seen that the total-body content of caesium-137 increased by a factor of 1.6 within the period under review.

ACKNOWLEDGEMENTS

This work was performed under the auspices of the Bundesministerium des Inneren, Federal Republic of Germany.

The authors are indebted to Miss R. GLATZEL and Miss K. MARTIN for their technical assistance.

REFERENCES

THE RETENTION AND EXCRETION OF CAESIUM-137
BY TWO MALE SUBJECTS

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Abstract — Résumé — Аннотация — Resumen

THE RETENTION AND EXCRETION OF CAESIUM-137 BY TWO MALE SUBJECTS. The whole-body counter
at the United Kingdom Atomic Energy Authority (UKAEA) Windscale and Calder Works has been used to make
a series of in vivo measurements of body radioactivity on two male employees who had received accidental
intakes of radioactive material. The contaminant consisted mainly of caesium-137, although small amounts
of other radionuclides were also present.

Body radioactivity determinations were made on the two men, during periods of 1 to 289 d and 10 to 169 d
after the day of intake, and the results indicated that the initial intakes of caesium-137 were approximately
0.59 µCi and 0.15 µCi respectively. The effective half times for the long component of body retention were 116 d and
68 d respectively. In the case of the man with the highest intake, the long component represented about 78% of
the initial body burden. The distribution of caesium-137 in his body was measured on two occasions within fourteen
days of intake, and about 15% of the retained body burden was found to be concentrated into a small volume in
the region of the chest.

Urine samples from both subjects were analysed for caesium-137. From the equations describing the
pattern of excretion in urine, and retention of caesium-137 in the body, it has been possible to make esti-
mations of the caesium-137 excreted in faeces. After the fifteenth day following intake, the average amount
of caesium-137 excreted per day in urine represented about 0.55% of the retained body burden. During the
same period the average urinary to faecal ratio was approximately 2.3.

RÉTENTION ET ÉLIMINATION DU CÉSIIIUM 137 CHEZ DEUX SUJETS DU SEXE MASCULIN. L’anthropo-
gammamètre des établissements de Windscale et Calder Hall a été utilisé pour une série de mesures in vivo
de la charge corporelle chez deux employés du sexe masculin qui avaient absorbé accidentellement des ma-
tières radioactives. Le césium 137 était le contaminant principal, mais d’autres radionuclides étaient également
présents, en petites quantités.

On a fait des dosages de l’activité du corps des deux hommes, au cours de périodes allant de 1 à 289 j et
de 10 à 169 j, après le jour de l’absorption; il ressort des résultats obtenus que les quantités de césium 137
absorbées initialement ont été d’environ 0,59 µCi et 0,15 µCi respectivement. Les périodes effectives de la
fraction «longue» de la quantité retenue par l’organisme ont été de 116 j et 68 j, respectivement. Chez le
sujet qui avait absorbé la dose la plus élevée, cette fraction «longue» représentait environ 78% de la charge
corporelle initiale. La distribution du césium 137 dans son organisme a été mesurée à deux occasions dans
les 14 j qui ont suivi l’absorption, et on a constaté qu’environ 15% de la charge corporelle retenue étaient con-
centrés dans un petit volume, au niveau de la poitrine.

On a dosé le césium 137 dans des échantillons d’urine prélevées sur l’un et l’autre sujet. À partir des
équations qui expriment le régime de l’élimination urinaire et la rétention du césium 137 dans l’organisme, il
a été possible d’évaluer la quantité de césium 137 éliminée dans les fèces. À partir du quinzième jour après
l’absorption, la quantité moyenne de césium 137 éliminée par jour dans l’urine représentait environ 0,55% de
la charge corporelle retenue. Au cours de la même période, le rapport élimination urinaire/élimination fécale a
été en moyenne de 2,3 environ.

ЗАДЕРЖКА И ВЫДЕЛЕНИЕ ЦЕЗИЯ-137 У ДВУХ ПАЦИЕНТОВ МУЖСКОГО ПОЛА.
Счетчик для измерения радиоактивности всего организма в Управлении по атомной энергии
Соединенного Королевства, заводы Уинскейл и Колбер, был использован для проведения серии
измерений радиоактивности организма у двух служащих (мужчин) после случайного погло-
щений радиоактивного материала. Загрязнитель состоял в основном из цезия-137, хотя при- сутствовали малые количества и других радиоизотопов.

Радиоактивность организма определялась у двух мужчин в период от 1 до 289 дней и от 10 до 169 дней после поглощения. Результаты показывают, что начальное поглощение цезия-137 варьировалось приблизительно 0,6 и 0,15 мккюр. Эффективный период полувыведе-ния для длительно задерживающихся в организме компонентов варьировал соответственно 116 и 68 дней. У мужчин, получившего большую дозу, длительно задерживающийся компонент составляла 78% первоначального содержания изотопа в организме. Распределение цезия-137 у него измерялось дважды в течение 14 дней после поглощения; было обнаружено, что около 15% всего оставшегося количества изотопа в организме сосредоточено в области легких.

Пробы мочи у обоих пациентов исследовались на содержание цезия-137 и с помощью уравнений, описывающих характер выделения изотопа с мочой и задержку цезия-137 в организ­ме, удалось определить выделение цезия-137 с экскрементами. На 15-й день после погло­щения среднее количество цезия-137, выделяемого за сутки с мочой, составляло около 0,55% количества, содержащегося в организме. В течение этого же периода отношение количеств, выделяющихся с мочой и экскрементами, составляло приблизительно 2,3.

1. INTRODUCTION

The retention and excretion of Cs\textsuperscript{137} by two male subjects who received accidental intakes of radioactive material at the UKAEA, Windscale Works, have been studied during the year following the incident. Intake was pri­marily by inhalation.

In vivo measurements of body radioactivity were made on both subjects by means of the Windscale Whole Body Counter (Fig. 1) [1]. Uriné samples, collected over periods of 24 h were analysed for Cs\textsuperscript{137}. The relationship between the amount of a radionuclide excreted, and the amount retained in the human body, is required in personnel monitoring programmes which depend upon excretion analyses. This relationship has been assessed in the present case, for Cs\textsuperscript{137} in urine and in faeces.

Results of the in vivo measurements indicated that the initial body burdens were 0.59 and 0.15 μС, respectively. These amounts represent approximately 0.01 of a "Maximum Permissible 13 Weeks' Intake" of soluble Cs\textsuperscript{137}, [2], as recommended by ICRP.
The pattern of body retention fitted a double exponential function for subject A, \((t > 1 \text{ d})\) but for Subject B who was not measured until \(10 \text{ d}\) after the intake, it was only possible to assess the second component of body retention. This was described by a single exponential function \((t > 10 \text{ d})\). Effective half-times for the retention of \(\text{Cs}^{137}\) were \(116 \text{ d}\) and \(68 \text{ d}\) respectively.

2. **IN VIVO MEASUREMENTS OF BODY RADIOACTIVITY**

2.1. **Whole-body radioactivity**

Measurements of the body content of gamma-ray-emitting nuclides were made inside the steel cubicle of the Windscale Whole Body Counter, using an array of four gamma-ray scintillation detectors each incorporating a sodium-iodide crystal \(4 \frac{3}{4} \text{ in.} \times 4 \text{ in.}\). The detectors were positioned two above and two below the prone subject (Fig. 1). To reduce any effects due to surface contamination the subjects showered prior to each measurement, and during measurements wore pyjamas.
The gamma-ray spectra of the body radioactivity of both subjects showed traces of gamma-rays with energies of 0.80 MeV, 1.46 MeV and 1.60 MeV, in addition to the predominant 0.66 MeV gamma-rays associated with the decay of Cs\textsuperscript{137} (Fig. 2). The photopeak at 1.60 MeV was observed on the earlier spectra only. The smaller peaks were associated with Cs\textsuperscript{134}, K\textsuperscript{40} and Ba\textsuperscript{140} + La\textsuperscript{140}. Naturally-occurring K\textsuperscript{40} (1.46 MeV) is observed in control subjects, together with Cs\textsuperscript{137} which arises from nuclear weapon fall-out (Fig. 2, Table I). The Cs\textsuperscript{134} and probably the Ba\textsuperscript{140} + La\textsuperscript{140} were associated with the accidental intake of Cs\textsuperscript{137}. This was supported by the identification of Cs\textsuperscript{134}, in addition to Cs\textsuperscript{137}, on an air sample collected at the time of the incident.

In assessing the body content of Cs\textsuperscript{137}, the counts in the region of the 0.66 MeV photo-peak were corrected for the contributions of the other radio-nuclides. Then the Cs\textsuperscript{137} values were corrected for the current contributions of Cs\textsuperscript{137} arising from nuclear weapon fall-out. Corrections for weapon fall-out were based upon the mean levels of Cs\textsuperscript{137} in a small group of control subjects (Table I) on whom measurements of body radioactivity are made periodically. The standard error on the corrected values (Table II) varied from about 5 to 10%. 

---

Fig. 2

Gamma-ray spectra of body radioactivity

- subject A, day 1
- subject A, day 50
- control subject, 8.4 nc Cs\textsuperscript{137}, 132 g K.
TABLE I

QUARTERLY MEAN AMOUNTS OF FALL-OUT Cs\textsuperscript{137} IN SUBJECTS FROM WEST CUMBERLAND

<table>
<thead>
<tr>
<th>Year</th>
<th>Quarter</th>
<th>Cs\textsuperscript{137} ((\text{nc}))</th>
<th>Cs\textsuperscript{137} ((\text{pc/g K}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961</td>
<td>2</td>
<td>9.3</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>8.1</td>
<td>61</td>
</tr>
<tr>
<td>1962</td>
<td>1</td>
<td>6.1</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>7.1</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10.1</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>14.0</td>
<td>92</td>
</tr>
<tr>
<td>1963</td>
<td>1</td>
<td>15.1</td>
<td>107</td>
</tr>
</tbody>
</table>

2.2. Distribution of radioactivity

In order to investigate the longitudinal distribution of Cs\textsuperscript{137} throughout the body, two series of measurements were made on Subject A by means of a collimated detector (Fig. 1). The detector incorporated a sodium iodide crystal \(2.5\) in diam. \(\times\) 5 in collimated by a cylinder of lead with a wall thickness of one inch. Unfortunately it was not possible to make similar measurements on Subject B.

The resulting distributions of Cs\textsuperscript{137} in the trunk of Subject A are shown in Fig. 3, together with the results of a similar series of measurements made along a Polythene phantom (Fig. 1) filled with an aqueous solution containing Cs\textsuperscript{137}. It was shown by RUNDO [3] using a similar counting geometry that the distribution of radio-caesium in a similar phantom closely resembled that in two male subjects, with the difference that the maximum response from the phantom occurred at 0.4 of its length, while that in his two subjects occurred at 0.48 of their lengths, measured from the head. The maximum response from Subject A occurred at about 0.2 of his length measured from the head. It may be concluded that the unusual distribution of Cs\textsuperscript{137} in Subject A was due to Cs\textsuperscript{137} retained in the chest.

To assess the excess amount of Cs\textsuperscript{137} in the chest the contribution from Cs\textsuperscript{137} already deposited in the muscles and circulation had to be allowed for. This was done by normalizing the response over the abdomen of Subject A to that of the phantom, and calculating the contribution in the region of the lungs, assuming the distribution to be the same as that in the phantom. The differences between the observed and calculated distributions gave the distribution of Cs\textsuperscript{137} in the chest, and these have been compared (Fig. 4) with the response of the detector to a small source of Cs\textsuperscript{137} shielded above and below by Polythene sheet of thickness 4 in. The similarity between the three distributions shows that the Cs\textsuperscript{137} in the chest was concentrated in a relatively small volume although the actual distribution on days 1 and 14 did differ
slightly. On day 1 the point of maximum response occurred 32 cm from the top of the subject's head, and the distribution was skew (Fig. 4).

On day 14, the point of maximum response occurred at about 34 cm from the top of the subject's head, and the distribution appeared to be symmetrical.

Comparison of the maximum count rates of the three distributions showed that the excess amounts of Cs\textsuperscript{137} in the chest on days 1 and 14 were approximately 90 nc and 60 nc. On the assumption that the retention was exponential, a half-time of about 23 d was indicated for the retention of Cs\textsuperscript{137} in the chest.

### TABLE II

**Cs\textsuperscript{137} IN VIVO AND IN URINE**

<table>
<thead>
<tr>
<th>Days since intake</th>
<th>In vivo Cs\textsuperscript{137} (nc)</th>
<th>Cs\textsuperscript{137} in urine (nc/24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subject A</td>
<td>Subject B</td>
</tr>
<tr>
<td>1</td>
<td>548</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>498</td>
<td>393</td>
</tr>
<tr>
<td>10</td>
<td>420</td>
<td>108</td>
</tr>
<tr>
<td>14</td>
<td>21</td>
<td>92</td>
</tr>
<tr>
<td>21</td>
<td>28</td>
<td>388</td>
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<td>30</td>
<td>38</td>
<td>78</td>
</tr>
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<td>49</td>
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<td>50</td>
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</tr>
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<td>76</td>
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<td>78</td>
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<td>56</td>
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<tr>
<td>94</td>
<td>98</td>
<td>291</td>
</tr>
<tr>
<td>98</td>
<td>280</td>
<td>28</td>
</tr>
<tr>
<td>140</td>
<td>201</td>
<td>28</td>
</tr>
<tr>
<td>169</td>
<td>174</td>
<td>20</td>
</tr>
<tr>
<td>206</td>
<td>137</td>
<td></td>
</tr>
<tr>
<td>253</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>289</td>
<td>81</td>
<td></td>
</tr>
</tbody>
</table>
Distributions of Cs\textsuperscript{137} in the trunk of subject A, and in a Polythene phantom (height of subject 170 cm).

--- day 1
--- day 14
--- phantom

Responses of detector to Cs\textsuperscript{137} in the chest and to a small source shielded by Polythene (height of subject 170 cm).

--- day 1
--- day 14
--- Cs\textsuperscript{137} source
3. Cs\(^{137}\) IN URINE

Periodic collections were made of the urine excreted by Subjects A and B during periods of 24 h. The samples were analysed for Cs\(^{137}\) and creatinine. Subject A produced several urine samples which were not representative of 24 h excretion. This fact, suspected from the relatively small volume of certain samples, and the correspondingly low creatinine values, was confirmed by the subject. Estimations of the probable 24 h excretion were made by multiplying the value for the amount of Cs\(^{137}\) in a particular urine sample by the ratio of his average amount of creatinine in complete 24-h samples to the amount of creatinine in the appropriate urine sample.

It has been shown [4, 5] that the amount of creatinine excreted per day in urine by an individual is relatively constant. Therefore, the mean value can be used as an index of complete 24-h samples. The mean daily amount of creatinine excreted in urine by Subject A was 1.33 ± 0.11 g, and for Subject B it was 1.53 ± 0.16 g. The amounts of Cs\(^{137}\) excreted in urine per day were normalized to these mean values.

Cs\(^{137}\) arising from weapon fall-out also contributed to the Cs\(^{137}\) excreted in urine. Appropriate corrections have been made to the urine results, based upon three 24-h urine samples given by two control subjects. The Cs\(^{137}\) in urine represented 0.54% of their retained body burdens. Therefore, 0.54% of the current mean amounts of Cs\(^{137}\) in control subjects was subtracted from the amounts of Cs\(^{137}\) excreted in urine by Subjects A and B. The standard error on each of the corrected values (Table II) was about 10 to 12%.

4. DISCUSSION OF RESULTS

4.1. The amounts of Cs\(^{137}\) retained in the body, and excreted in urine, have been fitted to double exponential functions for Subject A. Unfortunately, the first measurements were not made on Subject B until after the first exponential components had disappeared, therefore it has only been possible to assess the second part of the functions (Figs. 5 and 6). The functions are of the following forms

\[
R_t = a_1 e^{-\left(k_1 + \lambda\right)t} + a_2 e^{-\left(k_2 + \lambda\right)t}
\]

(1)

\[
U_t = b_1 e^{-\left(m_1 + \lambda\right)t} + b_2 e^{-\left(m_2 + \lambda\right)t}
\]

(2)

\(R_t\) - Cs\(^{137}\) (nc) retained in the body on day \(t\)
\(a_1\) and \(a_2\) - Cs\(^{137}\) (nc) components of body retention
\((k_1 + \lambda)\) and \((k_2 + \lambda)\) - effective decay constants of body retention
\(U_t\) - Cs\(^{137}\) excreted in urine per day (nc/24 h)
\(b_1\) and \(b_2\) - components of excretion in urine
\((m_1 + \lambda)\) and \((m_2 + \lambda)\) - effective decay constants of Cs\(^{137}\) in urine.

The values of these coefficients (Table III) have been derived from the experimental points by the method of least squares.

Several workers have found that a double exponential function adequately described the pattern of retention of caesium by the human body. One of the
more recent reports [6] gave the results of measurements made on four male subjects who had received oral administrations of radio-caesium. It was found that on average 13.3% of the intake was retained with a half-time of 1.4 d, and an average biological half-time of 134 d was reported for the
### COEFFICIENTS OF EQUATIONS (1) AND (2)

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Subject A</th>
<th>Subject B</th>
</tr>
</thead>
<tbody>
<tr>
<td>$a_1$ (nc)</td>
<td>132</td>
<td>33$^a$</td>
</tr>
<tr>
<td>$k_1 + \lambda$ (days$^{-1}$)</td>
<td>0.33</td>
<td>(b)</td>
</tr>
<tr>
<td>$\frac{0.693}{k_1 + \lambda}$ (days)</td>
<td>2.1</td>
<td>(b)</td>
</tr>
<tr>
<td>$a_2$ (nc)</td>
<td>457</td>
<td>115</td>
</tr>
<tr>
<td>$k_2 + \lambda$ (days$^{-1}$)</td>
<td>0.00595</td>
<td>0.0102</td>
</tr>
<tr>
<td>$\frac{0.693}{k_2 + \lambda}$ (days)</td>
<td>$116 \pm 1.6$</td>
<td>$68 \pm 2$</td>
</tr>
<tr>
<td>$b_1$ (nc/day)</td>
<td>12.4</td>
<td>(b)</td>
</tr>
<tr>
<td>$m_1 + \lambda$ (days$^{-1}$)</td>
<td>0.37</td>
<td>(b)</td>
</tr>
<tr>
<td>$\frac{0.693}{m_1 + \lambda}$ (days)</td>
<td>1.9</td>
<td>(b)</td>
</tr>
<tr>
<td>$b_2$ (nc/day)</td>
<td>2.4</td>
<td>0.66</td>
</tr>
<tr>
<td>$m_2 + \lambda$ (days$^{-1}$)</td>
<td>0.009</td>
<td>0.0074</td>
</tr>
<tr>
<td>$\frac{0.693}{m_2 + \lambda}$ (days)</td>
<td>$77 \pm 9$</td>
<td>$94 \pm 13$</td>
</tr>
</tbody>
</table>

(a) Calculated from the ratio $a_1/a_2$ of Subject A, and the value $a_2$ of Subject B.

(b) Not evaluated owing to insufficient data.

remaining 86.7%. In this study at Windscale, approximately 22% of the estimated initial body burden of 0.59 $\mu$C was retained by Subject A with a half-time of 2.1 d, and the remaining 78% was retained with an effective half-time of 116 d. The shorter period of retention was probably prolonged owing to the retention of part of the intake of Cs$^{137}$ in the lungs. Owing to a complete lack of data for the retention of Cs$^{137}$ during the first 10 d, it was not possible to draw similar conclusions for Subject B.

The previously mentioned value of 78% for the fraction of the intake retained with the longer half-time is about double the fraction which is quoted by the ICRP [2] for retention in the muscle.

The effective half-times for retention of Cs$^{137}$ by Subjects A and B were 116 d and 68 d, as compared with values extending from about 80 to 150 d [6, 7, 8]. These values represent some of the more recently published data, and are generally within the range covered by the ICRP [2] values of 70 d for the body and 138 d for retention in muscle.

**4.2.** A comparison between the amounts of Cs$^{137}$ retained in the chest of Subject A and in his whole body is given in Table IV. On average, about 15%
of the retained body burden of Cs\textsuperscript{137} appears to have been present in the chest during the first fourteen days after intake.

In order to explain this retention in terms of deposition in the lungs and lymph nodes it is necessary to suggest that Cs\textsuperscript{137} might have been present in a relatively insoluble form. The apparently normal behaviour of Cs\textsuperscript{137} in the remainder of the body indicates that the compound would need to be insoluble in the lungs, but soluble in the digestive system. In the absence of information on the retention of caesium in the lungs, the possibility cannot be entirely ruled out that there is a mechanism by which caesium is complexed and retained in the lungs and lymph nodes.

The rapid uptake of Cs\textsuperscript{137} by cartilage has been reported \cite{9} as a result of experiments performed with rats. A strong accumulation was detected in the cartilage of the trachea \cite{9}. This effect may have been present in Subject A and could have contributed to the observed retention of Cs\textsuperscript{137} in the region of his chest.

4.3. The relationship between the amount of Cs\textsuperscript{137} excreted in urine per day and the retained body burden, was found from equations (1) and (2), and is shown in Fig. 7. Differentiation of equation (1) gave an expression for the total amount of Cs\textsuperscript{137} excreted per day, and \( F_t \), the amount of Cs\textsuperscript{137} (nc) excreted per day in the faeces was deduced from the relationship \( F_t = \frac{dR}{dt} t - U_t \).

The variation of \( \frac{F_t}{R_t} \) during the 150 d after intake has been calculated in this way (Fig. 8).

The variations of \( U_t \) and \( F_t \) expressed as a percentage of the estimated initial intake of 0.59 \( \mu \)Cs\textsuperscript{137} are shown in Fig. 9 for Subject A.

The average amount of Cs\textsuperscript{137} excreted in urine by both subjects for \( t > 15 \) d was 0.55 \( \pm \) 0.1\% of the retained body burden, which agrees with the mean value of 0.54\% previously quoted in this paper for control subjects. These values may be compared with 0.6 \( \pm \) 0.2 reported by TAYLOR et al. \cite{8}. The present data for Subject A extends from the third day after intake, and the results indicate that the Cs\textsuperscript{137} excreted in urine (Fig. 7) decreased from about 2 to 0.6\% of the retained body burden during the first 15 d.

The mean, of the amounts of Cs\textsuperscript{137} excreted per day in urine expressed as a percentage of the total daily excretion of Cs\textsuperscript{137}, was approximately 70\% for 20 < \( t < 150 \) d (Fig. 10) as compared with values of 61\% (STEWART et al. \cite{10}) and 78\% calculated from the results of HAMMOND et al. \cite{8}. The
above value of 61% [10] was considered to represent the urinary pool, as compared with 51% for the total excretion in urine by Windscale Subject A and 58% and 77% for the longer components only of both the Windscale subjects.

The estimated intakes of Subjects A and B respectively were approximately 0.59 μC and 0.15 μC (Table III). These amounts represent about 0.01 of a Maximum Permissible 13 Weeks' Intake (39 μC) of soluble Cs\textsuperscript{137} [2].
Assuming that the equations for body retention ($R_t$) are valid to infinity, the total whole-body radiation doses received by Subjects A and B were approximately 30 and 5 mrem.

5. CONCLUSIONS

Half-times for the retention of Cs$^{137}$ by two male subjects aged 37 and 27 yr were found to be 116 and 68 d respectively. These values compare
favourably with the results of other workers [6, 7, 8] but were in the lower part of the range covered by the ICRP [2] values for retention of Cs\(^{137}\) in the body (70 d) and muscle (138 d).

The intake was primarily by inhalation, and in one of these subjects it was found that approximately 15\% of the body content was in the region of the chest during the first 14 d after intake, and was eliminated with an effective half-time of 23 d.

Whole-body retention, and urinary excretion of Cs\(^{137}\) could both be described by double exponential functions for one subject, while for the other subject, for whom the first component could not be evaluated owing to insufficient data, a single exponential function applied for \(t > 10\) d. The average fraction of the retained body burden excreted per day in urine was \(0.55 \pm 0.1\%\) of body content for \(15 < t < 150\) d, and on average 70\% of the Cs\(^{137}\) excreted per day was in urine.

ACKNOWLEDGEMENTS

I wish to thank Dr. J. C. Dalton of the Windscale Chemical Services Department for the biochemical analyses, and Mr. G. Green and Mr. E. H. Tucker who assisted in the measurements of body radioactivity.

The co-operation of the Windscale Medical Department has been greatly appreciated.

I wish to acknowledge the advice which I have received from members of the Windscale Health and Safety Department and the Authority Health and Safety Branch at Harwell.

REFERENCES

NOTE AU SUJET DE DEUX TYPES DE CONTAMINATION HUMAINE PAR LE $^{137}$Cs

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Abstract — Résumé — Аннотация — Resumen

NOTE ON TWO TYPES OF CONTAMINATION OF HUMAN BEINGS BY CAESIUM-137. The authors present an elimination curve for a case of occupational contamination by caesium-137. They also show how the caesium-137 body burden varied during 1963 in a group of persons who did not undergo occupational exposure.

NOTE AU SUJET DE DEUX TYPES DE CONTAMINATION HUMAINE PAR LE CÉSIUM 137. L’auteur présente une courbe d’élimination à la suite d’une contamination professionnelle par le césium 137. Il montre aussi l’évolution de la charge corporelle en césium 137 au cours de l’année 1963 sur un groupe de personnes non exposées professionnellement.

СООБЩЕНИЕ О ДВУХ ТИПАХ ЗАРАЖЕНИЯ ОРГАНИЗМА ЧЕЛОВЕКА ЦЕЗИЕМ-137. Дается кривая выделения после профессионального заражения цезием-137. Показана эволюция содержания в организме цезия-137 в течение 1963 года у группы лиц, не подвергавшихся профессиональному облучению.

NOTA RELATIVA A DOS TIPOS DE CONTAMINACIÓN HUMANA POR CESIO-137. El autor presenta una curva de eliminación consecutiva a una contaminación profesional por cesio-137. Expone, por otra parte, la evolución de la carga corporal de cesio-137 durante el año 1963, en un grupo de personas no expuestas profesionalmente.

Le premier cas concerne une contamination professionnelle par ingestion. Les premières mesures effectuées dans notre laboratoire n’ont eu lieu que plusieurs mois après la contamination et, de ce fait, nous ne disposons pas des valeurs initiales.

Les mesures ont été effectuées avec un anthroporadiomètre à cristal d’iodure de sodium de 20 cm de diamètre sur 10 cm de hauteur.

Les valeurs trouvées pendant un an se groupent parfaitement sur une seule droite en coordonnées semi-logarithmiques comme le montre la figure 1. Nous avons trouvé une période d’élimination de 100 j. Elle diffère sensiblement de celle reportée par la CIPR.

La quantité de césium présente lors de la première mesure était de 0.75 μc.

Quelques déterminations d’activité ont été faites sur l’urine. Le tableau I montre les valeurs trouvées par examen de l’urine, ainsi que les valeurs d’élimination calculées à partir des mesures sur l’individu, en tenant compte d’une période effective de 100 j.

Les mesures sont peu nombreuses, mais semblent en bon accord, et permettent de conclure que l’étalonnage du corps effectué avec un fantôme en plastique du type REMCAL est très satisfaisant dans le cas du $^{137}$Cs.

Le deuxième point sur lequel nous pouvons apporter quelques données concerne la contamination en $^{137}$Cs due aux retombées radioactives au cours de l’année 1963.
Figure 1
Résultats de mesures effectuées avec un autoresonance

Figure 2
Évolution de la teneur moyenne en césium
- Homme Cs/g de K (pm)
- Lait Cs/g de K (pc)
Eau de pluie, Cs retombé (unités arbitraires)
TABLEAU I
DÉTERMINATIONS D'ACTIVITÉ

<table>
<thead>
<tr>
<th>Jour de la mesure</th>
<th>Activité mesurée (pc)</th>
<th>Activité calculée (pc)</th>
<th>% d'écart</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>4940</td>
<td>4680</td>
<td>+5.4</td>
</tr>
<tr>
<td>187</td>
<td>1490</td>
<td>1450</td>
<td>+2.7</td>
</tr>
<tr>
<td>196</td>
<td>1880</td>
<td>1345</td>
<td>+2.6</td>
</tr>
</tbody>
</table>

TABLEAU II
ÉVOLUTION DE LA TENUEUR MOYENNE EN CÉSIUM

<table>
<thead>
<tr>
<th>Mois</th>
<th>Individu (pc/g de potassium)</th>
<th>Lait (pc/g de potassium)</th>
<th>Eau de pluie (césium retombé par mois; unités arbitraires)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janvier</td>
<td>67</td>
<td>36</td>
<td>33</td>
</tr>
<tr>
<td>Février</td>
<td>57</td>
<td>36</td>
<td>33</td>
</tr>
<tr>
<td>Mars</td>
<td>61</td>
<td>31</td>
<td>114</td>
</tr>
<tr>
<td>Avril</td>
<td>67</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Mai</td>
<td>77</td>
<td>50</td>
<td>165</td>
</tr>
<tr>
<td>Juin</td>
<td>91</td>
<td>110</td>
<td>310</td>
</tr>
<tr>
<td>Juillet</td>
<td>100</td>
<td>158</td>
<td>52</td>
</tr>
<tr>
<td>Août</td>
<td>146</td>
<td>188</td>
<td>193</td>
</tr>
<tr>
<td>Septembre</td>
<td>150</td>
<td>194</td>
<td>28</td>
</tr>
<tr>
<td>Octobre</td>
<td>148</td>
<td>140</td>
<td>17</td>
</tr>
<tr>
<td>Novembre</td>
<td>168</td>
<td>121</td>
<td>60</td>
</tr>
<tr>
<td>Décembre</td>
<td>170</td>
<td>136</td>
<td>56</td>
</tr>
</tbody>
</table>

Des mesures systématiques ont été faites environ tous les deux mois sur un groupe d'une vingtaine de personnes non soumis à une contamination professionnelle. Toutes les personnes mesurées ont présenté une augmentation similaire de leur teneur en césium. Le tableau II indique pour ce groupe l'évolution de la teneur moyenne en Césium par gramme de potassium. Une autre colonne montre la moyenne
de la teneur en césium dans le lait. Ces valeurs correspondent à des moyennes mensuelles calculées à partir d'échantillons journaliers d'un lait ayant une large diffusion dans la région parisienne. La colonne suivante indique l'évolution de la quantité de césium retrouvée dans l'eau de pluie au cours de la même période.

Ces valeurs reportées sur le graphique de la figure 2, montrent que l'évolution de différentes courbes suit un ordre logique, bien qu'il ne s'agisse que de résultats très fragmentaires.

REMERCIEMENTS

Nous remercions Mademoiselle S. BERTRAND, qui a effectué les mesures de spectrométrie γ et Mademoiselle D. BULLIER les dosages de césium dans l'eau de pluie.
HALF-LIFE STUDIES OF RADIOCAESIUM IN HUMANS

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RADATION PHYSICS DEPARTMENT, UNIVERSITY OF LUND, SWEDEN

Abstract — Résumé — Аннотация — Resumen

HALF-LIFE STUDIES OF RADIOCAESIUM IN HUMANS, The retention of caesium-137 in humans has been studied in several cases. Two adult men were intravenously administered a small quantity of caesium-137. They were followed about 300 days by frequent whole-body counting and with excreta collection during the initial period. The retention decreased as a sum of two exponentials. The slowest compartment decreased with a half-life of about 75 d.

One of them was also given caesium-137 orally 2 years later with the same excretion pattern obtained as after intravenous injection. The excretion rate of caesium-137 has also been studied in a different way for large groups of men, women and children through comparison with diet data.

From a group of 10 people, voluntarily changing their diet, the average excretion rate could be calculated from whole-body counting at an interval of six weeks. The excretion also has been obtained from a study on two people after an oral administration of caesium-132.

Detailed results on these studies will be given particularly with respect to the elimination rate of caesium, i.e. the biological half-life and its variation with sex and age. On the average, half-lives ranging from 30 to 90 d have been obtained.

ÉTUDES SUR LA PÉRIODE DE RADIOCÉSÉIUM CHEZ L'HOMME. La rétention de césium 137 chez l'homme a été étudiée sur plusieurs sujets. Ainsi, on a administré à deux hommes adultes, par voie intraveineuse, une petite quantité de césium 137. On les a suivis pendant 300 j environ en faisant de fréquents dosages de l'activité du corps et en recueillant les excréta au début de la période. La fonction qui représentait la décroissance de la rétention est une somme de deux exponentielles. La fraction qui décroissait le plus lentement avait une période d'environ 75 j.

Deux ans plus tard, on a administré au même régime d'élimination qu'après l'injection intraveineuse. On a aussi étudié le taux d'élimination de césium 137 par une méthode différente pour des groupes importants d'hommes, de femmes et d'enfants en faisant des comparaisons avec des données concernant leur régime alimentaire.

Pour un groupe de dix personnes qui avaient volontairement accepté un changement de leur régime alimentaire, on a pu calculer le taux d'élimination moyen en procédant à des dosages de l'activité du corps à des intervalles de six semaines. On a aussi obtenu ce taux pour deux personnes auxquelles on avait administré le césium 132 par voie buccale.

Les auteurs communiquent les résultats détaillés de ces études, notamment en ce qui concerne le taux d'élimination du césium, c'est-à-dire la période biologique et ses variations selon le sexe et l'âge. Dans l'ensemble, on a trouvé des périodes allant de 30 à 90 j.

ИССЛЕДОВАНИЕ ПЕРИОДА ПОЛУВЫВЕДЕНИЯ РАДИОАКТИВНОГО ЦЕЗИЯ У ЛЮДЕЙ. Изучалась задержка цезия-137 у людей при различных обстоятельствах. Двум взрослым мужчинам вводили внутривенно малые количества цезия-137. Пациенты находились под наблюдением 300 дней, в течение которых производились частые измерения радиоактивности всего организма и сбор выделений в начальный период. Степень задержки изотопа снижалась как сумма двух экспоненциальных величин. Найболее медленно изменяющейся величиной снижалась с периодом полувыведения около 75 дней.

Один из пациентов получил цезий-137 внутрь 2 года спустя, причем наблюдался тот же тип выведения, как и после внутривенного введения. Скорость выведения цезия-137 изучалась также другим способом у большой группы мужчин, женщин и детей путем сравнения данных исследования днём.

При обследовании группы из 10 добровольцев, изменивших свою диету, удалось возможно рассчитать среднюю скорость выведения на основании измерения радиоактивности.
1. INTRODUCTION

Since 1960 the retention and metabolism of different radionuclides in humans has been studied at our laboratory. These studies have played an important part in our investigation both of various radioactive contamination problems in the biosphere and the use of radionuclides for medical purposes.

One branch of our research programme has been the measurement of retained radiocaesium. The total-body retention has usually been obtained by whole-body counting techniques, but assay of carefully collected samples of the totally excreted urine and faeces has proved valuable, especially in the initial period following administration.

So far only a few results of our metabolic caesium studies have been published, and then very briefly. As more detailed knowledge in this field is desirable, we have made a compilation of our results and present them at this Symposium. For a recent review of other published data, see RUNDO [4].

2. ARTIFICIAL ADMINISTRATION OF RADIOCAESIUM

In September 1960 Cs$^{137}$Cl solution was administered to two male subjects, A and B:1 (a second study of B was performed two years later, B:2; see below) by intravenous injection, preceded by accurate determination of the amount of Cs$^{137}$. Subject A obtained 148 nc and B:1 304 nc. The total-body retention was then determined by whole-body counting in a 42-cm chair arrangement using a 5 in x 4 in NaI(Tl) crystal [1]. All excreta were collected during the three days after the administration. At this time the principal purpose of the investigation was the calibration of the chair geometry.
For cases A and B:1 no change of the sensitivity of the counter due to redistribution in the body could be detected after 30 h. The total-body retention was measured frequently during 9 and 12 months for subjects A and B:1 respectively. After 10 d the measured retention could be accurately represented by a one-exponential function for both subjects, corresponding to a biological half-time of 89 and 73 d for A and B:1 respectively.

Detailed analysis of the initial retention pattern was possible by using the results of both excreta assays and whole-body counting. Considerable Cs\(^{137}\) excretion was observed during the first few hours after administration compared to the excretion rates found thereafter, and after subtracting the slow excretion component the remaining fast fraction could not be accurately represented by one second exponential only. In adding a third exponential with a biologic half-time of approximately 2 h it was possible to describe the initial phase much better.

Similar results were obtained for two male subjects, С and D, who obtained orally 1240 nc and 1190 nc, respectively, of Cs\(^{132}\)Cl solution. These subjects were carefully measured by a whole-body counter, using a scanning bed technique\(^1,2\). which gave accurate results also during the initial period after administration. However, the slow component of the retention curve could not be studied with the same accuracy as in the case of Cs\(^{137}\), owing to the short half-life of Cs\(^{132}\).

In these four cases retention can be described by a sum of three exponentials. The result of the analysis is displayed in Table I, showing the fractions \(a_1\), \(a_2\), and \(a_3\) of the administered activity being excreted with rates corresponding to the biologic half-times \(T_1\), \(T_2\), and \(T_3\), which are also given. Although the method of collecting excreta at discrete time points means that the data for analysing the initial period are relatively poor (the first urine sample obtained 3 to 5 h after administration), it is fully evident that a small fraction of the administered activity, 1 to 5%, is eliminated very quickly from the body, corresponding to a biologic half-time of 2 to 3 h. The results obtained so far indicate that \(a_1\) may be larger at intravenous injection than at oral administration; however, further studies are needed in order to exclude a possible effect of biologic variability.

The data plotted in Fig. 1 have been obtained by subtraction of the slow component from the observed total body retention of subject С. This procedure requires a smooth transfer from total-body retention determined by excreta measurement to the same quantity obtained by whole-body counting. The scanning bed geometry is particularly convenient in such a case, owing to its insensitivity to redistribution. The curve shows the retention of the fast components as a percentage of the administered activity. In Fig. 1 the second component is extrapolated and subtracted from the curve, and the obtained difference illustrates the new fast fraction \((a_1, T_1)\).

In case A the available data are insufficient for a reliable estimate of \(T_1\) and \(T_2\). Moreover, the varying accuracy ascribed to the data in Table I illustrates the difficulties encountered in analysing excretion data from irregularly-collected samples.

The caesium metabolism of subject В was also studied 2 yr later after an oral intake of 267 nc Cs\(^{137}\) as CsCl solution; this case is indicated as B:2. As the first urine sample covered the first 16 h, \(T_1\) could not be determined. We can only say that \(T_1 = 2\) to 3 h fits the obtained retention curve,


<table>
<thead>
<tr>
<th>Subject</th>
<th>A</th>
<th>B:1</th>
<th>B:2</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (a)</td>
<td>28</td>
<td>45</td>
<td>47</td>
<td>31</td>
<td>38</td>
<td>28</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73</td>
<td>74</td>
<td>74</td>
<td>83</td>
<td>88</td>
<td>72</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method</th>
<th>Cs$^{137}$</th>
<th>Cs$^{137}$</th>
<th>Cs$^{137}$</th>
<th>Cs$^{132}$</th>
<th>Cs$^{132}$</th>
<th>Cs$^{137}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. v.</td>
<td>Activity (nc)</td>
<td>i. v.</td>
<td>per os</td>
<td>per os</td>
<td>food intake</td>
<td></td>
</tr>
<tr>
<td>Date of adm.</td>
<td>148</td>
<td>304</td>
<td>287</td>
<td>1240</td>
<td>1190</td>
<td>80</td>
</tr>
</tbody>
</table>

| $a_1$ (%) | 4 ± 1 | 5 ± 1 | 1 - 2 | 2.0 ± 0.5 | 1 - 2 | --- c) |
| $T_1$ (h) | 1.5 - 5 | 2.0 ± 0.5 | --- b) | 2.5 ± 0.5 | 2 - 3 | --- c) |
| $a_2$ (%) | 8 ± 2 | 9 ± 1 | 11 ± 1 | 2.0 ± 0.5 | 1 - 2 | 14 ± 3 c) |
| $T_2$ (d) | --- a) | 1.1 ± 0.2 | 1.1 ± 0.1 | 1.5 ± 0.3 | 0.5 ± 1.0 | 0.7 ± 0.2 c) |
| $a_3$ (%) | 88 ± 2 | 86 ± 1 | 87 ± 1 | 96.0 ± 0.5 | 96.9 ± 0.5 | 86 ± 3 |
| $T_3$ (d) | 89 ± 2 | 73 ± 2 | 63 ± 2 | 72 ± 2 | 85 ± 7 | 80 ± 10 |

Notes:

a) Inconsistent data.

b) The procedure of the initial measurements made it impossible to calculate this parameter.

c) The data did not allow a separation of the first two components. The values of $a_2$ and $T_2$ include the effect of the first fraction, $a_1$ and $T_1$.

an extrapolation of which indicates a value of $a_1$ of 1 to 2%. The obtained value of $T_3$, 63 ± 2 d, deviates significantly from that 2 yr earlier, 73 ± 2 d. No explanation of this observation is available. However, the first study was made in the autumn and the second in the summer. It should be mentioned that a temperature effect on the caesium metabolism in mice has been found by FURCHNER and RICHMOND [3], showing an increased excretion rate at lower temperatures.

Subject E (Table I) obtained his Cs$^{137}$ body activity by eating naturally-contaminated reindeer meat (25 nc/kg fresh meat) on seven days out of a period of 16 d. All excreta were collected during this time and also during the following 11 d. Whole-body counting was performed during these periods but only a couple of times during the following two months. Therefore the determination of $T_3$ and $a_3$ is less accurate than in the other cases studied, and no separate estimate of the parameters of the two fast components could
TABLE II

URINARY AND FAECAL EXCRETION DATA OF RADIOCAESIUM, OBTAINED FROM FIVE MALE SUBJECTS*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Collection period (d)</th>
<th>Excreted activity per day in % of adm. amount</th>
<th>Fraction in faeces, ( \frac{F}{U+F} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(U)</td>
<td>(F)</td>
</tr>
<tr>
<td>A</td>
<td>0 - 0.8</td>
<td>5.7</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>0 - 2.8</td>
<td>2.9</td>
<td>0.5</td>
</tr>
<tr>
<td>B:1</td>
<td>0 - 1.0</td>
<td>7.4</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>0 - 3.2</td>
<td>3.4</td>
<td>0.2</td>
</tr>
<tr>
<td>C</td>
<td>0 - 0.9</td>
<td>3.9</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>0 - 3.9</td>
<td>1.7</td>
<td>0.2</td>
</tr>
<tr>
<td>D</td>
<td>0 - 1.0</td>
<td>3.1</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>0 - 3.0</td>
<td>1.6</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>0 - 3 after 1st intake</td>
<td>2.9</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>0 - 5 after 2nd intake</td>
<td>1.7</td>
<td>0.4</td>
</tr>
<tr>
<td>E</td>
<td>0 - 6 after 3rd intake</td>
<td>1.6</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>0 - 5 after 4th intake</td>
<td>1.5</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>0 - 12 after last intake</td>
<td>0.6</td>
<td>0.1</td>
</tr>
</tbody>
</table>

* Cf. TABLE I. U = urine, F = faeces.

be made. In Table I the values of \( a_2 \) and \( T_2 \) for subject E also include the effect of the first fraction \( a_1 - T_1 \).

The fraction of radiocaesium excreted in faeces has recently been subject to special interest (Rundo [4], Rosoff et al. [5]). In Table II we have collected the data obtained on faecal and urinary excretion in the initial period and, in one case, on a more long-term study. The large amount of radiocaesium excreted on the first day is noticeable. In agreement with
Retention of the fast components per cent of administered activity

Fig. 1

The biologic retention of the fast components of Cs\textsuperscript{132} in subject C referred to the administered amount of activity. The slow (third) component is mathematically eliminated from the full retention curve. The rest is indicated by circular points and the fraction belonging to the first component by square symbols. The bars indicate 2 S. D.

RUNDO's results the daily faecal excretion in the initial period is 0.2 to 0.4\% of the administered activity.

3. CHANGE OF DIETARY INTAKE OF RADIOCAESIUM

In April and May 1962, in connection with our measurements of the enhanced levels of body activity of people in northern Sweden a special study was performed on a group of subjects from the Lapp peoples' high school at Jokkmokk. With 5 males and 4 females, all of them about 20 yr old, and with the 52-yr old male headmaster (H-M) it was agreed that their main sources of Cs\textsuperscript{137} intake, reindeer meat and fresh-water fish, should be omitted from their meals for a period of 5 weeks. They were first measured in our semi-portable whole-body counter [6] at Jokkmokk. On their way back from a two-weeks' trip abroad they were again measured, 36 d later, in the iron room whole-body counter at Lund. All these people (10) showed a pronounced decrease (average 32\%) of their initial Cs\textsuperscript{137} level; the latter ranged from 90 to 260 nc. Thus it was possible to obtain a rather good estimate of the average excretion rate with these two measurements. In a control group of 12 subjects from the same school there was a decrease of only 14\%.

In Table III the results are summarized. The initial levels have been corrected for intake of Cs\textsuperscript{137} just before the start of the investigation, assuming a value for a\textsubscript{0} of 87\%. Except for one subject this correction mounted to less than 1\% of the initial body activity.

In this study a certain but small intake of Cs\textsuperscript{137} by normal food (milk, etc.) could appear. A reliable correction for this effect proved impossible. Therefore the measured excretion rate should be a minimum value. Moreover, for one of the boys the biologic half-time became $81\pm\frac{30}{15}$ d and for one of the girls $97\pm\frac{14}{15}$ d. If these subjects are omitted, 5 and 10 d shorter average half-time is obtained, as shown in Table III.
TABLE III

BIOLOGIC HALF-TIME ($T_3$) OBTAINED AS A RESULT OF A TEMPORARILY INTERRUPTED NORMAL DIETARY INTAKE OF CS$^{137}$

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age range (yr)</th>
<th>Weight (kg)</th>
<th>$T_3$ (d)</th>
<th>2 S.D. (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 males</td>
<td>18 - 25</td>
<td>64</td>
<td>64</td>
<td>8</td>
</tr>
<tr>
<td>only 4 males</td>
<td>20 - 25</td>
<td>64</td>
<td>59</td>
<td>6</td>
</tr>
<tr>
<td>4 females</td>
<td>19 - 21</td>
<td>53</td>
<td>67</td>
<td>7</td>
</tr>
<tr>
<td>only 3 females</td>
<td>19 - 21</td>
<td>55</td>
<td>57</td>
<td>8</td>
</tr>
<tr>
<td>H - M (male)</td>
<td>51</td>
<td>58</td>
<td>73</td>
<td>15</td>
</tr>
</tbody>
</table>

These results strongly indicate a half-time of the slow component in the range 50 to 70 d both for 20 yr-old women and men from the actual district of Sweden.

4. BODY BUILD-UP OF Cs$^{137}$ FROM FOOD INTAKE

In a joint study with a Finnish group [7] the present authors had the opportunity to use whole-body counting results together with food consumption data and food activity data in an attempt to calculate average retention rates of Cs$^{137}$ for various groups of Finnish Lapps. Details of this study are given in ref. [7]; in this paper the results only are summarized and set out in Table IV. The age range in the adult groups is large, but most men are 20 to 50 yr old and most women 20 to 60 yr old. The mean age of the boys is 11.5 yr. The short half-time of the latter group is of special

TABLE IV

AVERAGE BIOLOGIC HALF-TIME ($T_3$) OF FINNISH LAPPSS

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of subjects</th>
<th>Average weight (kg)</th>
<th>Age range (yr)</th>
<th>Average age (yr)</th>
<th>$T_3$ (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>50</td>
<td>63</td>
<td>16 - 75</td>
<td>40</td>
<td>64 ±10</td>
</tr>
<tr>
<td>Females</td>
<td>33</td>
<td>57</td>
<td>17 - 76</td>
<td>44</td>
<td>65.5 ±10</td>
</tr>
<tr>
<td>Boys</td>
<td>17</td>
<td>33</td>
<td>10 - 13</td>
<td>11.5</td>
<td>44 ±10</td>
</tr>
</tbody>
</table>
interest, as it means a faster Cs metabolism in children than in adults. The half-times of the adult group agree well with the data for Swedish Lapps (Table III).

5. THE Cs\textsuperscript{137} METABOLISM IN THE NEWBORN AND THEIR MOTHERS

In our laboratory SVENSSON, BENGTSSON and NAVERSTEN \cite{8} have studied the retention of Cs\textsuperscript{137} and Cs\textsuperscript{132} in mothers and their newborn. The results are summarized in Table V. For comments the reader is referred to \cite{8}. In the present paper we have reported on all studies of radiocaesium metabolism performed in our laboratory to date.

\begin{table}
\centering
\begin{tabular}{|l|c|c|c|}
\hline
Subject & Before partus (d) & After partus (d) & Baby (d) \\
\hline
F & 33 & 67 ± 3 & 21 ± 5 \\
G & -- & 73 ± 10 & -- \\
H & -- & 32 ± 2 & 25 ± 3 \\
\hline
\end{tabular}
\caption{BIOLOGIC HALF-TIME (T\textsubscript{3}) OF RADIOCAESIUM IN MOTHERS AND NEWBORN}
\end{table}

6. CONCLUSIONS

A diagrammatic representation of all values of T\textsubscript{3}, the slow component, is presented in Fig. 2. From this diagram it is evident that the biologic

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Fig_2.png}
\caption{The biologic half-time (T\textsubscript{3}) of radiocaesium, obtained from studies of individuals and groups of people in Sweden and Finland. The number of subjects in a group is given below the plotted average value of the group. The age range (16-76 yr) of group "50" and "33" is indicated in the diagram.}
\end{figure}
half-time of caesium varies with age. No difference between Lapp groups and other Swedish control persons is observed. From the newborn there seems to be a much faster caesium metabolism; this should be confirmed by further studies. The present material is not useful for an estimate of $T_3$ older people, but it is very likely that no general increase occurs with age.

The investigations reported above show that a sum of three exponentials describes human caesium retention quite accurately. The first fast component with a biologic half-time of about 2 h has not been reported in the literature before. However, it is well known that a three-component retention function for radiocaesium is valid for several mammalian species [9].

Evidently a rather large biologic variability of the various parameters of caesium metabolism occurs. Therefore further studies of different age groups, at different times of the year, etc., are desirable.

ACKNOWLEDGEMENT

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REFERENCES

THE EFFECT OF CHLOROTHIAZIDE ON CAESIUM-137 EXCRETION IN HUMAN SUBJECTS

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Abstract — Résumé — Аннотация — Resumen

THE EFFECT OF CHLOROTHIAZIDE ON CAESIUM-137 EXCRETION IN HUMAN SUBJECTS. The present study was carried out to determine factors that influence caesium metabolism in normal human subjects with particular interest in finding a therapeutic regimen for reducing the body burden of caesium.

Since caesium and potassium are chemically similar, and are both localized in the intracellular compartment of the body, principally in muscle, it seemed possible that chlorothiazide, which has a marked potassium diuretic effect, might also increase caesium excretion.

Four normal subjects were given a single dose of 0.1 μc of caesium-137 by mouth. Two subjects were given chlorothiazide 2.0 g/d for a total of three consecutive days starting 1 h after the caesium intake. The chlorothiazide dose was repeated at two weeks. The other two subjects were used as controls. The body burden of caesium-137 was measured by a whole-body counter at intervals up to 320 d. Daily urine collections were made for three control days and 20 d following caesium intake. The samples were analysed for electrolytes and caesium activity.

Although chlorothiazide increased K excretion to 1.5 times the control values, it had no significant effect on caesium excretion or in reducing the body burden of caesium. In all subjects a small fraction of caesium (10-20%) was excreted rapidly with a biological half-life (T1/2) of less than 1 d. The remainder was excreted at a constant rate with T1/2 of 90 to 155 d. More than 70% of the caesium eliminated from the body per day was excreted by the kidney. T1/2 of K was also calculated by the formula

\[ T_{1/2}K = \frac{\text{Total body K}}{\text{Urine K}} \times 0.693 \times 0.8 \]

assuming 80% of the total potassium excreted is by kidney. T1/2 of K was 35 to 42 d. The discrimination ratio

\[ T_{1/2}K / T_{1/2}K = 2.1 \text{ to } 3.8 \]

These results demonstrate that caesium and potassium are not utilized interchangeably. Caesium is retained preferentially over potassium and changes in potassium turnover have no effect on caesium turnover.

Studies are being carried out at the present time to determine the effect of basal metabolism on caesium excretion and these results will also be reported.

EFFET DE LA CHLOROTHIAZIDE SUR L'ÉLIMINATION DU CÉSIUM 137 CHEZ L'HOMME. L'étude avait pour objet de déterminer les facteurs qui influent sur le métabolisme du césium chez des sujets normaux, en vue notamment d'établir une thérapie qui permettrait de réduire la charge corporelle de césium.

Êtant donné que le césium et le potassium sont chimiquement semblables et qu'ils sont localisés l'un et l'autre dans le compartiment intracellulaire de l'organisme, principalement dans le tissu musculaire, il a semblé aux auteurs que la chlorothiazide, qui stimule fortement l'élimination urinaire du potassium, pouvait augmenter aussi la quantité de césium éliminé.

 Ils ont administré à quatre sujets normaux une dose unique de 0,1 μc de césium 137 par voie buccale. Deux des sujets ont alors reçu de la chlorothiazide à raison de 2.0 g/d pendant trois jours consécutifs, à compter d'une heure après l'absorption du césium. La dose de chlorothiazide a été administrée à nouveau après deux semaines. Les deux autres sujets ont servi de témoins. La charge corporelle de césium 137 a été mesurée à l'aide d'un anthropogammamètre, à des intervalles de temps allant jusqu'à 320 j. Les auteurs ont recueilli les urines de 24 h, d'abord pendant trois jours à des fins de contrôle, puis pendant les 20 j qui ont suivi l'absorption de césium. Ils ont analysé les échantillons afin de déterminer les électrolytes et l'activité du césium.
la chlorothiazide a augmenté la quantité de potassium éliminée, qui a atteint jusqu'à 1,5 fois les valeurs témoins, mais elle n'a pas eu d'effet significatif sur l'élimination du césium et n'a pas non plus réduit sensiblement la charge corporelle de césium. Chez tous les sujets, une faible fraction de Cs (10 à 20%) a été éliminée rapidement, la période biologique (Tb) étant inférieure à 1 j. Le reste a été éliminé à un taux constant, Tb étant de 90 à 155 j. Plus de 70% du césium éliminé quotidiennement par l'organisme a été évacué par voie rénale. Les auteurs ont également calculé Tb de K en appliquant la formule

\[
T_bK = \frac{K_{\text{total du l'organisme}}}{K_{\text{de l'urine}}} \times 0,693 \times 0,8
\]

en supposant que 80% du potassium éliminé l'est par voie rénale. Tb de K était de 35 à 42 j. Le rapport TbcS/TbK était de 2,1 à 3,8.

Il ressort de ces résultats que le césium et le potassium ne sont pas utilisés indifféremment. Le césium est retenu de préférence au potassium et les variations du taux de renouvellement du potassium n'affectent pas le renouvellement du césium.

Les auteurs poursuivent actuellement des études visant à déterminer l'effet du métabolisme basal sur l'élimination du césium: ils en présenteront également les conclusions.

ВЛИЯНИЕ ХЛОРТИАЗИДА НА ВЫДЕЛЕНИЕ ЦЕЗИЯ-137 У ЛЮДЕЙ. Целью работы являлось определение факторов, влияющих на метаболизм цезия у здоровых людей, и, в частности, определение терапевтического режима, ведущего к уменьшению содержания цезия в организме.

Поскольку цезий и калий обладают сходными химическими свойствами и оба располагаются внутриклеточно, главным образом в мышцах, вполне возможно, что хлортиазид, оказывающий выраженный калиевый диуретический эффект, может увеличивать и выделение цезия.

Четверо обследуемых получили внутрь однократно по 0,1 мккюри цезия-137. Двое из них давали хлортиазид по 2,0 г в день в течение 3 дней через час после приема цезия. Прием хлортиазида повторяли через две недели. Двух других обследуемых использовали в качестве контроля. Содержание цезия 137 в организме измеряли с интервалами с помощью счетчика для измерения радиоактивности всего организма до 320 дней. Сбор суточного количества мочи производился в течение 3 контрольных дней после приема цезия. Образцы мочи исследовались на содержание электролитов и уровень активности цезия.

Хотя хлортиазид и повышал в 1,5 раза по сравнению с контролем выделение K, он не оказывал заметного влияния на выделение цезия или уменьшение его содержания в организме. У всех обследованных небольшие фракции цезия-137 (10–20%) выделялись быстро с периодом полувыведения (Tb) менее одного дня. Остальное количество выделялось с постоянной скоростью при Tb от 90 до 155 дней. Более 70% всего выделяемого организмом цезия за сутки выделяется почками. Tb для K также вычислялось по формуле:

\[
T_bK = \frac{\text{Общее содержание K в орг-ме}}{\text{Содержание K в моче}} \times 0,698 \times 0,8,
\]

при условии, что 80% общего количества калия выделяется почками. Tb для калия составляло от 35 до 42 дней. Коэффициент дискриминации TbcS/TbK составлял от 2,1 до 3,8.

Эти результаты показывают, что не существует взаимозаменяемого усвоения цезия и калия. Задержка цезия происходит в большей степени по сравнению с калием, и изменения в кругообороте калия не влияют на кругооборот цезия.

В настоящее время проводятся исследования по определению влияния основного обмена на выделение цезия, о результатах которого будет также сообщено.

INFLUENCIA DE LA CLOROTIAZIDA SOBRE LA EXCRECIÓN DE CESIO EN EL HOMBRE. Los autores procuraron determinar los factores que influyen en el metabolismo del cesio en sujetos humanos normales, y se dedicaron particularmente a encontrar un régimen terapéutico tendiente a reducir la carga corporal de cesio.

Dado que el cesio y el potasio son químicamente semejantes y ambos se localizan en los compartimientos intracelulares del cuerpo, principalmente en los músculos, se estimó posible que la clorotiazida, que ejerce un efecto diurético notable sobre el potasio, pueda fomentar también la excreción de cesio.

Se administró por vía oral una dosis única de 0,1 mc de cesio-137 a 4 sujetos normales. A dos de ellos se les dio clorotiazida a razón de 2,0 g/día, durante tres días consecutivos en total, comenzando una hora después
de la administración de cesio. La dosis de clorotiazida se repitió a las dos semanas. Los otros dos sujetos sirvieron de testigos. Mediante un antropogammámetro se midió periódicamente la carga corporal de cesio-137 por espacio de 320 d. Se recogieron muestras diarias de orina, primordialmente durante 3 d, como referencia, antes del tratamiento, y luego, durante 20 d a contar de la administración de cesio. En las muestras se determinaron los electrolitos y la actividad del cesio.

Por más que la clorotiazida incrementó la excreción de potasio hasta 1,5 veces con respecto a los valores de referencia, no se comprobó que tuviera ningún efecto apreciable sobre la excreción de cesio ni que redujera la carga corporal del mismo. Todos los sujetos excretaron rápidamente una pequeña fracción de cesio (10 a 20%) con un periodo biológico (Tb) inferior a 1 d. El resto fue excretado en proporción constante con un Tb de 90 a 155 d. Más del 70% del cesio se excretó diariamente por vía renal. El Tb del potasio se calculó también por la fórmula:

$$T_{bK} = \frac{\text{K total en el cuerpo}}{K \text{ en la orina}} \times 0.693 \times 0.8$$

admitiendo que el 80% del potasio total excretado lo sea por vía renal. El $T_{bK}$ del K fue de 35 a 42 d. La razón de discriminación $T_{bK}/T_{bC}$ osciló entre 2.1 y 3.8.

Estos resultados demuestran que el cesio y el potasio no se utilizan de manera intercambiable. El cesio es retenido con preferencia al potasio y las alteraciones de la renovación del potasio no ejercen ninguna influencia sobre la del cesio.

Los autores prosiguen actualmente sus estudios con el propósito de determinar el efecto del metabolismo basal sobre la excreción de cesio y oportunamente darán los resultados a que lleguen.

An investigation was carried out to explore the therapeutic value of the diuretic, chlorothiazide (Diuril), in reducing the body burden of caesium-137 in human subjects. Caesium and potassium are chemically similar and, in some respects, are metabolized in the same way [1-3]. Acetazolamide, which has a potassium diuretic effect, has been shown to increase caesium excretion in rats [4] and mice [5]. We believed that chlorothiazide had a greater potassium diuretic effect associated with hypokaliemia and, therefore, conceivably a greater effect on caesium excretion than acetazolamide [6].

In a subsidiary experiment, the effect of thyroid extract on the biological half-life of caesium was also studied. If caesium turnover is dependent on cellular metabolism, then thyroid hormone, in doses sufficient to increase basal metabolism, would be expected to increase the rate of caesium excretion.

METHOD

Four normal male subjects were investigated. They were between 25 and 35 yr of age and weighed between 110 and 180 lb. They were given a single dose of 0.1 μc of Cs137 by mouth. Two control subjects (case 1 and case 2) followed no special dietary or therapeutic regime. Two subjects (cases 3 and 4) were given chlorothiazide (Diuril) at a dose of 2.0 g/d in divided doses. The diuretic was started one hour after caesium ingestion and continued for a total of three days. After two weeks the chlorothiazide was repeated for a further three days. Apart from moderate salt restriction, designed to augment the potassium diuresis, the diet was that normally followed by these two subjects.
The total body caesium activity was measured at intervals up to 180 and 320 d in the four subjects. In the chlorothiazide studies (cases 3 and 4) daily 24-h urine collections were made starting two days before caesium ingestion and continued for 20 d. The samples were analysed for caesium-137 and for sodium (Na), potassium (K) and chloride (Cl). Blood samples were taken the day before and the morning after each period on chlorothiazide and analysed for Na, K and Cl. In the control studies (cases 1 and 2) 24-h urine collections were made for 6 d after caesium intake and at intervals up to 20 d. The samples were analysed for caesium-137 activity. The urine excretion and percentage retention of caesium activity of the subjects on chlorothiazide were compared to similar data obtained for the two control subjects.

The total-body caesium activity was measured with the use of the whole-body counter as described in a previous publication [7]. Briefly, the intensity of the 0.66 MeV gamma ray of caesium-137 was measured with the use of a single 5-in sodium iodide (NaI) crystal and a 100-channel pulse height analyser. The subjects were seated in the reclining chair position with the crystal suspended above the abdomen. The counts equal to 100% body burden of caesium-137 were determined from the three-hour total-body measurement plus the fraction of caesium-137 excreted in the urine by that time. Although there were significant changes in counting geometry initially, subsidiary experiments showed that the geometry remained constant for all measurements after three hours.

The urine caesium activity was also measured by gamma spectrometry using the 0.66-MeV gamma ray. The urine caesium-137 counts were expressed as percentage of a caesium-137 standard which was equal to the ingested dose and measured with similar geometry at the same time as the urine samples. The total body and urine caesium-137 determinations are accurate to within ±5%.

As an additional experiment, a single oral dose of radioactive caesium-134 was given to an obese 33-yr-old man who was on an intensive programme for weight reduction consisting of a low calorie diet and the administration of dried thyroid. The low calorie diet was maintained throughout the period of investigation. Dried thyroid was started 28 d after caesium ingestion, increased gradually from 2 grains (gr) per day to 12 gr per day over a month and continued at this level for the remainder of the study. The total body caesium-134 activity was measured at intervals up to 100 d utilizing the whole-body counter and measuring the 0.6-MeV gamma ray of caesium-134. The per cent retention of caesium over this interval was compared with similar data obtained for the control subjects.

RESULTS

The urine caesium excretion and the 20-d per cent caesium retention in the subjects treated with chlorothiazide and the controls are summarized in Table I. It will be seen that there was no significant difference between the subjects treated with chlorothiazide and the controls.

Chlorothiazide increased urine K 1.5 to 2.0 times the control value throughout each three-day period on diuretic and reduced serum K by 20%.
TABLE I

EFFECT OF CHLOROTHIAZIDE (DIURIL) ON URINE EXCRETION OF CAESIUM-137 AFTER ORAL INTAKE

<table>
<thead>
<tr>
<th></th>
<th>Total urine Cs(^{137}) excretion 0-3 d (% dose)</th>
<th>Mean urine Cs(^{137}) excretion per day at 2 weeks (% of body burden)</th>
<th>Cs(^{137}) retained in the body at 20 d (% dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>12.3</td>
<td>0.70</td>
<td>69</td>
</tr>
<tr>
<td>Case 2</td>
<td>6.3</td>
<td>0.44</td>
<td>80</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 3</td>
<td>11.3</td>
<td>0.63</td>
<td>72</td>
</tr>
<tr>
<td>Case 4</td>
<td>9.3</td>
<td>0.56</td>
<td>75</td>
</tr>
</tbody>
</table>

The whole-body retention of caesium-137 in four subjects after oral intake. The measurements obtained at intervals up to 320 d are shown for cases 1 and 2 and the curves obtained from similar data for cases 3 and 4, followed for 180 d, are also shown.

The diuresis of Na and Cl was transient with no change in serum concentration.

The per cent retention of caesium-137 over a period of 320 d for the control subjects (cases 1 and 2) is shown in Fig. 1. The data are plotted on semilog paper against time and appear to fit a two term exponential equation (i.e. \( Q = a_1 e^{-\lambda_1 t} + a_2 e^{-\lambda_2 t} \)). \( Q \) is the per cent activity retained in the body, \( \lambda_1 \) and \( \lambda_2 \) are measures of the two rates of excretion and \( a_1 \) and \( a_2 \) are the fractions of the initial body burden excreted at the respective rates. The two biological half-lives \( T_{b1} \) and \( T_{b2} \) are equal to \( \frac{0.693}{\lambda_1} \) and \( \frac{0.693}{\lambda_2} \) respectively.
vely. The curves obtained from the data for cases 3 and 4 followed for 180 d are also shown in Fig. 1. Values for $a_1$, $a_2$, $\lambda_1$ and $\lambda_2$ for the four subjects are shown in Table II. A small fraction 12 to 20% was excreted rapidly with $T_{b_1}$ of less than 1 d. The remainder was excreted at a slower constant rate with the value for $T_{b_2}$ varying from 90 to 155 d in the four subjects.

**TABLE II**

<table>
<thead>
<tr>
<th>RETENTION OF CAESIUM FOLLOWING A SINGLE EXPOSURE</th>
<th>OF Cs$^{137}$ EXPRESSED AS A TWO-TERM EXPONENTIAL EQUATION:</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Q = a_1 e^{-\lambda_1 t} + a_2 e^{-\lambda_2 t}$</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case 1</th>
<th>$a_1$</th>
<th>$\lambda_1$</th>
<th>$a_2$</th>
<th>$\lambda_2$</th>
<th>$T_{b_2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>17%</td>
<td>&gt; 0.7</td>
<td>83%</td>
<td>0.0077</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Case 2</td>
<td>12%</td>
<td>&gt; 0.7</td>
<td>88%</td>
<td>0.0045</td>
<td>155</td>
</tr>
<tr>
<td>Case 3</td>
<td>20%</td>
<td>&gt; 0.7</td>
<td>80%</td>
<td>0.0055</td>
<td>125</td>
</tr>
<tr>
<td>Case 4</td>
<td>15%</td>
<td>&gt; 0.7</td>
<td>85%</td>
<td>0.0064</td>
<td>108</td>
</tr>
</tbody>
</table>

$Q$ = percent Cs$^{137}$ activity retained in the body at time $t$.

$\lambda_1$ and $\lambda_2$ are the two rates of excretion expressed in days$^{-1}$.

$a_1$ and $a_2$ are the fractions of the initial body burden excreted at the respective rates $\lambda_1$ and $\lambda_2$.

$T_{b_2} = \frac{\ln 2}{\lambda_2}$ and is the biological half-life for the fraction $a_2$.

The total-body potassium was also measured by whole-body counter, measuring the 1.46-MeV gamma ray of potassium-40. The total-body $K$ and the 24-h urine $K$ are shown in Table III. An estimate of the biological half-life for potassium ($T_{bK}$) was calculated from the equation $T_{bK} = \frac{\text{Total body } K}{\text{Urine } K} \times 0.693 \\times 0.8$

**TABLE III**

<table>
<thead>
<tr>
<th>POTASSIUM DATA</th>
<th>Total body potassium (g/d)</th>
<th>Urine potassium (g/d)</th>
<th>$T_b$ of potassium (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>130</td>
<td>1.73</td>
<td>42</td>
</tr>
<tr>
<td>Case 2</td>
<td>165</td>
<td>2.25</td>
<td>41</td>
</tr>
<tr>
<td>Case 3</td>
<td>146</td>
<td>2.3</td>
<td>35</td>
</tr>
<tr>
<td>Case 4</td>
<td>187</td>
<td>2.6</td>
<td>40</td>
</tr>
</tbody>
</table>
EFFECT OF CHLOROTHIAZIDE ON CAESIUM-137 EXCRETION

× 0.8 assuming that 80% of daily K excretion is eliminated in the urine (8, 9). The values for $T_{bK}$ obtained from this calculation are shown in Table III. The $T_{bK}$ varied from 35 to 42 d. The values for $T_b$ of caesium were greater than the values for $T_b$ of potassium by a factor of 2.1 to 3.8. $T_b$ of caesium, which varied by a factor of 1.7 in the four male subjects of comparable age, showed no correlation to the total body potassium or to $T_b$ of potassium.

The percentage of caesium retention for the obese subject on low calorie diet and dried thyroid is shown in Fig. 3. It will be seen that thyroid therapy had no effect in reducing the body burden of caesium. The caesium retention at 100 d was 50% as compared to a range of 38 to 56% in the previous four studies. During this period the subject lost 74 lb. Although he did not appear to be clinically hyperthyroid at any time, the serum protein bound iodine increased from 5.5 μg% before the experiment to 12.5 μg% while on 12 gr of dried thyroid per day.

![Fig. 2](image-url)

**Fig. 2**

Effect of low calorie diet and dried thyroid therapy on whole-body retention of caesium-134 following a single oral dose (case 5).

CONCLUSIONS

Although chlorothiazide caused a sustained increase in potassium excretion of 1.5 to 2.0 times the control values, it had no significant effect on caesium excretion. These results support the evidence of other research workers (10, 11) that Cs and K are not utilized interchangeably in normal biological systems. Although the two elements are related, the body has an increased binding capacity for Cs than for K. Additional evidence to support this theory is a comparison of the $T_{bCs}$ and $T_{bK}$. In our study the long half-life $T_{bK}$ of caesium ranged from 90 to 155 d and $T_b$ of potassium from 35 to 42 d in the four subjects.

Also, the administration of dried thyroid in a dose sufficient to raise the serum protein bound iodine to 12.5 μg% had no effect on the rate of loss of caesium from the body. It is almost certain that this large dose of thyroid increased cellular metabolism with enhanced tissue breakdown. One would, therefore, expect increased excretion of the intracellular ions including Cs and K. On the other hand, the low calorie diet and rapid weight loss might have influenced the results.
In our experience an increase in diet K [11], the diuretic chlorothiazide and thyroid therapy are of no significant value in reducing the body burden of caesium.

REFERENCES

THE STUDY OF BINDING AND DISTRIBUTION OF CAESIUM-137 IN THE BLOOD

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Abstract — Résumé — Аннотация — Resumen

THE STUDY OF BINDING AND DISTRIBUTION OF CAESIUM-137 IN THE BLOOD. It is known that the resorption of caesium-137 in the body of man and other mammalians is about 100%, but the fate of resorbed caesium-137 in the blood is not fully resolved. Some authors mentioned a small accumulation of this substance in the erythrocytes without nucleus (mammalian) and more in the erythrocytes with nucleus (avian).

The purpose of this study is to try to establish the character of binding and distribution in the fractions of the blood for caesium-137. In vitro experiments were performed with caesium-137 sulphate in the blood of rats.

During these experiments the time and temperature of incubation was varied and it was established that:
1. the greatest part of radioactivity is in the plasma of the blood;
2. with increase of the time of incubation the radioactivity of the blood cells increases; and
3. with increase of the temperature the same effect is obtained.

These results are discussed in the light of the chemical and physical theories of binding.

The results of the study of the distribution of caesium-137 in the fractions of plasma and erythrocytes are mentioned.

ÉTUDE DE LA LIAISON ET DE LA DISTRIBUTION DE ÇÉSIUM 137 DANS LE SANG. On sait que la réorption de césium 137 dans l'organisme de l'homme et des autres mammifères est d'environ 100%, mais on ne sait pas encore exactement ce que devient césium 137 réorbé dans le sang. Certains auteurs mentionnent une petite accumulation de cette substance dans les érythrocytes sans noyaux (mammifères) et une plus grande dans les érythrocytes à noyaux (oiseaux).

Cette étude a pour but d'essayer de déterminer pour le césium 137 le caractère de la liaison et de la distribution dans les fractions du sang. Les auteurs ont fait des expériences in vitro sur du sulfate de césium 137 dans du sang de rat.

Au cours de ces expériences, ils ont fait varier le temps et la température de l'incubation et ont établi que:
1. la plus grande partie de la radioactivité se trouve dans le plasma sanguin,
2. la radioactivité des cellules du sang augmente avec le temps d'incubation,
3. la radioactivité des cellules du sang augmente aussi avec la température.

Les auteurs analysent ces résultats en se fondant sur les théories chimiques et physiques de la liaison, le mémoire mentionne les résultats de l'étude sur la distribution de césium 137 dans les fractions de plasma et les érythrocytes.

ИССЛЕДОВАНИЕ ПРОЦЕССА СВЯЗЫВАНИЯ И РАСПРЕДЕЛЕНИЯ ЦЕЗИЯ-137 В КРОВИ. Известно, что резорпция цезия-137 в организме человека и других млекопитающих равна почти 100%, но обмен резорциицованного цезия-137 в крови еще недостаточно изучен. Некоторые авторы упоминали о незначительной аккумуляции этого вещества в эритроцитах без ядер у млекопитающих и лучшей в эритроцитах с ядрами (у птиц).

Цель данного исследования заключается в попытке установить характер связывания и распределения цезия-137 во фракциях крови. Эксперименты in vitro были выполнены с сернокислым цезием-137 в крови крыс.

Во время этого эксперимента время и температура инкубации менялись, и было установлено следующее:
1) наибольшая часть радиоактивности содержится в плазме крови;
2) с увеличением срока инкубации возрастает радиоактивность кровяных телец;
3) с увеличением температуры достигается тот же эффект.

Эти результаты обсуждаются в соответствии с химическими и физическими теориями связывания.

Упоминаются результаты изучения распределения цезия-137 во фракциях плазмы и эритроцитах.
ESTUDIO DE LA FIJACIÓN Y DISTRIBUCIÓN DEL CESIO-137 EN LA SANGRE. Es sabido que el coeficiente de reabsorción del cesio-137 en el organismo del hombre y de otros mamíferos es del orden de 100%; pero no se conoce cabalmente el ciclo del cesio-137 reabsorbido en la sangre. Algunos autores señalan leves acumulaciones de esta sustancia en los eritrocitos anucleados (en los mamíferos) y aún más en los eritrocitos nucleados (en las aves).

Los autores se propusieron determinar el carácter de la fijación y la distribución del cesio-137 en las fracciones sanguíneas. Realizaron experimentos in vitro con sulfato de cesio-137 en la sangre de la rata.

Durante estos experimentos, fueron modificando el tiempo y la temperatura de incubación y comprobaron que:

1. la mayor parte de la radiactividad se concentra en el plasma sanguíneo,
2. Al prolongar la incubación, aumenta la radiactividad de los hematocitos,
3. El mismo efecto se obtiene al elevar la temperatura.

Los autores examinan estos resultados teniendo presentes las teorías químicas y físicas de la fijación.

Mencionan asimismo los resultados del estudio de la distribución del cesio 137 en las fracciones de plasma y los eritrocitos.

Isotopes of caesium are important by-products of nuclear fission. Two of them are long-lived isotopes: caesium-134, with a half-life of 2.3 yr, and caesium-137, with a half-life of about 29 yr. They reach the human organism through complicated ecological chains.

Retention of caesium-134 and of caesium-137 in some mammalian varieties, including man, approaches 100% [1, 2]. The literature on their distribution and excretion is abundant.

Adequate attention has not been paid to the behaviour of caesium in the blood. Caesium belongs to the same group of elements as potassium and rubidium. All three have similar physical and chemical characteristics. One would, therefore, expect similar physiological behaviour.

LOVE and BURCH [3] established that potassium and rubidium are more easily incorporated in human erythrocytes than caesium. They attribute this phenomenon to differences in the diameters of the atoms, and consider that potassium could be easily exchanged for rubidium, but poorly for caesium.

PERRI [4] found that caesium-134 penetrates erythrocytes with nuclei (avian), but not anuclear erythrocytes. On the other hand, rubidium-86 penetrates both kind of cells equally well.

It is of interest to study the distribution and binding of caesium in the various fractions of the blood. This kind of study is important both from the radiobiological/dose, damage of the tissue/and radiotoxicological/possible way of ecorporization/points of view.

We intend to study the behaviour of caesium-137 in rat blood and human blood, performing in vitro experiments followed by in vivo experiments with rats. Here are presented results of our first in vitro experiments with the blood of rats.

METHOD

The first series was directed to the dynamics of penetration of caesium-137 into erythrocytes. The experiment was performed with caesium-137 SO₄ in 0.1 N HNO₃. The pH was adjusted to 7.2 with NH₄OH. Further di-
Solution was performed with Ringer solution to obtain a specific activity of 0.1 μc/ml.

The blood was obtained by heart puncture of rats under narcosis. The anticoagulant "Liquemin" was used. One-ml samples of the blood were incubated with 5 μc of caesium-137 during periods of 30 min., 1, 2, 4 and 24 h at following temperatures: 0, 8, 20 and 37°C. In this way the influence of time and temperature on the rate of penetration of caesium-137 into the blood cells was studied.

Every result indicated in the following graphs represents the average value of 3 samples from 3 different animals.

After incubation, the radioactivity of the whole blood was measured. After centrifugation /30 min on 3000 r/min/ and each fraction of the blood was diluted to 1 ml with Ringer solution and its activity measured. Erythrocytes were washed subsequently 3 times with Ringer solution and the activity measured. All results were normalized to volumetric fractions obtained by haematocrite.

Measurements of gamma-activity were performed with a scintillation detector. The radioactivity of every blood sample was measured three times, and an average value obtained after statistical selection with the Chauvenet criterion. The relative error was ±5% and reliability 68% (K = 1).

RESULTS

The percentage of the activity of caesium-137 in the plasma, erythrocytes and in washed erythrocytes, relative to the activity of the whole blood,

| TABLE I |
| PERCENTAGE COUNTS OF CAESIUM-137 IN PLASMA RELATIVE TO BLOOD |

<table>
<thead>
<tr>
<th>Incubation time (d)</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0°C (%)</td>
</tr>
<tr>
<td>1</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>97.5</td>
</tr>
<tr>
<td>4</td>
<td>83.1</td>
</tr>
<tr>
<td>24</td>
<td>76.4</td>
</tr>
<tr>
<td>Mean values</td>
<td>82</td>
</tr>
</tbody>
</table>
COUNTS PER MINUTE WASHED ERYTHROCYTES PER MILLILITRE

<table>
<thead>
<tr>
<th>Incubation time (d)</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-5°C</td>
</tr>
<tr>
<td></td>
<td>(cpm/ml)</td>
</tr>
<tr>
<td>1</td>
<td>144 ± 9</td>
</tr>
<tr>
<td>1</td>
<td>154 ± 9</td>
</tr>
<tr>
<td>2</td>
<td>203 ± 3</td>
</tr>
<tr>
<td>4</td>
<td>228 ± 6</td>
</tr>
<tr>
<td>24</td>
<td>269 ± 3</td>
</tr>
<tr>
<td>Mean values</td>
<td>199.6</td>
</tr>
</tbody>
</table>

are presented in Tables I and II and Fig. 1 (a), (b), (c) and (d). Figure 1 shows data for one of the temperatures of incubation with time of incubation as a variable.

The data from washed erythrocytes are, perhaps, most illustrative of the penetration of caesium-137. Figure 2 shows the influence of the incubation time and temperature. Every line represents one incubation time with temperature as a variable.

The influence of these two factors on penetration of caesium-137 into the erythrocytes is synergistic. From Fig. 2 it could be concluded that at lower temperatures the time of incubation does not have a great influence. At higher temperatures the effect of incubation time is more accentuated.

The activity after incubation of 24 h at 37°C is lower than after 4 h at the same temperature. This could be explained by the fact that we did not add any nutrient to our solution. The vitality of erythrocytes after 24 h at 37°C is probably lower and some changes in the permeability of the membrane may have occurred.

The rate of penetration of caesium-137 into erythrocytes as a function of temperature could give some information about the type of process. Generally if uptake decreases with increasing temperature, the process could be ascribed to adsorption. This behaviour could be explained by increased kinetic energy of adsorbed molecules with increased temperature.

In this case the radioactivity of erythrocytes increased with the temperature and incubation time, indicating that some biochemical process may be involved. The binding rate of caesium-137 inside the erythrocytes might increase with temperature and time.

We are proceeding with these experiments in the hope of identifying the fractions in the erythrocytes and plasma to which caesium-137 is attached.
Activity of caesium-137 in plasma, erythrocytes and washed erythrocytes relative to activity of whole blood. Data for temperatures of incubation with time of incubation as variable.

Fig 1 (a), (b), (c) and (d)
Similar experiments will be performed with human blood. These results will be reported later.

**Fig. 2**

Influence of incubation time and temperature

**SUMMARY**

The kinetics of penetration of caesium-137 into erythrocytes was studied. From the results it could be concluded that:

1. The greater part of the activity is present in the plasma;
2. With increase of the incubation temperature, the activity of the blood cells increases and that of plasma decreases;
3. The increase of the incubation time has a similar effect;
4. The influence of temperature and time is synergistic; and
5. From these data it could be deduced that the process involved in penetration of caesium-137 into erythrocytes is of biochemical nature and not simple adsorption.

**REFERENCES**

CAESIUM-137 CHLORIDE RETENTION FOLLOWING ACCIDENTAL INGESTION

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Abstract — Résumé — Аннотация — Resumen

CAESIUM-137 CHLORIDE RETENTION FOLLOWING ACCIDENTAL INGESTION. Four men became contaminated with caesium-137 chloride due to leaks in a 100 c source. The source was believed to be completely leakproof, since the caesium chloride was contained in a welded stainless-steel capsule which was covered with an outer steel jacket of standard Oak Ridge design. Most of the contamination occurred while the men were cleaning the components of a pneumatic device used to move the source. The most heavily-contaminated individual placed his mouth over the end of a transport tube and attempted to blow some "dust" out of the tube. The other men handled various parts of the transport mechanism and wiped "dust" out of holes with their fingers. None of the men washed their hands before eating lunch. When radioactive contamination was discovered on the following day, immediate efforts were made to decontaminate the men. Arrangements for whole-body counts were also made and, on the fifth day following contamination, the men reported to the Radiation Exposure Evaluation laboratory. The body burdens on the fifth day ranged from 35 - 970 nc of caesium-137. During the next five to six days the burdens dropped rapidly and on the eleventh day ranged from 28 - 780 nc. After the eleventh day the body burdens of caesium-137 changed much more slowly. Whole-body counts made between the 11th and 160th day yielded biological half-lives of 76, 95 and 126 d for the three most heavily-contaminated individuals. During the period of rapid excretion all urine and faeces were collected and counted. These counts indicated a considerable superficial contamination prior to the eleventh day since only a portion of the removed caesium-137 was found in the urine and stool specimens. The body burdens of the four men are compared with normals of the same size, build, age and diet habits. A short discussion of normal burdens is included. A brief description of the counting system, data handling techniques and calibration procedures is also included.

RÉTENTION DE CHLORURE DE CÉSIIU137 APRÈS UNE INGESTION ACCIDENTELLE. Quatre ouvriers ont été contaminés par du chlorure de césium 137 à la suite d’une fuite dans une source de 100 c. La source était considérée comme parfaitement étanche, car le chlorure de césium était contenu dans une capsule en acier inoxydable soudée et recouverte d’une gaine extérieure en acier, d’un type couramment employé à Oak Ridge. La contamination s’est produite essentiellement pendant que les hommes nettoyaient les éléments d’un dispositif pneumatique servant à déplacer la source. L’ouvrier le plus atteint avait soufflé dans un tube servant au transport de la source pour enlever les <<poussières>>. Les autres avaient manipulé différemment les parties du mécanisme de transport et essuyé avec les doigts des <<poussières>> qui s’étaient déposées dans des trous. Aucun d’eux ne s’était lavé les mains avant d’aller déjeuner. La contamination radioactive fut découverte le lendemain et on s’est immédiatement efforcé de décontaminer les quatre hommes. On a pris également des dispositions pour leur faire subir un examen au moyen d’un anthropogammamètre, et le cinquième jour après la contamination, ils se sont présentés au Laboratoire d’évaluation des radioexpositions. Les charges corporelles étaient alors de 35 à 970 nc de césium-137. Durant les cinq ou six jours qui ont suivi cet examen, les charges corporelles ont diminué rapidement et le onzième jour elles étaient de 28 à 780 nc. Après le onzième jour, les charges corporelles de césium 137 ont diminué beaucoup plus lentement. Entre le onzième et le 160e jour, des dosages de l’activité du corps ont révélé des périodes biologiques de 75, 95 et 126 d chez les trois hommes les plus gravement contaminés. Durant la période d’élimination rapide, on a recueilli et examiné toutes les urines et toutes les matières fécales et dosé leur activité. Ces dosages ont révélé une contamination superficielle importante avant le onzième jour, car une fraction seulement du césium 137 éliminé se trouvait dans
les échantillons d'urine et de fèces; les charges corporelles, des quatre hommes ont été comparées à celles d'hommes non contaminés ayant la même taille, la même corpulence, le même âge et les mêmes habitudes alimentaires. Les charges corporelles normales font l'objet d'un bref examen. L'auteur fait également une description succincte de l'appareil de comptage, des méthodes employées pour le traitement des données et des procédés d'étalonnage.

ЗАДЕРЖКА ХЛОРИДА ЦЕЗИЯ-137 ПОСЛЕ СЛУЧАЙНОГО ПОПАДАНИЯ ЕГО В ОРГАНИЗМ. Четыре человека было заражены хлоридом цезия-137 из-за утечки в источнике мощностью 100 кюри. Предполагалось, что источник был полностью герметичен, так как хлорид цезия был помещен в капсулу из сваренной нержавеющей стали, заключенную во внешнюю стальную оболочку стандартной конструкции, разработанной в Окridge. Основное заражение произошло, когда эти люди чистили компоненты пневматического приспособления, которое использовалось для перемещения источника. Один рабочий, получивший серьезное поражение, взяв в рот конец соединительной трубы и попытался выдуть "пыль" из этой трубы. Остальные держали в руках различные части транспортного механизма и вычищали "пыль" из отверстий пальцами. Никто из четырех не вымыл рук перед едой. Когда на следующий день было обнаружено радиоактивное заражение, немедленно были приняты меры для дезактивации. Были также приняты меры для измерения радиоактивности всего организма, и на пятый день после поражения эти люди были направлены в Лабораторию по определению радиационного облучения. Содержание изотопа в организме на пятый день составляло от 35 до 970 ммккюри цезия-137. В течение последующих пяти-шести дней содержание изотопа быстро уменьшалось и на одиннадцатый день составляло 28—180 ммккюри. После одиннадцатого дня уровень активности цезия-137 в организме менялся гораздо медленнее. При измерении уровня радиоактивности всего организма, произведенного между одиннадцатым и 160-м днем, период полувыведения равнялся 76; 95 и 126 дн. у трех наиболее тяжело по-раженных людей. В период быстрого выделения собирались моча и кал и производилось измерение активности. Эти измерения указали на значительное поверхностное загрязнение до 11-го дня, поскольку только часть выведенного цезия-137 была обнаружена в пробах мочи и кала. Содержание изотопа в организме у 4-х человек сравнивалось с данными для здоровых людей такого же роста, веса и диетических привычек.

Включается краткое обсуждение вопроса о нормальном содержании изотопов в организме здоровых людей. Включается также краткое описание счетной системы, методов обработки данных и процедур калибровки.

RETENCIÓN DEL CLORURO DE CESIO-137 DESPUÉS DE UNA INGESTIÓN ACCIDENTAL. Las pérdidas de una fuente de cloruro de cesio-137, de 100 c, contaminaron a 4 trabajadores. Se suponía, antes del accidente, que la fuente era completamente hermética, ya que el cloruro de cesio estaba encerrado en una cápsula sellada de acero inoxidable, recubierta con una camba de acero del diseño adoptado normalmente en Oak Ridge. La contaminación mayor ocurrió mientras los hombres limpiaban las piezas de un dispositivo neumático utilizado para desplazar la fuente. El individuo más gravemente contaminado había aplicado la boca al extremo de un tubo de transporte y soplado para tratar de expulsar el "polvo" del mismo. Los otros habían tocado varias partes del mecanismo de transporte y limpiado el "polvo" de los agujeros con los dedos. Ninguno se había lavado las manos antes de comer. Al día siguiente, cuando se descubrió que habían sufrido la contaminación radiactiva, se procuró descontaminarlos inmediatamente. Asimismo, se dispuso lo necesario para efectuar una antropogammametria y al quinto día a contar de la contaminación, los hombres concursaron al Laboratorio de Evaluación de la Exposición a la Radiación. Las cargas corporales de cesio-137 determinadas en esa oportunidad variaron entre 36 y 970 nc. Durante los 5-6 d siguientes, las cargas disminuyeron rápidamente y al undécimo día estuvieron comprendidas entre 28 y 780 nc. Después del undécimo día, las cargas corporales de cesio-137 se redujeron con una lentitud mucho mayor. El recuento antropogammamétrico entre el 11º y el 160º día indicó períodos biológicos de 76, 95 y 126 d, respectivamente, para los tres individuos más gravemente contaminados. Durante el período de excreción rápida, se recogió y sometió a recuento toda la orina y las heces, los resultados de estas determinaciones indican que existía una contaminación superficial considerable antes del undécimo día, ya que en las muestras de orina y de heces sólo se encontró una porción del cesio-137 eliminado. En la memoria se comparan las cargas corporales de estos cuatro hombres con los valores normales para personas que tienen la misma altura, contextura física y edad y el mismo régimen alimenticio. Se realiza también un breve examen de las cargas normales. Asimismo, se describe someramente el sistema de recuento, las técnicas de elaboración de los datos y los procedimientos de calibración utilizados.
1. INTRODUCTION

The four cases of accidental ingestion of caesium-137 that are reported here resulted from a leak in a 100-c caesium-137 chloride source which was thought to be leak-proof. The CsCl was contained in a welded stainless steel capsule with an outer steel jacket of standard Oak Ridge design. The source was moved pneumatically from its shielded storage container to an exposed position for various shielding experiments. On the day of the accident, the source tended to stick in a pneumatic riser tube and had to be returned to its storage container while the transport system was dismantled and cleaned. The riser tube contained dust which was not suspected of radioactivity at the time of the cleaning operation. Monitoring on the following day disclosed radioactive contamination of the work area and the four men who worked with the source.

The four men involved in the accident will be identified by the letters A, B, C and D. The letters are in order of decreasing degree of contamination. The manner in which each individual ingested the radioactive material is as follows:

1. "A" held the riser tube to his mouth and attempted to blow the dust out of the tube. He also handled various parts of the transport mechanism and did not wash before eating.
2. "B" washed several components of the transport assembly but did not wash his own hands before eating.
3. "C" handled several parts of the assembly and did not wash before eating.
4. "D" handled tools which were used to dismantle the assembly. He also touched the outside of the riser tube and did not wash before eating.

2. EXPERIMENTAL PROCEDURES

2.1. Description of counting system

The body-burden measurements which are reported in this study were made in a low background counting room. The room is nine feet wide by ten feet deep by eight feet high and is shielded on all sides by eight inches of steel and one eighth of an inch of lead. The detector of this system is a four-inch-thick by eight-inch diameter thallium-activated sodium iodide crystal assembly. The subject is counted in a 90° chair with seat and back at 45° relative to the floor. The chair runs on tracks which are attached to the floor to insure reproducible geometry. The crystal axis passes through the apex at the bottom of the chair. The crystal face is 50 cm from this apex. A 512-channel pulse height analyser is used to sort and store the pulses from the detector. The multi-channel analyser is equipped with binary coded decimal (BCD) reader and punch accessories in addition to oscilloscope, typewriter and x-y plotter read-out modes.
2.2. Data format

A case history folder is maintained for all counting subjects. This folder contains the name, age, height, weight, sex, date of initial count, place of birth, address, occupation, dietary habits, history of exposure to radio-isotopes, medical history, results of all counts and any other information pertinent to the case. Each folder is assigned a case number.

A log entry is made for every count. This entry includes the count serial number, case number, date, time, name of subject, occupation of subject, amplifier gain, live counting time, gross count, net count rate (0.1 - 3.0) and any necessary remarks.

After each count, the contents of the memory of the analyser are transferred to binary coded decimal tape. This tape is identified by the count serial number in the log. If the tape represents the count of a person, the tape is filed by case number. Background, calibration and other tapes are filed by count serial number.

2.3. Calibration procedures

(a) Energy versus analyser channel number

Only half of the memory of the analyser is used to store pulses from the detector. The other half of the memory is, therefore, available for storage of reference information which can be transferred from the first half of the memory or read into the analyser by the BCD tape reader. A tape of the spectrum obtained from the original accurate calibration of the analyser against a mixed caesium-137 and cobalt-60 source is kept on file. The analyser is calibrated by comparing a current count of the same source with the reference tape. The comparison is accomplished by viewing the electronically overlapped spectra on an oscilloscope. This technique provides extremely consistent energy calibrations with a minimum of effort.

(b) Activity

A Remcal Phantom is used to calibrate the counting system in cases involving adults of near average size. This hollow plastic phantom is designed to approximate the size and shape of a 70 kg man. The interior of the phantom contains compartments which simulate the larger body organs. In general, the compartments of the phantom are loaded with assayed amounts of activity which correspond to the distribution in the subject under study. The distribution in the subject is determined by a whole-body scan. Since the distribution of caesium in the body is nearly uniform, all compartments in the phantom, excluding the organs, were loaded with a uniform aqueous solution of caesium-137 and KCl. The solution contained 140 g of potassium and the contents of a sealed vial source which contained slightly over one microcurie of caesium-137. The organs of the phantom were filled with distilled water. A caesium-137 band between 0.58 and 0.71 MeV was used for the activity calibrations and all body burden determinations. The calibration factor obtained from the Remcal Phantom was $1.24 \times 10^4$ net counts per minute per microcurie in the caesium-137 band. A review of the proce-
dures which were used in the assay of the caesium-137 indicated that most of the experimental errors would tend to produce an underestimate of caesium-137 activity. Therefore, the above calibration factor represents a maximum possible value.

We have found experimentally that a point source at the centre of a horizontal, water-filled, five-gallon, polyethylene bottle has approximately the same detection efficiency as a uniformly distributed activity when the point source is placed 30 cm from the face of our detector. A calibration with a 0.0565 µc caesium-137 standard source yielded a calibration factor of 1.065 X 10^4 net counts per minute per microcurie in the caesium-137 band.

Doctor Howard Andrews at the National Institutes of Health (NIH), Bethesda, Maryland, kindly consented to determine the caesium-137 burdens of two men who had been counted at our facility. The NIH group found caesium-137 body burdens of 23.7 and 18.1 nc in the two men. The corresponding net counts per minute in our caesium-137 band were 260 and 184 respectively. Calibration factors of 1.10 X 10^4 and 1.02 X 10^4 net counts per minute per microcurie in the caesium-137 band were obtained from these measurements.

It is believed that a calibration factor of 1.10 X 10^4 net counts per minute per microcurie in the caesium-137 band represents the best estimate of the sensitivity of our counting system to caesium-137 body burdens.

2.4. Data processing

(a) General procedures

Immediately after each count the contents of the memory of the analyser are displayed on the screen of an oscilloscope and any unusual feature is noted in the log. A record of the pulse height analysis is then punched on BCD tape for future reference. The analyser is used to sum the contents of all 255 channels (0.1 - 3.0 MeV) and the live counting time, gross count, gross rate and net rate are then recorded in the log. The contents of the channels under any photopeaks of interest are automatically summed and recorded. If a counting subject is suspected of being contaminated or has an abnormally high count rate, a previous count of the subject is read into, the analyser from the BCD tape file. When the subject does not have a tape on file, the tape of a person of the same size, build, age, dietary habits and geographical area is used. The old and new pulse height analyses are then compared by electronically overlapping them on an oscilloscope.

(b) Calculations of caesium-137 burdens

Since everyone now has a caesium-137 body burden which is superimposed on a variety of both naturally-occurring and artificially-produced radionuclides, the determination of small caesium-137 burdens is somewhat complicated. The most difficult problem in the calculation of a caesium-137 burden is the correction which must be made for contributions to the caesium-137 band by other nuclides in the body. A number of possible techniques are available for estimating the correction for other nuclides. Unfortunately, the most accurate methods are also excessively complicated
and time-consuming. Our estimate of the contribution to the caesium-137 band (0.58 - 0.71 MeV) by other nuclides is based on the assumption that the contribution per channel in the band is equal to the contribution per channel in an energy range between 0.83 and 1.01 MeV. A careful analysis of the count versus channel data of several normal individuals indicates that our assumption will produce an error which is negligible when compared with the variance of caesium-137 burdens. The following procedure was used to calculate all caesium-137 burdens:

1. The net count-rates in the caesium-137 and 0.83 to 1.01 MeV bands were calculated.

2. The net count-rate per channel in the 0.83 to 1.01 MeV band was computed and multiplied by the number of channels in the caesium-137 band. The result of this calculation represents the contribution to the caesium-137 band by other nuclides.

3. The contribution term was then subtracted from the net count rate in the caesium-137 band to obtain the count rate in the band due to caesium-137.

4. The count-rate due to caesium-137 was then multiplied by the calibration factor 1.10 × 10^4 cpm/µc in the caesium-137 band.

3. RESULTS

3.1. Accidentally-exposed individuals

The caesium-137 body burdens of the accidentally-exposed individuals are listed in Table I. The day of exposure is defined as day zero in Table I and in all future references to time. The caesium-137 burdens of the four men on the fifth day were approximately as follows: A - 1.09 µc; B - 0.786 µc; C - 0.206 µc; D - 0.0395 µc. The activity was observed to decrease rapidly during the next few days. Scans which were made with a flat field collimated 3 in × 3 in NaI detector showed that the hands of B, C and D were contaminated. Urine and stools were collected between the fifth and fifteenth days. The caesium-137 found in the excreta accounted for only a small portion of the decrease in activity between the fifth and eleventh days. Therefore, most of the loss of activity during this period was probably due to removal of superficial contamination. On the eleventh day the body burdens were as follows: A - 0.883 µc; B - 0.546 µc; C - 0.160 µc; D - 0.0316 µc. After the eleventh day the rate of decrease of whole-body activity changed much more slowly. The loss of caesium-137 after the eleventh day appeared to follow a simple exponential relationship out to the 163rd day when the study was terminated. The following biological half-lives were determined: A - 95 d; B - 76 d; C - 126 d. The half-lives have been corrected for the caesium-137 present in uncontaminated persons. The correction in each case was based on the average caesium-137 burden of ten selected individuals who were counted within one month of time zero and closely approximated the weight, height, body build and diet of the contaminated individuals.
TABLE 1

CAESIUM-137 BURDENS OF ACCIDENTALLY-EXPOSED INDIVIDUALS

<table>
<thead>
<tr>
<th>Day</th>
<th>Body burden (μC)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>0</td>
<td>---</td>
</tr>
<tr>
<td>5</td>
<td>1.09</td>
</tr>
<tr>
<td>6</td>
<td>1.02</td>
</tr>
<tr>
<td>7</td>
<td>1.01</td>
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<td>10</td>
<td>0.933</td>
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<tr>
<td>11</td>
<td>0.833</td>
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<td>13</td>
<td>0.838</td>
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<tr>
<td>14</td>
<td>0.838</td>
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<td>17</td>
<td>0.826</td>
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<tr>
<td>19</td>
<td>0.800</td>
</tr>
<tr>
<td>21</td>
<td>0.789</td>
</tr>
<tr>
<td>24</td>
<td>0.764</td>
</tr>
<tr>
<td>26</td>
<td>0.767</td>
</tr>
<tr>
<td>28</td>
<td>0.768</td>
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<tr>
<td>32</td>
<td>0.723</td>
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<td>33</td>
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<td>34</td>
<td>0.739</td>
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<td>35</td>
<td>0.737</td>
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<tr>
<td>38</td>
<td>0.699</td>
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<td>40</td>
<td>0.707</td>
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<td>42</td>
<td>0.677</td>
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<td>80</td>
<td>0.532</td>
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<tr>
<td>97</td>
<td>0.460</td>
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<tr>
<td>129</td>
<td>0.372</td>
</tr>
<tr>
<td>163</td>
<td>0.293</td>
</tr>
</tbody>
</table>

3.2: Normal caesium-137 burdens

During the past three years we have noted a marked increase in the caesium-137 burdens of normal individuals. The increase has not been uni-
TABLE II

CAESIUM-137 BURDENS OF NORMAL INDIVIDUALS

<table>
<thead>
<tr>
<th>Month</th>
<th>Year</th>
<th>Group size</th>
<th>Average (pc/kg)</th>
<th>Standard deviation (pc/kg)</th>
<th>Significance level of difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>September</td>
<td>1962</td>
<td>14</td>
<td>79.0</td>
<td>56.5</td>
<td></td>
</tr>
<tr>
<td>October</td>
<td>1962</td>
<td>11</td>
<td>85.3</td>
<td>20.6</td>
<td>0.1</td>
</tr>
<tr>
<td>November</td>
<td>1962</td>
<td>16</td>
<td>104.3</td>
<td>29.4</td>
<td></td>
</tr>
<tr>
<td>December</td>
<td>1962</td>
<td>(Insufficient cases available)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>January</td>
<td>1963</td>
<td>7</td>
<td>102.3</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td>February</td>
<td>1963</td>
<td>16</td>
<td>102.7</td>
<td>31.3</td>
<td></td>
</tr>
<tr>
<td>March</td>
<td>1963</td>
<td>22</td>
<td>103.7</td>
<td>18.4</td>
<td>0.01</td>
</tr>
<tr>
<td>April</td>
<td>1963</td>
<td>13</td>
<td>129.5</td>
<td>36.7</td>
<td></td>
</tr>
<tr>
<td>May</td>
<td>1963</td>
<td>17</td>
<td>143.1</td>
<td>31.2</td>
<td></td>
</tr>
<tr>
<td>June</td>
<td>1963</td>
<td>18</td>
<td>142.8</td>
<td>39.8</td>
<td>0.1</td>
</tr>
<tr>
<td>July</td>
<td>1963</td>
<td>20</td>
<td>168.8</td>
<td>50.5</td>
<td></td>
</tr>
<tr>
<td>August</td>
<td>1963</td>
<td>15</td>
<td>158.5</td>
<td>32.8</td>
<td></td>
</tr>
<tr>
<td>September</td>
<td>1963</td>
<td>22</td>
<td>146.41</td>
<td>43.2</td>
<td></td>
</tr>
</tbody>
</table>

* Using t-test for difference between two means.

form but has occurred in steps that are separated by periods of little change. Since normal changes in caesium-137 burden could affect the observed retention times of the accidental exposure cases, we decided to investigate normal burdens around the time of exposure. Counting data from young adult males who had no known abnormal contamination was grouped by month of count. The average caesium-137 burden and the standard deviation for each group are listed in Table II. The number of individuals in each group and the significance level of differences between monthly means are also included. All changes which appeared to be significant were subjected to a t-test for difference between two means. Differences significant at the 0.1 level were found between October and November, 1962 and between June and July, 1963. A difference significant at the 0.01 level was found between February and March, 1963.

4. DISCUSSION AND CONCLUSIONS

The average monthly caesium-137 burden from September 1962 through September 1963 of 191 normal adult male counting subjects was 122.2 pc/kg of body weight with an average standard deviation of 34.1 pc/kg. The relative standard deviation is, therefore, 27.8%, which is several times greater than the variation observed in potassium-40 burdens. This very large vari-
ance in caesium-137 burdens can be explained in terms of a pooling of the variances associated with intake, uptake and retention of caesium-137. We know that certain groups of Laplanders and Eskimos have exceptionally large caesium-137 burdens due to a uniform diet which contains relatively large amounts of caesium-137. We also know that certain foods, particularly milk, contain large amounts of caesium-137. Since there is little uniformity in the American diet, the consumption of foods which are rich in caesium-137 varies significantly among individuals. For example, the consumption of milk in our normal groups ranged from that included in cooked foods to over one litre per day. We do not have adequate data concerning the uptake of caesium contained in food, but we do know that there is a large variance in retention. The biological half-lives observed in the accidentally-contaminated individuals ranged from 76 d to 126 d. It should also be noted that the retention times were not a function of the level of contamination since the least contaminated case had the longest biological half-life.

DISCUSSION

E. OBERHAUSEN: With regard to the paper by D. Djurić et al. on the binding and distribution of Cs\textsuperscript{137} in the blood, we showed in a paper published about a year ago that Cs\textsuperscript{137} is transported actively into the cells in the same way as potassium. By measuring the influx and efflux of caesium and potassium we showed that the transportation rate for caesium is much less than that for potassium. We also showed that caesium and potassium are both transported by passive diffusion out of the cell, and that the rate for caesium is much lower than the rate for potassium; we found a ratio of caesium to potassium of 1 to 3 in the erythrocytes. This suggests the opposite of what we find for the whole body. I think that caesium penetration into and retention in the erythrocytes differs considerably from its behaviour with regard to the other body cells.

This might also explain the large differences, which Dr. Yamagata describes in his paper, between blood content and whole-body content, i.e. the speed of caesium penetration into the blood is very low and it therefore takes a long time for equilibrium to be established between the whole body and the erythrocytes.

A. KAUL: I would like to comment on the obvious discrepancies between our results, described in the paper by U. Nay et al. and those of other authors for the distribution of fall-out Cs\textsuperscript{137} in muscular tissue and compact bone.

Between 1960 and 1962 N. Yamagata (UN Document A/AC. 82/G./L.691; UN Document A/AC. 82/G./L. 396; Bull., Inst. Publ. Health 9 (1960) 72) and G. E. Harrison (Brit. J. Radiol. 36 (1963) 745) had observed a specific Cs\textsuperscript{137} activity in marrow-free bone one-half to one-third of that in muscular tissue. In some cases (rib bones) the measured specific activities even proved to be equal. Similar results had been observed for stable caesium. The authors estimated the Cs\textsuperscript{137} and Cs\textsuperscript{133} content of the skeleton to be about 6% of the total-body content.

In our cases, spring 1964, the corresponding Cs\textsuperscript{137} burden of the skeleton proved to be about 1% of the total body content. The specific Cs\textsuperscript{137} content
of the marrow-free femoral bone was 5 to 10% that of muscular tissue. We tried to explain these differences by the fact that we have today a kind of acute rather than chronic caesium poisoning from fall-out, resulting in a relatively high soft tissue burden and an unusually low skeleton burden due to the slow turnover of caesium in bone. This is a hypothesis we have advanced to explain the different observations mentioned above. We would be interested to know if anyone can give another explanation.

K. Lidén: The theory put forward by Dr. Kaul is interesting and should be studied further.

N. Yamagata: In this connection we can expect equilibrium between dietary Cs$^{137}$ and whole-body caesium probably this year or next year. I hope therefore to tabulate the Cs$^{137}$ in hard bone and in bone marrow during the next year or so.

K. McNeill: In Fig. 2 of the paper by G. Svensson, showing an apparent change in the biological half-life of caesium at childbirth, was the caesium administered at the time zero shown in the figure?

K. Lidén: No, it was administered chronically over a period ending well before time zero.

J. Rundo: Could a possible explanation of the change in biological half-life at parturition be that initially the observed turnover was a combination of the long turnover in the mother and a very short turnover in the baby, while after parturition the short-half-life in the baby was not contributing?

G. Bengtsson: In answer to Dr. Rundo I would like to mention that in one case we found a half-life of about 30 d after parturition.

R. D. Jordan: I would like to clear up, at least partially, the question about the ages of the subjects reported in our paper. The individuals with 76- and 95-d half-lives were between 23 and 25 yr old. The case with a 126-d half-life was 30 yr old. All subjects were males. The two with shorter half-lives were of average size and were lean. The man with the 126-d half-life was a very muscular negro of over-average size.

E. Oberhausen: With regard to the paper by Y. Naversten et al., I may say we have found very high Cs$^{137}$ concentrations in the kidneys of rats soon after injection. I think this is in very good agreement with the rapid elimination rate Dr. Naversten and Dr. Lidén found in humans immediately after injection or ingestion of Cs$^{137}$.

K. Lidén: I should like to thank Dr. Oberhausen for this interesting comment.

Could Dr. Hesp give us any information about the chemical nature of the radioactive caesium contaminant in the lungs of subject A described in the paper by R. Hesp? Can he explain the high faecal excretion in this case?

R. Hesp: The only information which I have about the nature of the contamination is that the intake followed a minor release of relatively volatile material. I cannot suggest any reason why the faecal excretion during the five days after intake was so high (Fig. 9), but I must emphasize that the faecal excretion was calculated from the relationship for body retention and urinary excretion, and that no direct faecal analyses were carried out.

It has been drawn to my notice by colleagues that the concentration of caesium in cartilage has been reported in the literature, and I wonder whether one of the factors contributing to the apparent concentration in the chest is caesium in tracheal cartilage.
R.A. DUDLEY: The use of Cs\textsuperscript{132} for studying caesium metabolism, and especially for calibrating whole-body counter measurements of Cs\textsuperscript{137}, has been mentioned several times. As many of you know, the International Atomic Energy Agency last year distributed Cs\textsuperscript{132} sources of calibrated activity on two occasions. It expects to make another such distribution in June of this year. The Cs\textsuperscript{132} gamma-ray spectrum is virtually identical with that of Cs\textsuperscript{137}. It is this fact, of course, which makes Cs\textsuperscript{132} so useful in calibrating for self-absorption of Cs\textsuperscript{137} gamma rays in the body.
CAESIUM-137 IN GROUPS OF POPULATIONS

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Abstract — Résumé — Аннотация — Resumen

CAESIUM-137 IN GROUPS OF POPULATIONS. This review is a synthesis of results obtained by authors who have submitted papers on caesium-137 burdens in population groups and was prepared at the request of the scientific secretariat of this Symposium.

LE CÉSIUM 137 DANS LES GROUPES DE POPULATION. Cette étude fait la synthèse des résultats obtenus par des auteurs qui ont présenté des mémoires sur la charge corporelle de césium 137 dans les groupes de population; elle a été établie à la demande du secrétariat scientifique du Colloque.

ЦЕЗИЙ-137 В ГРУППАХ ПОПУЛЯЦИЙ. Этот обзор представляет собой обобщение результатов, полученных авторами, которые представили доклады относительно содержания цезия-137 в группах популяций, и был подготовлен по просьбе научного секретариата симпозиума.

EL CESIO-137 EN GRUPOS DE POBLACIÓN. El presente estudio constituye una síntesis de los resultados obtenidos por autores que han presentado memorias sobre la carga corporal de cesio-137 en distintos grupos de población, y se ha preparado a petición de la Secretaría científica de este Simposio.

The Scientific Secretary of this Symposium has asked me to compare the Cs137 body burdens in various regions on the basis of the papers presented at this Symposium. I have tried to do so, although all the data are not readily comparable. Some of the authors report only total-body burdens, others Cs137 activities per kilogram body weight and still others Cs137 values per gram of potassium. When necessary I have recalculated the values per gram of potassium, using in the conversion as the potassium content for males 1.9 g, and for females 1.8 g per kilogram body weight. If the weight of the subjects was not reported I have used 70 kg. The curves thus obtained for "normal" populations are presented in Fig. 1. In four cases are reported the values for males, and in three cases the mean values for both sexes. Figure 2 presents the total-body values for Lapps and Eskimos (males) from regions where the reindeer and caribou meat consumption is the greatest.

The body burden of a group of the population depends mainly on three factors:

(a) the amount of fall-out in the region, which determines the Cs137 level of the locally-produced foodstuffs;
(b) the type of diet, a typical milk diet having a relatively high Cs137 content; and
(c) the average biological half-time of Cs137 in the population group in question. This again depends on the age of the subjects in the group measured. There also seem to be regional differences, the average half-time of the slow component of excretion being 60 to 70 d in Scandinavia and in other regions 105 to 140 d.

It is well known that the amount of fall-out is highest between the 40th and 50th northern latitudes. Within this zone it is rather similar around the globe. In Sweden and Finland, for instance, the amount of fall-out is
In spite of the fact that the groups are not quite comparable, the following conclusions can probably be drawn from Fig. 1. In the first place, body burdens in Japan are much lower than in the other regions. Japan is a typical rice diet country, the consumption of milk and dairy products being low. Another factor may be the considerable consumption of Pacific Ocean fish which still has an extremely low Cs\textsubscript{137} content.

The curves of the United States, Italy, Germany, and France (Nos. 1-4) run fairly parallel with each other but are below the curves of southern Finns.

<table>
<thead>
<tr>
<th>Curve No.</th>
<th>Location</th>
<th>Subjects/ measurement</th>
<th>Sex</th>
<th>Age limits (yr)</th>
<th>(mean)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Maryland, United States of America</td>
<td>7-22</td>
<td>male</td>
<td>adults</td>
<td></td>
<td>[2]</td>
</tr>
<tr>
<td>2</td>
<td>Bologna, Italy</td>
<td>13'</td>
<td>male</td>
<td>16-45</td>
<td></td>
<td>[3]</td>
</tr>
<tr>
<td>3</td>
<td>Saar, Fed. Rep. of Germany</td>
<td>100-400</td>
<td>both</td>
<td>22-70 (-40)</td>
<td></td>
<td>[4]</td>
</tr>
<tr>
<td>4</td>
<td>France</td>
<td>6-112</td>
<td>male</td>
<td>18-63 (~35)</td>
<td></td>
<td>[5]</td>
</tr>
<tr>
<td>5</td>
<td>Helsinki, Finland</td>
<td>11-49</td>
<td>both</td>
<td>24-46 (21)</td>
<td></td>
<td>[6]</td>
</tr>
<tr>
<td>6</td>
<td>Cumberland, United Kingdom</td>
<td>4-11</td>
<td>male</td>
<td>20-45</td>
<td></td>
<td>[7]</td>
</tr>
<tr>
<td>7</td>
<td>Japan</td>
<td>5</td>
<td>both</td>
<td>22-43 (28)</td>
<td></td>
<td>[8]</td>
</tr>
</tbody>
</table>
Cs\textsuperscript{137} IN GROUPS OF POPULATIONS

![Graph showing Cs\textsuperscript{137} total-body burdens of male Lapps and Eskimos](image)

<table>
<thead>
<tr>
<th>Curve No.</th>
<th>Location</th>
<th>Subjects/measurement</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lapps, Jokkmok, Sweden</td>
<td>20-35</td>
<td>male</td>
<td>20-65</td>
<td>[9]</td>
</tr>
<tr>
<td>2</td>
<td>Lapps, Inari, Finland</td>
<td>9-33</td>
<td>male</td>
<td>20-50</td>
<td>[10]</td>
</tr>
</tbody>
</table>

(No. 5) and Englishmen from West Cumberland (No. 6). Curve No. 3\* is based on a large number of subjects, namely, 15,000, and is therefore statistically quite significant.

The cause of the somewhat higher body values of the Finnish subjects is without doubt the Finnish diet. Finland has the highest milk consumption per capita in the world. The dietary intake of Cs\textsuperscript{137} for the particular groups of Finnish men and women measured was determined and was found to be 240 pc/d for women, 400 pc/d for men, corrected for food preparation losses and food left over. This gives a mean intake for both sexes of 320 pc/d per subject after July, 1963. This value is about twice as high as that reported by Huycke and Oberhausen\* for people in Germany, which is 175 pc/d, and

\* HUYCKE, E.J. and OBERHAUSEN, E. "Measurement of caesium-137 in the normal person", these Proceedings.
which was calculated from the increase of body burdens, assuming a biological half-time of 140 d. The higher Cs\textsubscript{137} intake by Finns is evidently partly compensated for by a shorter biological half-time. As we heard in the previous session, the biological half-time of these subjects was estimated to be about 62 d, this being based on the dietary intake of Cs\textsubscript{137} and the measured increase of body burdens after 10 July. If the half-time were longer, the body burdens ought to be higher than those actually measured, or the dietary intake of Cs\textsubscript{137} grossly over-estimated.

The average body burdens of male reindeer-breeding Lapps from Inari, Finland, Jokkmokk, Sweden and Alaskan Eskimos [1] from Anaktavuk Pass, are compared in Fig. 2. These values are about 40 times higher than those shown in Fig. 1, varying from 2000 to 7000 pc/g K. It is interesting to note that the two points of Alaskan Eskimos from the region of greatest caribou meat consumption lie exactly on the curve of the reindeer Lapps from Finland. The smaller seasonal variation in the body burden of the Swedish Lapps compared with Finnish Lapps is due to a better availability of refrigerators and a more regular meat consumption in Jokkmokk than in Inari.

Four of the authors whose body burden values are presented in Fig. 1 also give Cs\textsubscript{137} concentrations in milk in the same region. These results are illustrated in Fig. 3. The levels in the Saar and in Paris a year ago were about half of those in Helsinki and in another region of France, but after the increase the level in France seems to stay higher than the one in Helsinki. The sharp increase began in France in April but in Helsinki much later, at the beginning of July; this is in agreement with the differences in climate. The milk data illustrate qualitatively the changes in the dietary intake of Cs\textsubscript{137} but for a more detailed analysis of changes of body burdens the Cs\textsubscript{137} content of the total diet should be accurately known. Even in Finland milk represents only about half of the total Cs\textsubscript{137} intake; in most other countries definitely less. For the two groups of Finns meat was the second most important source of Cs\textsubscript{137}, 25% of the total intake, while cereals, fruits and vegetables both represented 10 to 15%. Both groups of Finnish subjects measured had a very low fish consumption value but there are groups of the population in Finland who eat plenty of fresh-water fish and to them the fish may be the most important source of Cs\textsubscript{137} at the present time. Last fall the fresh-water fish in Finland contained up to 15 nc Cs\textsubscript{137}/kg fresh weight while beef contained 1 nc and milk only 200 pc. On the other hand, in regions where, for example, canned meat, poultry or ocean fish are important components of the diet, the increase of the Cs\textsubscript{137} content of the total diet is certainly much slower than the increase of the Cs\textsubscript{137} level in milk. In the southern countries, where plenty of green vegetables are grown and consumed even during winter months, they may be a very important source of Cs\textsubscript{137} during periods of a rapid increase in fallout. A rather illustrative whole-body spectrum in this respect is given in Fig. 2 of the paper by Pellerin, Moroni and Remy.\textsuperscript{*} The spectrum contains marked peaks of Ba\textsubscript{140} + La\textsubscript{140}, Zr\textsubscript{90} + Nb\textsubscript{95}, and Ru\textsubscript{103}. Of about one hundred persons measured in the Loire valley about half gave this type of spectra, and all had supposedly gone through a shower before measurement. We have recorded

\textsuperscript{*} PELLERIN, P., MORONI, J. P. et REMY, M. L., "Premiers résultats d'une étude systématique des contaminations internes consécutives aux retombées radioactives", these Proceedings.
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To summarize, I should like to recommend that all authors reporting Cs\textsuperscript{137} body burdens in groups of populations, would also report the number, age, weight, height, sex and potassium content of the subjects measured, as well as the standard deviation of the values reported, and that they would preferably calculate the values separately for both sexes and for certain age groups, in order that the results could be compared more accurately. I should also like to recommend that the body burdens of Cs\textsuperscript{137} should preferably be reported per kilogram body weight for three reasons:

1. The goal of whole-body counting studies is the determination of the radiation dose, not the Cs\textsuperscript{137} body content per se.

2. Body weight can be determined much more accurately and also more rapidly than the potassium content and with the present levels Cs\textsuperscript{137} also gives better counting statistics than potassium. Therefore, it is not feasible to base the caesium results on the less accurate potassium values.

3. The potassium content of man is a variable ranging from 1.5 to 2.5 g/kg body weight in different groups of populations. For in-

\begin{table}
\centering
\begin{tabular}{|c|c|c|}
\hline
Curve No. & Location & Reference \\
\hline
2 & Helsinki, Finland & [6] \\
3 & Paris, France & [12] \\
4 & France & [5] \\
\hline
\end{tabular}
\caption{Cs\textsuperscript{137} in milk (pc/l)}
\end{table}
stance, adult male Lapps contain on an average \(2.4 \pm 0.1\) g K/kg body weight, while city people contain 1.9 g.

It is recommended, however, that, if possible, the Cs\(^{137}\) values per gram of potassium be recorded as well since our knowledge on the inter-relationship of caesium and potassium metabolism in man is still limited.

With the above prerequisites fulfilled, the results of Cs\(^{137}\) body burdens in different groups of populations can be accurately compared, but not yet interpreted. For this purpose the amount of fall-out in the region, the composition of the diet of the population, the Cs\(^{137}\) content of the main dietary items, and/or the biological half-time of Cs\(^{137}\) in the population should be known. In addition to milk at least meat, fresh-water fish, cereals, fruits and vegetables should also be analysed.

With the rapidly growing number of whole-body counting results, better comparability and better information on the Cs\(^{137}\) intake will soon make possible a more accurate evaluation of the role of this genetically perhaps most important radioactive contaminant with regard to the radiation burden of mankind.

REFERENCES

[12] JEANMARE, L., "Note au sujet de deux types de contamination humaine par le \(^{137}\)Cs", these Proceedings.
FIRST RESULTS OF A SYSTEMATIC STUDY OF INTERNAL CONTAMINATION DUE TO FALL-OUT. Since September 1961 the Service Central de Protection contre les Rayonnements Ionisants (Central Radiological Protection Service) has carried out more than 500 examinations with whole-body counter. Numerous individuals were examined at intervals of three or six months, and, in many cases, the urine was radioanalysed during these examinations. A systematic examination of the urine sample by gamma-spectrometry generally preceded the radiochemical study. A comparative study of the results of the various examinations yielded a certain amount of data on internal contamination from radioactive fall-out. 

1. Caesium-137 was the only artificial radioisotope which was consistently detected by the whole-body counter. The changes occurring in the mean body burden could be observed throughout the entire period of the examinations. The normal variation in body burden depending on sex could also be observed.

2. For the low-level activities usually found, it was possible to study the ratio of the urinary excretion of caesium-137 to the total body burden of this isotope. The results seemed to confirm the ratios found by other authors for higher levels of contamination.

3. The presence of fission products with moderate half-lives, particularly zirconium-95 and niobium-95, and, to a lesser extent, ruthenium-103, could be observed as a transitory phenomenon at certain times.

4. A knowledge of the total body burden of strontium-90 would be extremely useful, but, in the case of low-level activities, this isotope cannot be measured directly with the whole-body counter. The authors therefore tried to estimate the order of magnitude of this burden in two different ways. A first approximation was arrived at by studying caesium-137, since the percentages of strontium-90 and caesium-137 in radioactive fall-out evolve along very similar lines. Then, the urinary excretion of strontium-90 in a number of individuals was measured in an attempt to deduce the body burden of, at least, to infer a maximum value for the isotope.

PREMIERS RÉSULTATS D'UNE ÉTUDE SYSTÉMATIQUE DES CONTAMINATIONS INTERNES CONSÉCUTIVES AUX RETOMBÉES RADIOACTIVES. Depuis septembre 1961, plus de 500 examens à l'anthropogamma-mètre ont été pratiqués par le Service central de protection contre les rayonnements ionisants. De nombreuses personnes sont soumises à des examens trimestriels ou semestriels et des radioanalyses urinaires sont fréquemment associées à ces examens; une exploration systématique de l'échappement d'urine par spectrométrie γ précède en général l'étude radiochimique. L'étude comparative des résultats de ces divers examens permet de dégager certains faits relatifs à la contamination interne due aux retombées radioactives:

1. Le césium 137 est le seul radioisotope artificiel constamment retrouvé par examen à l'anthropogamma-mètre. L'évolution de la charge totale moyenne peut être suivie durant toute la période de temps couverte par l'ensemble des examens. On peut constater accessoirement la variation, par ailleurs classique, de la charge radioactive selon le sexe.

2. Les auteurs ont pu étudier, pour les faibles activités habituellement rencontrées, le rapport entre l'excrétion urinaire du césium-137 et la charge corporelle totale de ce radioisotope. Les résultats paraissent confirmer les relations établies d'autres auteurs pour des contaminations plus importantes.

3. En ce qui concerne les produits de fission à vies moyennes, les zirconium 95 + niobium 95 en particulier (et plus accessoirement le ruthénium 103), leur présence a pu être constatée de façon transitoire à certaines périodes.
4. La connaissance de la charge corporelle totale de strontium 90 serait une donnée capitale, mais la mesure directe de ce radioisotope à l'anthropogammamètre ne peut être réalisée pour de faibles activités. Les auteurs ont donc tenté d'évaluer l'ordre de grandeur de cette charge par deux voies différentes: tout d'abord, l'étude du césium 137, dont le pourcentage dans les retomées radioactives évolue de façon sensiblement parallèle à celui du strontium 90, permet de réaliser une première approximation. Ils ont de plus mesuré l'excrétion urinaire du strontium 90 chez un certain nombre de sujets, pour tenter d'en déduire la charge totale ou, tout au moins, une limite supérieure pour ce radioisotope.

ПЕРВЫЕ РЕЗУЛЬТАТЫ СИСТЕМАТИЧЕСКОГО ИССЛЕДОВАНИЯ ВНУТРЕННЕГО ЗАРАЖЕНИЯ ОТ ВЫПАДЕНИЯ РАДИОАКТИВНЫХ ОСАДКОВ. С сентября 1961 года Центральная служба защиты от ионизирующих излучений провела свыше 500 обследований с помощью счетчика для измерения радиоактивности всего организма человека. Многие лица обследовались в течение трех или шести месяцев. При этих обследованиях часто использовался радиоанализ мочи, в целом радиохимическому исследованию предшествовало систематическое изучение образцов мочи с помощью гамма-спектрометрии. Сравнительное изучение результатов этих различных исследований позволяет выявить некоторые факты, относящиеся к внутреннему заражению в результате радиоактивных выпадений:

1. Цезий-137 является единственным искусственным радиоизотопом, который постоянно обнаруживался при обследованиях с помощью счетчика для измерения радиоактивности всего организма. Эволюция общего среднего содержания изотопа может быть прослежена в течение всего периода времени, отведенного на все исследования. Дополнительно можно отметить изменения, и, в том же обычный, радиоактивного заражения в зависимости от пола.

2. Что касается обычно встречающихся слабых активностей, то нам удалось изучить связь между выделением с мочой цезия-137 и общим содержанием этого изотопа в организме. Результаты, кажется, подтверждают установленные другими авторами соотношения для более серьезных заражений.

3. Что касается продуктов деления со средним периодом полуразпада, в частности циркония-95 и ниобия-95 (и иногда рутения-103), то их присутствие может обнаружено в определенные периоды.

4. Знание общего содержания стронция-90 в организме человека было бы очень полезным, однако при небольших активностях прямо определить этот изотоп с помощью счетчика для измерения радиоактивности невозможно. Поэтому авторы стремились определить величину заражения двумя различными путями. Предварительная оценка была сделана путем изучения цезия-137, поскольку процентное содержание стронция-90 и цезия-137 в радиоактивных выпадениях находится примерно на одном и том же уровне. Затем были замерены выделения стронция-90 с мочой у некоторых обследованных, с целью вывести отсюда общее содержание или по крайней мере установить высший предел для этого изотопа.

RESULTADOS INICIALES DE UN ESTUDIO SISTEMÁTICO DE LAS CONTAMINACIONES INTERNAS DE BIDAS A LA PRECIPITACIÓN RADIOACTIVA. En septiembre de 1961, el Servicio Central de Protección contra las Radiaciones Ionizantes del Ministerio de Salud Pública de Francia empezó a efectuar exámenes antropogammétricos, hasta la fecha se comprobaron más de 500 exámenes de esa índole. Se somete a exámenes trimestrales o semestrales a un gran número de personas y, frecuentemente, junto con dichos exámenes se efectúan radianalisis de orina; en general, antes del estudio radioquímico, se procede a una exploración sistemática de la muestra de orina por espectrometría gamma. El estudio comparado de los resultados de estos diversos exámenes ha permitido deducir ciertos hechos relativos a la contaminación interna debida a la precipitación radiactiva:

1. El cesio-137 es el único radioisótopo artificial cuya presencia queda constantemente demostrada por el examen antropogammamétrico. La variación del valor medio de la carga corporal total puede ser observada durante todo el periodo que abarca el conjunto de los exámenes. Además, es posible comprobar la variación, por otra parte bien conocida, de la carga radiactiva en función del sexo.

2. los autores han podido estudiar la relación existente entre la excreción urinaria de cesio-137 y la carga total de este isótopo en el organismo, en correspondencia con las demás actividades que se registran habitualmente. Los resultados parecen confirmar las relaciones establecidas por otros autores para grados de contaminación más elevados.

3. En lo que se refiere a los productos de fisión de periodo medio, en particular el cinc-95 + niobio-95 (y en menor grado el tantalo-103), se pudo comprobar que aparecen transitoriamente en determinados períodos.

4. El conocimiento de la carga total de estroncio-90 en el organismo humano tendría notable importancia, pero la medición directa de este isótopo mediante el antropogammametro no puede realizarse cuando se trata
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de bajas actividades. Por lo tanto, los autores procuraron evaluar el orden de magnitud de dicha carga por
dos métodos diferentes: primeramente, el estudio del cesio-137, cuya concentración en las precipitaciones
radioactivas sigue una evolución sensiblemente paralela al del estroncio-90, permite hallar una primera aproxi-
mación. Además, los autores midieron la excreción urinaria de estroncio-90 en cierto número de sujetos, con
el propósito de deducir así la carga total o, por lo menos, encontrar un límite superior para la concentración
de dicho isótopo.

Dans le cadre de la surveillance systématique de la contamination
interne des individus, le Service central de protection contre les rayonne-
ments ionisants a contrôlé plus de 500 personnes depuis 1961.

Le présent travail a pour objet l'étude de la contamination par les re-
tombées radioactives, à partir des données qui ont pu être recueillies lors
de ces contrôles.

I. LES SUJETS ÉTUDIÉS

Ils sont de trois origines différentes: les éléments de la population,
les travailleurs de certaines industries conventionnelles, les travailleurs
des industries nucléaires.

Cependant, du fait des conditions sanitaires excellentes dans lesquelles
ils sont placés, les travailleurs des industries nucléaires que nous avons
contrôlés n'ont qu'exceptionnellement présenté, jusqu'à présent, des con-
taminations radioactives spécifiques de leur activité professionnelle. Il
s'ensuit qu'en général nous avons été amenés, sur le plan de l'évolution de
leur contamination interne par les retombées radioactives, à les classer
a posteriori avec les individus de la population.

Par contre, certains travailleurs des industries classiques se trouvent
parfois, du fait de leur profession, nettement plus exposés aux retombées.
Tel est le cas des spécialistes procédant à la révision des moteurs à réaction
des avions intercontinentaux volant à haute altitude. Les aubes et tuyères de
ces réacteurs, qui brassent des flux d'air de l'ordre de 100 m³/s, accumu-
ulent en effet les poussières radioactives en quantités suffisantes pour
que l'on puisse, après un vol transcontinental, mesurer des débits de doses
de l'ordre de plusieurs mr/h à leur contact [1].

II. LES TECHNIQUES DE SURVEILLANCE

A. Les voies de contamination

Le processus de contamination interne le plus courant est lié à la con-
tamination de la chaîne alimentaire, et la surveillance de cette dernière
nous a fourni des éléments essentiels, notamment [2] en ce qui concerne
le strontium 90 et le césium 137 dans le lait (fig.1). En particulier, la
détermination du césium 137 dans le lait de l'alimentation est effectuée,
après élimination éventuelle de l'iode par passage sur résine anionique,
par dessication et calcination, les cendres étant comptées au spectromètre
gamma dans un cristal à puits.
Dans le cas particulier des travailleurs de l'industrie aéronautique, nous avons complété ces éléments par le contrôle de l'inhalation et de l'ingestion accidentelle, par examen de prélèvements atmosphériques, de frottis de surfaces, et des vêtements de travail.

B. La surveillance des individus

La surveillance a porté sur la spectrométrie humaine totale, et sur la radioanalyse des urines.

a) Spectrométrie gamma totale

Nos compteurs humains comportent des enceintes d'acier non radioactif de 20 cm d'épaisseur moyenne, et des cristaux de 20 cm de diamètre et 10 cm de haut (avec conducteurs de lumière de 8 cm en iodure de sodium non activé) donnant, pour le pic de 662 keV du césium 137, une résolution de 10% dans les conditions de la mesure sur l'homme. Les spectromètres, à 512 canaux transistorisés, comportent un aiguilleur permettant d'enregistrer simultanément les données de 4 détecteurs, ainsi que les accessoires nécessaires au dépouillement des spectres complexes. Les étalonnages en sont effectués, pour différents produits de fission, à l'aide de fantômes constitués d'éléments cylindriques en polyéthylène.

b) Radioanalyses

La détermination du strontium 90 est effectuée selon la méthode classique [3] par précipitations nitriques nécessaires pour éliminer le calcium, le baryum et le radium. Le strontium séparé est conservé pendant 15 j en présence d'yttrium entraîneur. On sépare alors l'yttrium par précipitation oxalatique, et ce précipité est compté sous compteur automatique à faible
mouvement propre (inférieur à 0.5 cpm). D'autre part, la mesure de l'activité du césium 137 est effectuée parallèlement par spectrométrie gamma. Les étalonnages de ces différents dosages ont été conduits à partir de solutions étalons en provenance d'Amersham, par la méthode pondérale de l'AEC [3].

III. LES RÉSULTATS

a) Produits de fission à vies courtes et moyennes

Dans les semaines qui suivent immédiatement les tests nucléaires dans l'atmosphère, de minimes quantités d'iode 131 ont pu être détectées sur les spectres obtenus au compteur humain total, mais il s'agit de quantités de l'ordre du seuil de détection, et ce phénomène a été très transitoire, comme on pouvait s'y attendre.

Dés traces de baryum 140 – lanthane 140 ont été trouvées au mois de mars 1962 (fig. 2); mais ici encore, il s'agit de quantités minimes, à la limite de la détection.

La contamination par le zirconium 95 – niobium 95 (fig. 2) est relativement plus importante en 1962 et 1963: sur un ensemble d'une centaine de personnes examinées en mars 1962, plus de la moitié présentent les pics du zirconium 95 – niobium 95, à des activités comprises entre quelques milliers et une dizaine de milliers de pc; on note également la présence, à des taux moindres, de ruthénium 103.

Il est intéressant de remarquer que ces mesures ont été effectuées dans une même localité, à deux cent cinquante kilomètres de Paris environ.
la même date, les mesures effectuées dans la région parisienne présentent beaucoup plus rarement des activités décelables de ces isotopes; la raison de cette dissemblance pourrait être due à la consommation de produits maraîchers locaux, constituant un circuit plus court dans la chaîne alimentaire.

Ces mêmes produits de fission à vies moyennes sont retrouvés sur les travailleurs en contact avec des réacteurs d'avions. Ici, les activités sont nettement plus importantes, quoique plusieurs centaines de fois inférieures aux quantités maximums admissibles pour ces divers éléments (fig. 3).

Il faut noter que les personnes ayant présenté de telles activités lors d'un examen ont présenté des spectres sensiblement normaux aux examens suivants, espacés de six mois, et que leurs charges en césium 137 ainsi que les excréptions de strontium 90 sont normales: il s'agit donc de contaminations minimes, transitoires.

b) Étude de la charge en césium 137

La figure 4 montre l'évolution de cette charge pour l'un des sujets. On constate que la charge s'est maintenue à une valeur voisine de 10 000 pc en 1961 et 1962 et a augmenté en 1963 de plus de 100%; on atteint actuellement une valeur de l'ordre de 26 000 pc.
Figure 4
Evolution dans le temps de la charge individuelle en césium 137.

a) Représentation graphique.
b) Spectre gamma individuel.

--- Spectre effectué le 21/10/1963.
----- Spectre effectué le 31/7/1963.
Cette augmentation de la charge totale en césium 137 est bien illustrée par la figure 5 qui représente la variation dans le temps de la moyenne mensuelle de toutes les mesures (tableau I); nous avons porté sur cette figure, non la charge en césium 137, mais le rapport entre cette charge et la quantité de potassium naturel (colonnes 4 et 5 du tableau I). L'augmentation de ce rapport est nette à partir de 1963; elle semble ensuite assez régulière, atteignant l'ordre de 200 pc par gramme de potassium naturel au début de 1964. (La figure 1 présente, à titre de comparaison, les valeurs moyennes mensuelles de l'activité du césium 137 dans le lait, et l'on constate un certain parallélisme entre les deux graphiques.) Lorsqu'on considère non plus le rapport $^{137}\text{Cs}/K$ naturel mais la charge en césium 137 seule (figure 6,
### TABLEAU I
**MOYENNES MENSUELLES DES CHARGES INDIVIDUELLES EN CÉSIUM 137**

<table>
<thead>
<tr>
<th>Mois</th>
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<th>Femmes (pc)</th>
<th>Hommes (pc/g de K)</th>
<th>Femmes (pc/g de K)</th>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
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### TABLEAU II

RÉSULTATS COMPARATIFS DES RADIOANALYSES URINAIRES ET DES EXAMENS AU COMPTEUR HUMAIN TOTAL

<table>
<thead>
<tr>
<th>No</th>
<th>Date</th>
<th>Volume (ml)</th>
<th>Potassium naturel</th>
<th>Câsium 137</th>
<th>Strontium 90</th>
<th>Potassium naturel</th>
<th>Câsium 137</th>
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<td></td>
<td></td>
<td>(g/24 h)</td>
<td>(g/l)</td>
<td>(pc/24 h)</td>
<td>(g/l)</td>
<td>(pc/24 h)</td>
<td>(g/l)</td>
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* Examens témoins
tableau I, colonnes 2 et 3), on retrouve la disparité bien connue [4] entre les charges moyennes chez l'homme et chez la femme, liée à la moindre musculature de cette dernière. La présentation précédente (fig. 5) comporte l'avantage d'effacer cette disparité.

Pour ces charges de l'ordre de quelques dizaines de milliers de pc, l'excrétion quotidienne du césium 137 est de l'ordre de 100 à 200 pc, soit environ 0,6 pc d'excrétion pour 100 pc de charge. Différents auteurs ont déduit ces valeurs de mesures faites à partir de contaminations plus importantes [5, 6] et nos résultats (tableau II, colonnes 6 et 14) paraissent les confirmer pour les faibles activités.

c) Étude de la charge en strontium 90

La détermination de la charge en strontium 90 est, on le sait, particulièrement importante à cause de la longue période résultante de cet élément, associée à sa localisation osseuse. De nombreux auteurs [7, 8, 9, 10], ont tenté une évaluation de cette charge et de son évolution dans le temps, soit à partir de modèles du métabolisme du strontium, soit par l'analyse directe d'échantillons osseux, soit même par contamination volontaire par le strontium 85 [11]. Mais la charge des individus en strontium 90 peut encore être indirectement évaluée par l'étude par spectrométrie γ totale de la charge en césium 137, dont l'activité, dans les retombées suffisamment anciennes, est dans un rapport constant avec l'activité du strontium 90 [12, 13]. On retrouve, dans les différents éléments de l'alimentation, des rapports différents, mais, là encore, constants [2]. L'étude de la charge en césium 137 permet donc d'évaluer a posteriori non seulement des activités ingérées de cet isotope, mais aussi les activités du strontium 90 qui leur étaient associées lors de cette ingestion. (La brièveté relative de la période-résultante du césium 137 conduit à renouveler fréquemment les examens.) D'autre part, la mesure directe du strontium 90 dans les urines permet de confirmer certains éléments de cette évaluation [11, 14, 15].

C'est par cette méthode que nous surveillons notamment, depuis février 1962, un groupe de travailleurs en contact avec les moteurs à réaction contaminés à haute altitude. A part d'exceptionnelles et transitoires contaminations, d'ailleurs à des niveaux très bas, par des produits de fission à vies moyennes (fig. 3), les charges en césium 137 relevées tous les six mois étaient strictement comparables à celles enregistrées chez des personnes non exposées professionnellement; les examens d'urine pratiqués récemment chez ces travailleurs montrent (tableau II, colonnes 6 à 8) des excréptions comparables à celles relevées sur les examens témoins. Nous pouvons donc en conclure que leur charge en strontium 90 est actuellement du même ordre que celle du reste de la population.

L'élimination urinaire du strontium 90 (tableau II, colonnes 9 et 10) donne des résultats du même ordre de grandeur que ceux des témoins et de la littérature [10]: 5 pc/l.

Finalement, si l'on admet les valeurs données par la littérature [7, 9], les mesures indirectes que nous avons pratiquées permettent de conclure que, vraisemblablement, la charge globale en strontium 90 des sujets que nous avons contrôlés s'établit actuellement à un niveau comparable à celui de la population dans son ensemble: un à quelques picocuries par gramme
de calcium, soit un à quelques milliers de picocuries pour la totalité du squelette, valeurs très éloignées de la charge maximum admissible de l’ICRP (0,2 μc pour la population) [15].

IV. CONCLUSIONS:

a) La contamination de la population par les produits de fission à vies longues des retombées se situe actuellement à un niveau très faible. Les charges individuelles moyennes actuelles sont de l’ordre de 20 000 pc pour le cézium 137, et de l’ordre du millier de picocuries pour le strontium 90.

b) La détermination de la charge individuelle en cézium 137, associée à la détermination de l’élimination urinaire du strontium 90, est une méthode possible d’évaluation de la charge en strontium 90.

c) Enfin, nos résultats semblent confirmer, pour les très faibles contaminations liées aux retombées, les rapports des excrétions urinaires aux charges individuelles, déjà connues pour les contaminations importantes.

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MEASUREMENT OF CAESIUM-137 IN THE NORMAL PERSON

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LANDSTUHL/PFALZ, FEDERAL REPUBLIC OF GERMANY

Abstract — Résumé — Аннотация — Resumen

MEASUREMENT OF CAESIUM-137 IN THE NORMAL PERSON. During the period June 1959 to October 1963 the Landstuhl whole-body counter has measured the caesium-137 content of more than 15,000 normal persons. The monthly averages of these measurements indicate a steady increase in the caesium-137 content since June 1962. This increase has become more rapid during the period June 1963 to October 1963.

A further evaluation of the monthly averages since June 1962 indicates a mean biologic half-life of caesium-137 of 140 d for persons older than 22 yr. A comparison of the mean caesium-137 content of persons between 8 and 17 yr of age with those older than 22 appears to indicate that the biologic half-life of caesium-137 is shorter in the younger people. This is in agreement with earlier data from this counter concerning measurements of caesium-137 content between June 1959 and December 1960; these data showed a lower caesium-137 content in children than in adults.

Another evaluation of recent data from this unit concerns the standard deviation (sigma) of the caesium-137 content in a large population. From this population the sigma of measured caesium/g body potassium values is 33%. This is more than twice the sigma of the body potassium content of this same population. By comparing a group of persons who have undergone several repeat assays over an extended period of time with the monthly means of the total population measured, it has been found that the large sigma of caesium-137 content cannot be caused solely by the varying diets of the population measured.

DOSAGE DU CÉSIUM 137 CHEZ UN SUJET NORMAL. Au cours de la période allant de juin 1959 à octobre 1963, l'anthropogammamètre de Landstuhl a été utilisé pour mesurer la charge corporelle de césium 137 chez plus de 15,000 sujets normaux. D'après les moyennes mensuelles de ces mesures, la charge corporelle de césium 137 a augmenté constamment depuis juin 1962. Cette augmentation s'est accélérée au cours de la période allant de juin 1963 à octobre 1963.

Une analyse plus poussée des moyennes mensuelles depuis juin 1962 met en évidence pour le césium 137 une période biologique moyenne de 140 d chez les sujets âgés de plus de 22 a. En comparant la charge corporelle moyenne de césium 137 chez ces sujets âgés et celle qui est présente chez les sujets âgés de 8 à 17 a, on constate que la période biologique du césium 137 est plus courte chez les sujets plus jeunes. Cette observation concorde avec les données obtenues précédemment au moyen du même appareil entre juin 1959 et décembre 1960; ces données indiquaient aussi que la charge corporelle de césium 137 était plus faible chez l'enfant que chez l'adulte.

Une autre analyse des données obtenues récemment porte sur l'écart type (sigma) de la charge corporelle en césium 137 pour une population nombreuse. Dans cette population, l'écart type des valeurs mesurées de la quantité de césium par gramme de potassium de l'organisme est de 33%, soit plus de deux fois l'écart type de la charge corporelle de potassium pour la même population. En comparant les résultats obtenus pour un groupe de sujets qui ont été soumis à plusieurs dosages au cours d'une période prolongée aux moyennes mensuelles pour l'ensemble de la population sur laquelle les mesures ont été effectuées, les auteurs ont constaté que l'importance de l'écart type de la charge corporelle de césium 137 ne peut pas être uniquement due à la diversité des régimes alimentaires de la population sur laquelle les mesures ont été effectuées.


Дальнейшая оценка среднемесячных величин с июня 1962 года указывает на то, что средний период полувыведения цезия-137 составляет 140 дней для лиц старше 22 лет. Срав-
The potassium and caesium-137 content of a large number of normal persons has been determined since June 1959.[1]. These measurements have been accomplished through the use of a 2-pi whole-body liquid scintillation counter developed by ANDERSON and collaborators at Los Alamos [2]. By the end of December 1963, a total of 15,000 persons had been measured. Figure 1 shows the mean values, in picocuries caesium-137 per gram body potassium, measured during the period from July 1959 through December 1963. Only the results of those persons older than 22 yr of age at the time of measurement were considered in the calculation of the monthly means.

An earlier study showed the ratio of caesium-137 per gram of body potassium in children and young people to be different from that in adults [3]. This conclusion was confirmed by the results of measurements made from July 1959 to December 1960, a period when the caesium content in humans remained relatively stable, and a subsequent period starting in April 1960 when a decrease having a half-life of 12 months was evident.

It was shown by these measurements that the ratio of caesium-137 per gram of potassium is smallest in children. This ratio then increases up to 22 yr of age; and in adults the ratio appears independent of age. If it is assumed that there is no difference in the ratio of caesium-137 per gram of potassium in the foods consumed by children and adults, the results of these measurements can only be interpreted to show that the ratio of the biological
half-lives of caesium and potassium is proportionately smaller in children than it is in adults.

The possibility of verifying these earlier results occurred with the rise in the caesium-137 content of humans since approximately June 1962; the rise has become especially significant since June 1963 to the present time.

In the case of the smaller ratio of caesium-137 per gram of potassium in children at a time of equilibrium, the decrease of the mean caesium content was caused by a shorter biological half-life of caesium. This difference may not appear significantly at the very beginning of a period of increasing caesium content, but will become apparent only after some time has passed. In an ideal situation in which the two biological half-lives, adults to children, have a ratio of 2:1, and the caesium content of the foodstuffs remains constant over a relatively long period of time, the difference of the caesium content between children and adults would be as shown in Fig. 2. The calculation of the curve for adults is based on a biological half-life of 140 d for caesium-137, and for children a biological half-life of 70 d is assumed.

The measured increase of the caesium content in the general population certainly has not occurred under the ideal conditions which are assumed in Fig. 2.

The data as shown in Table I verified that the measured caesium level of milk from the Saarland area of Western Germany during the period of June 1962 through June 1963 remained relatively constant. Forty picocuries caesium-137 per litre of whole milk was the mean value used as a standard during this period. From July to September 1963, the caesium content of milk rose by a factor of approximately three to 125 pc/l.

If we assume that the caesium content in the milk is representative of the aggregate intake of caesium by man, then it is possible to make a more
E.J. HUYCKE and E. OBERHAUSEN

Fig. 2
Difference in caesium content between children and adults

TABLE I

CAESIUM-137 (pc/1) IN MILK FROM THE SAAR

<table>
<thead>
<tr>
<th></th>
<th>1962 Individual measurements</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>September</td>
<td>54 36 37</td>
</tr>
<tr>
<td></td>
<td>October</td>
<td>49 40 30 36</td>
</tr>
<tr>
<td></td>
<td>November</td>
<td>21 30 49 31 30 30 31 30 28</td>
</tr>
<tr>
<td></td>
<td>December</td>
<td>31 32 26 31 37 33 33</td>
</tr>
<tr>
<td></td>
<td>1963</td>
<td></td>
</tr>
<tr>
<td></td>
<td>January</td>
<td>28 45 46 33 43</td>
</tr>
<tr>
<td></td>
<td>February</td>
<td>59 42 35 41</td>
</tr>
<tr>
<td></td>
<td>March</td>
<td>27 42 39 46 41</td>
</tr>
<tr>
<td></td>
<td>April</td>
<td>29 35</td>
</tr>
<tr>
<td></td>
<td>May</td>
<td>36 32 56 56</td>
</tr>
<tr>
<td></td>
<td>June</td>
<td>74 78</td>
</tr>
<tr>
<td></td>
<td>July</td>
<td>130 102 161 148</td>
</tr>
<tr>
<td></td>
<td>August</td>
<td>109 84 123 134 138</td>
</tr>
<tr>
<td></td>
<td>September</td>
<td>152 130 124 114</td>
</tr>
<tr>
<td></td>
<td>October</td>
<td>104 90</td>
</tr>
</tbody>
</table>

accurate analysis of the curve of the average caesium content of the total population. This analysis of the curve was made with the assumption that a constant caesium intake took place between June 1962 and June 1963. In July 1963 there was a noticeable jump to a much higher caesium content in the milk, and for the next several months the value remained fairly constant.
A comparison of the measured values of the caesium content rise between June 1962 and June 1963, with the calculated curve taking into consideration the initial content of the person of 30 pc/g K, indicates good agreement as may be seen from Fig. 3. In the calculated curve a biological half-life of 140 d for caesium-137 was assumed. The agreement is not so good if a biological half-life of 120 d is assumed. From this ascending curve it can be further calculated that the average mean caesium intake remained at 53 pc caesium-137 per day during this time. There is also fair agreement between the calculated and the measured curves of the ascent between July and September 1963. By calculation this results in a daily caesium-137 intake of 175 pc. The amount of the daily caesium intake calculated from the curve is in the same ratio as measured in the milk. The daily intake is equivalent to the caesium-137 content in 1.5 l milk.

When a comparison of the measured average caesium content of the population over 22 yr of age is made with that of young people, it will result in data as presented in Table II.

The data in this Table demonstrate that the difference between adults and children is relatively narrow at the beginning of the rise of caesium content, and then the difference becomes greater as the ascent of the caesium content continues.

A further interpretation concerns those persons who have had their caesium levels assayed several times. On the average there was a time interval of slightly more than one year between the first and second measurements for the same person. These replicate measurements at various time intervals can be used to obtain a more accurate picture of the reason for the existing variation of the caesium-137 content of the human. Earlier measurements have shown that in humans older than 22 yr of age, the content
TABLE II

<table>
<thead>
<tr>
<th>Total population measured over 22 yr of age</th>
<th>Population measured, 8-17 yr of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average body burden, Cs$^{137}$, June-Aug. 1962</td>
<td>43 pc/g K</td>
</tr>
<tr>
<td>Average body burden, Cs$^{137}$, April-June 1963</td>
<td>93 pc/g K</td>
</tr>
</tbody>
</table>

of caesium-137/g of body potassium is independent of age. A statistical analysis of the caesium measurements taken in monthly groups reveals a standard deviation of approximately 33% for the individual measurements. In contrast to this, the standard deviation for potassium content was a maximum of 15% for persons in a given age group. It was first assumed that the standard deviation for caesium content, greater by a factor of two than the deviation of the potassium measurements, was caused by the various diets of the persons being measured.

In analysing the data of the persons with repeat assays the following method was used. A ratio for each such assay was constructed by comparing the person's individual caesium value with the mean value for all the persons
measured that month. Ratios were similarly established for the subsequent measurements. This gives relative values of the caesium content of the individual compared with the total population. Then the first such ratio of an individual person was divided by his second ratio to establish an expression of relative caesium content at the different times the person was measured. This comparison of the relative values of the first and second measurements gives an indication of how much the caesium content of the individual has changed between the two measurements with relation to the total population. The distribution of these numerical expressions of relative caesium content is shown in Fig. 4. To allow symmetry of this histogram, ratios greater than 1.0 were expressed as reciprocals and displayed on the right half of the histogram. The standard deviation of the data of this histogram is 20%.

Although this statistical procedure results in the comparison of the measurement evaluation of the single individuals, there is still a standard deviation of 20% considering the ratios of first and subsequent measurements.

According to this result it does not seem likely that the large standard deviation of the caesium-137 content in humans is caused only by the various diets of the different people who have been measured.

REFERENCES

IN VIVO MEASUREMENTS OF Cs\(^{137}\) WITH A HUMAN BODY COUNTER

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Abstract — Résumé — Аннотация — Resumen

IN VIVO MEASUREMENTS OF CAESIUM-137 WITH A HUMAN BODY COUNTER. Data are given of the first measurements of human body radioactivity made in Italy with the whole-body counter built by the authors in 1962.

The counter shielding is made of iron bricks 16 cm thick. Measurements inside are 270 cm \(\times\) 200 cm \(\times\) 200 cm. The detectors are a 9 in \(\times\) 4 in NaI (Tl) crystal and three 30 cm \(\times\) 20 cm \(\times\) 17 cm plastic scintillators which can be used separately, in parallel, or in anticoincidence and in coincidence with the crystal.

The counter has been used for determining the behaviour of the caesium-137 body content from fall-out in the whole population and for estimating the caesium-137 retention in a subject accidentally contaminated.

The first measurements of caesium-137 body content from fall-out were taken on 13 subjects in December 1962 and continued regularly at three-month intervals. A gradual increase was noted in the average caesium-137 content of the population throughout the whole of 1963 up to the value of 124 pc/g of potassium in September.

In a case of accidental contamination from caesium-137 (about two years before the counter was built) measurements were made in order to determine both the effective half-life of the long-term component and the initial intake of the radionuclide.
Счетчик использовался для определения всего населения поведения в организме цезия-137, поглощенного в результате выпадения радиоактивных осадков и для оценки за­держки цезия-137 у лиц, подвергшихся аварийному заражению.

Первые измерения содержания цезия-137 в результате выпадения радиоактивных осадков были проведены у 13 человек в декабре 1962 года. Затем они проводились регулярно с трехмесячными интервалами. Отмечалось постепенное увеличение среднего со­держания Цезия-137 у населения на протяжении 1963 года до величины 124 мккюри на грамм калия в сентябре месяце.

В случае аварийного заражения Цезия-137 (за два года до создания счетчика) прово­дился измерения с целью определения как эффективного периода полувыведения долгосрочного компонента, так и первоначального поглощения радиоэлемента.

MEDIDAS DE CESIO-137 IN VIVO CON UN ANTROPOGAMMÁMETRO. Se dan datos de las primeras medidas de radiactividad en el cuerpo humano realizadas en Italia con el antropogammedmetro construido por los autores en 1962.

El blindaje del contador se compone de bloques de hierro de 16 cm de espesor y sus dimensiones interiores son de 270 cm x 200 cm x 200 cm. Los detectores consisten en un cristal de NaI(Tl) de 9 x 4 pulgadas y 3 centelleadores de plástico que pueden utilizarse separadamente, en paralelo o bien en anticoincidencia y la coincidencia con el cristal.

El contador se ha utilizado para determinar el comportamiento del cesio-137 procedente de precipitaciones radiactivas en el organismo desde el punto de vista de la población como conjunto, y para-evaluar la retención del cesio-137 en un individuo accidentalmente contaminado.

Las primeras medidas fueron realizadas en 13 individuos en diciembre de 1962 y continuaron efectuándose regularmente con intervalos de tres meses. Se observó un aumento gradual del contenido medio de cesio-137 en la población a lo largo de todo el año 1963 hasta llegar a un valor de 124 pc/g de potasio en el mes de septiembre.

En un caso de contaminación accidental con cesio-137 (ocurrido dos años antes de que el contador fuese construido), se han efectuado medidas a fin de determinar el período efectivo del componente de larga duración y evaluar asimismo la cantidad de radioelemento inicialmente absorbida.

1. INTRODUCTION

In 1962 the United Nations, on the bases of data obtained by investigators of various countries, calculated the total dose commitment to the gonads, the cells lining bone surfaces, and to the bone marrow [1], due to fallout from nuclear explosions up to the end of 1961. The partial contribution to the total dose given by the most important radionuclides was also estimated. These data are shown in Table I.

As one can see, Cs137 gives a significant contribution to the fall-out dose to various organs. It contributes 26% to the gonads, 15% to the cells lining surfaces, and 21% to the bone marrow.

The evaluation of the body burden of this radioelement is therefore interesting.

For this reason direct measurements of the Cs137 body burdens have also been regularly performed in Italy since December 1962, as soon as the whole-body counter built by the "Reparto di Bologna del Gruppo di Dosi­metria e Standardizzazione del Laboratorio di Dosimetria e Protezione Sanitaria del C.N.E.N." [2, 3], was operating.

Moreover, in view of the importance of radiocaesium as a contaminant and the scarcity of data on its metabolism in man, a subject accidentally contaminated was examined to determine some parameters which describe biological retention.
TABLE I

DOSE COMMITMENT FROM NUCLEAR TESTING

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Source of radiation</th>
<th>Dose commitment for period of testing</th>
<th>1954-1961 (total mrem)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gomads</td>
<td>External Cs(^{137})</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Internal Cs(^{137})</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>C(^{14})</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>Cells lining bone surfaces</td>
<td>External Cs(^{137})</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Sr(^{90})</td>
<td></td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>Internal Cs(^{137})</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>C(^{14})</td>
<td></td>
<td>116</td>
</tr>
<tr>
<td></td>
<td>Sr(^{89})</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>External Cs(^{137})</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Sr(^{90})</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Internal Cs(^{137})</td>
<td></td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>C(^{14})</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Sr(^{89})</td>
<td></td>
<td>0.08</td>
</tr>
</tbody>
</table>

2. DESCRIPTION OF THE COUNTER

A total view of the apparatus is given in Fig. 1. It essentially consists of a shielding, a detector and a data processing unit.

2.1. Shielding

The shielding room was built up with 16-cm-thick iron bricks and plates which reduce the background by a factor of about 50.
The inner dimensions of the room (length 2.70 m, width 2.10 m, and height 2.10 m) are such that a wide choice of detector-to-subject geometric arrangements is allowed.

A 3-mm-thick interior lead lining was added for reducing substantially the background radiations with energies below 500 keV [4]. The overall weight of the shielding is about 60 t (metric). The place where the steel room is located is air-conditioned and air-filtered.

2.2. Detector

The detector used is a 9-in-diam x 4-in-high NaI(Tl) cylindrical monocrystal (supplied by the Harshaw Chemical Company) viewed by four 3-in Dumont 6363 photomultipliers selected for low radioactive impurities.
The resolving power of the unit for Cs$^{137}$ and K$^{40}$, measured in vivo, is 10.7% and 8% respectively (full width at half maximum).

The crystal holder allows vertical and horizontal displacements and rotations around a horizontal axis perpendicular to the vertical plane where translations are possible.

The geometric arrangement used for the measurements is the tilting chair technique. Such an arrangement has been adopted because it gives a response independent of individual body build for those isotopes which distribute throughout the whole body, like Sc and K [5]. This arrangement is shown in Fig. 2 where one can see the interior of the shielded room.
The patient sits on a chair with the back and the seat perpendicular to each other. The chair is tilted backwards 45° degrees from the horizontal. The crystal face is tilted 10° from the horizontal towards the back of the chair; the centre of the crystal is on the bisector of the back-seat angle. If the distance between the centre of the crystal and the back of the chair is larger than 40 cm, the measurement of K⁴⁰ and Cs¹³⁷ body burdens is independent of individual body build.

2.3. Electronics

The electronic chain is of a conventional type for scintillation counters. The pulse height analysis is performed by a 512-channel Laben analyser, equipped with a typewriter, a tape recorder and a spectrum stripper.

3. COUNTER CALIBRATION FOR Cs¹³⁷

A typical spectrum of a normal human is shown in Fig. 3. The photopeaks of Cs¹³⁷ from fallout and K⁴⁰, the natural radioisotope of potassium, are evident.

![Typical spectrum of a human](image)

Usually the Cs¹³⁷ content of the body is expressed in terms of the potassium present in the whole body.

As Cs and K have the same distribution pattern throughout the body, their ratio is easily calculated as follows: known quantities of Cs¹³⁷ and K are diluted in a distilled water-filled phantom large enough to simulate a human body as far as self-absorption and self-scattering is concerned. The ratio M between Cs¹³⁷ and K⁴⁰ photopeak areas is determined by taking a gamma spectrum of the phantom. Performing an identical spectrum of the subject the respective ratio N is calculated.
MEASUREMENTS $^{137}$Cs WITH BODY COUNTER

Then, the human body $^{137}$Cs contamination expressed in pc/g potassium, is given by the equation:

$$R = \frac{NP}{M}$$

where $P$ stands for the ratio between $^{137}$Cs, in pc, and $K$, in grams, dissolved in the phantom.

For the determination of the absolute value of the $^{137}$Cs content, in pc, one must know the $K$ content, in grams, of the body, that is, one must calibrate the counter also for potassium. This may be done with the aid of an internal tracer. Potassium-42 is a very suitable isotope for this biological tracing, because it has a relatively short half-life (12.5 h), an energy of 1.52 MeV very close to the $^{40}$K energy (1.46 MeV) and it reaches equilibrium with natural potassium in a reasonable time (12 h).

For the calibration, 5 $\mu$C of $^{42}$K is orally administered to the patient and an equal amount is diluted in two litres of distilled water. A second solution is also prepared diluting a known quantity of natural potassium in the same volume of water.

The $K$ content, in grams, of the body is given by the expression:

$$K = A\left(\frac{B}{C}\right)\left(\frac{D}{E}\right)$$

where:

- $A$ = in vivo $^{40}$K photopeak counting rate in cps
- $B$ = mass, in grams, of natural potassium contained in the solution
- $C$ = $^{40}$K photopeak counting rate of the solution in cps
- $D$ = $^{42}$K photopeak counting rate of the solution in cps
- $E$ = in vivo $^{42}$K photopeak counting rate in cps (corrected for excretion and K contribution) measured 14 h after the administration.

The factor $(B/C)(D/E)$ is constant, because, by this method, the measurement of the body $K$ content is independent of the patient's body build. Therefore this factor has been determined on a few subjects with different body builds [3] (from a minimum of 44 kg and 1.59 m to 78 kg and 1.75 m) administering $^{42}$K to them. The average value was found to be 73.5 with a standard error of 1.2.

Considering the error affecting this factor and that $A$ amounts to about 1.5 cps, plus background contribution of 1.3 cps measurements of the $K$ body burden can be made with a standard deviation of about $\pm 4\%$ in 30-min counting time. With the same counting time, errors of about $\pm 7\%$ are obtained in the determination of the $^{137}$Cs content.

4. IN VIVO MEASUREMENTS OF THE $^{137}$Cs AMOUNT FROM FALL-OUT

Evaluations of the $^{137}$Cs content of the human body due to fall-out began in December 1962, as soon as the whole-body counter was in operation for the purpose of estimating the dose commitment to the Italian population.

Periodical determinations have been made at three-month intervals on a group of 13 normal male subjects from 16 up to 43 yr old (height: maximum 1.79 m, minimum 1.65 m; weight: maximum 88.8 kg, minimum 53.8 kg).
TABLE II

AVERAGE Cs\(^{137}\) CONTENT IN A CONTROL GROUP
OF SUBJECTS RESIDENT IN BOLOGNA

<table>
<thead>
<tr>
<th>Date</th>
<th>Average Cs(^{137}) content (m(\mu)c)</th>
<th>Cs(^{137})/g K (pc)</th>
<th>Radiation dose-rates to the whole body (mrem/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 1962</td>
<td>7.0</td>
<td>56</td>
<td>1.23</td>
</tr>
<tr>
<td>March 1963</td>
<td>10.6</td>
<td>74</td>
<td>1.65</td>
</tr>
<tr>
<td>June 1963</td>
<td>11.7</td>
<td>81</td>
<td>1.84</td>
</tr>
<tr>
<td>September 1963</td>
<td>17.7</td>
<td>124</td>
<td>2.76</td>
</tr>
<tr>
<td>December 1963</td>
<td>21.3</td>
<td>150</td>
<td>3.34</td>
</tr>
</tbody>
</table>

In Table II are given the average values of the measurements performed to date.

In the first columns experimental data of the measurements are listed, in the last one the calculated dose commitment to the whole body in mrem/yr, based on the ICRP criteria [6] is given. The same data are also plotted in diagram A of Fig. 4. In abscissa there is the time and in ordinate the in vivo Cs\(^{137}\) concentration in pc/g potassium. In Fig. 4 the behaviour of the Cs\(^{137}\) body burdens calculated by other authors is also given. Diagram B has been obtained by RUNDO at Harwell [7], C by MILLER at Argonne [8] and D by ANDERSON at Los Alamos [9].

Fig. 4

Caesium-137 concentrations obtained by various authors since 1956
The last three diagrams show an increase of the Cs$^{137}$ body burden up to 1959-1960, then a decrease follows which goes on through the first months of 1962 (due to a dilatory period in nuclear testing at that time).

The determinations made in Italy are subsequent to those of the other authors and show a progressive increase of the in vivo Cs$^{137}$ concentration. Such increase may be ascribed to the accumulation of the radionuclide in diet and, therefore, in humans, due to nuclear explosions in 1961 and 1962. The increase has been almost continuous throughout the whole of 1963. The Cs$^{137}$ concentration rose from 56 pc/g potassium in December 1962 (very close to that obtained by Rundo at Harwell during the same period [10]) up to 150 pc/g potassium in December 1963. Such high concentrations had never been reached before the new series of nuclear tests in 1961. The maximum values registered in 1959 and 1960 by Rundo, Miller and Anderson were found to be 63, 65 and 92 pc/g potassium, respectively.

With the measurements here performed it was possible to evaluate the average dose commitment to the whole body in the subjects examined during 1963. This dose was calculated to be 2.1 mrem, about twice as much as the average dose/yr estimated by other authors from 1954 up to 1962.

5. LONG-TERM RETENTION OF Cs$^{137}$ BY MAN

The biological retention of Cs$^{137}$ may be expressed as the sum of two exponentials. The first exponential corresponds to the short half-time component, and the second one to the long-term component of retention. In a case of accidental contamination it was possible to determine the biological retention of the radionuclide. The contamination dates from December 15, 1960. But in our case, it has been impossible to determine the short-term component because the first measurement was performed 838 d after the

<table>
<thead>
<tr>
<th>Date</th>
<th>Interval after contamination (d)</th>
<th>Cs$^{137}$ content (µC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 1, 1963</td>
<td>837</td>
<td>1.47</td>
</tr>
<tr>
<td>July 2, 1963</td>
<td>929</td>
<td>1.15</td>
</tr>
<tr>
<td>July 12, 1963</td>
<td>939</td>
<td>1.12</td>
</tr>
<tr>
<td>Sept. 5, 1963</td>
<td>994</td>
<td>0.73</td>
</tr>
<tr>
<td>Oct. 29, 1963</td>
<td>1048</td>
<td>0.64</td>
</tr>
</tbody>
</table>
exposure. We were therefore forced to limit our investigation to the evaluation of the effective half-time of the long-term component.

The importance of determining such a value was pointed out by the remarkable disagreement between data found in the literature on this subject.

The disagreement is simply due to different individual biological behaviour; in fact even among persons of the same experimental group wide differences were noted. For instance, in two individuals contaminated with Cs\textsuperscript{137}, MILLER and STEINGRABER [11] found that the effective half-times of the long-term component were 92.5 and 157 d respectively.

In Table III data are given of the five measurements performed on the patient during the period 1 April - 30 October, 1963 for the purpose of estimating the effective half-time of the long-term component of retention. Dates and time intervals since the presumed exposure are given in the first columns; in the last one the Cs\textsuperscript{137} body burdens in \( \mu \text{c} \) are reported. The same data are also plotted in Fig. 5, where the abscissae represent days from exposure and the ordinates the body content of Cs\textsuperscript{137} in \( \mu \text{c} \); the reported errors are equal to three times the standard deviation.

\[ \text{Fig. 5} \]

Whole-body retention of Cs\textsuperscript{137} by a normal adult male subject

Considering that a considerable time has elapsed since the exposure, the analytical expression of retention may be written as follows:

\[ A = A_0 e^{-0.693 (t/T)} . \]

According to this function the best fit for our experimental points gives 165 d for the effective half-time \( T \) of the long-term component and 52.2 \( \mu \text{c} \) for the initial amount \( A_0 \) of such component.

Evidently even the knowledge of all the parameters of this function is not enough to calculate the exact dose commitment to the body from internal exposure. As a matter of fact one must also know the behaviour of the short-
lived component of retention. However, STEWART [12] and RICHMOND[13], who could study the behaviour of the radioelement in the body since the very beginning, established that the contribution of such a component to the total dose is negligible. According to Stewart the short-lived component represents 6% of the total intake and its effective half-time is 4.9 d. According to Richmond this component would amount to 13% of the total intake, but the respective half-time would be 1.39 d. It follows that the dose commitment from the short-time component of retention is less than 0.2% of the total dose.

Neglecting the contribution of such component and, using the parameters previously calculated and referring them to the subject's body weight (58.2 kg), we have been able to estimate the total dose commitment to the whole body from Cs\textsuperscript{137} intake, based on the ICRP criteria [6]. Such dose was found to be 6.4 rem.

The dose to the whole body during the first year after exposure amounted to 5 rem, which is the maximum permissible value for occupational exposure.

6. SUMMARY

Data are given of the measurements made in Italy with the whole-body counter built by the authors in 1962.

The total-body counter has been used for determining the behaviour of the Cs\textsuperscript{137} body content from fall-out in the whole population and for estimating the Cs\textsuperscript{137} retention in a subject accidentally contaminated.

The first measurements of Cs\textsuperscript{137} body content from fall-out were taken on 13 subjects in December 1962 and continued regularly at three-month intervals. A gradual increase was noted in the average Cs\textsuperscript{137} content throughout the whole of 1963 up to the value of 150 pc/g of potassium in December.

In a case of accidental contamination from Cs\textsuperscript{137} (about two years before the counter was built), measurements were made in order to determine the effective half-life of the long-term component, which was found to be 165 d.

REFERENCES


THE TIME ANALYSIS AND FREQUENCY DISTRIBUTION OF CAESIUM-137 FALL-OUT IN MUSCLE SAMPLES

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Abstract — Résumé — Аннотация — Resumen

THE TIME ANALYSIS AND FREQUENCY DISTRIBUTION OF CAESIUM-137 FALL-OUT IN MUSCLE SAMPLES. For low concentrations of artificial radioactivity in the body, detrimental effect will be most likely in that fraction of the population having many times the average amount. A meaningful evaluation of the nuclear fall-out hazard can only be made if the frequency distribution of radioactivity in the population is known. Attempts to determine the shape of the distribution curve from Kulp’s data on strontium-90 concentration in children’s bones have met limited success because of the small sample size and lack of strontium-90-calcium equilibrium in bone. To overcome these limitations, we have measured the caesium-137 content in approximately 900 muscle samples. These tissue samples were removed during post-mortem operations from January 1959 to August 1963. The use of caesium-137 as a fission product monitor assures that all members of the group, regardless of their age, were essentially in equilibrium with the radioactive environment at the time of death.

The period of investigation coincides with the first weapon test moratorium and the resumption of largescale testing in the fall of 1961. Average caesium-137 in the samples was relatively constant throughout 1959, decreased a factor of two during 1960, and remained relatively stable until the early summer of 1962. Since mid-1962 the average level of caesium-137 radioactivity in the sample population has steadily increased and was four times greater than the 1962 minimum by the summer of 1963.

Time-independent histograms of the data have been assembled by fitting a polynomial to the raw data (sample radioactivity as a function of data of death). This pooled data has been tested statistically against normal, log-normal, and gamma frequency distributions. Results indicate that the experimental distribution is definitely not Gaussian and is best fitted by a gamma distribution. By using the empirically derived gamma distribution it is possible to predict the fraction of the population having N times the average activity for any level of fall-out. We have tested this model for the fourfold increase in activity since mid-1962 and have found it to predict accurately the present distribution of caesium-137 radioactivity between individual members of the sample population.
On a établi des histogrammes indépendants du temps en ajustant un polynôme aux données brutes (radioactivité des échantillons en fonction de la date du décès). On a comparé statistiquement les données ainsi ajustées à une distribution suivant la loi de Laplace-Gauss, à une distribution suivant la loi de Galton et à une distribution gamma. Les résultats indiquent que la distribution expérimentale ne suit absolument pas la loi de Laplace-Gauss et qu'elle correspond le mieux à une distribution gamma. En utilisant la distribution gamma déduite empiriquement, on peut prévoir, pour n’importe quelle valeur de la retombée, quelle fraction de la population aura une charge corporelle égale à N fois la valeur moyenne. Les auteurs ont vérifié ce modèle pour l’augmentation quadruple de l’activité qui s’est produite depuis 1962 et ils ont constaté qu’il permettait de prévoir avec précision la distribution actuelle de la radioactivité due au césium 137 entre les différents membres de la population d’échantillons.

АНАЛИЗ ВРЕМЕНИ И ЧАСТОТА РАСПРЕДЕЛЕНИЯ ОСАДКОВ ЦЕЗИЯ-137 В ОБРАЗЦАХ МЫШЦ. При низких концентрациях искусственно-радиоактивности в организме вредные для эффекта, по всей вероятности, можно обнаружить у той части населения, у которой количество радиоактивности во много раз превышает средний уровень. Достоверная оценка опасности, от выпадения радиоактивных осадков может быть сделана только тогда, когда известна частота распределения радиоактивности у населения. Попытки определить форму кривой распределения на данных Калла по концентрации стронция-90 в костях у детей имели ограниченный успех из-за малого размера образца и отсутствия равновесия стронций-90—калий в костях. Для преодоления этих недостатков авторы измеряли содержание цезия-137 в образцах мышц. Образцы тканей были взяты во время вскрытия трупов с января 1959 по август 1963 года. Использование цезия-137 в качестве индикатора продуктов деления показывает, что все члены группы, независимо от их возраста, находятся в равновесии с радиоактивной средой во время смерти.


Были составлены независимые от времени гистограммы данных путем подборки многочисленных наблюдений. Эти собраные вместе данные позволили статистически по сравнению с нормальной, логнормальной и гамма-частотой распределения. Результаты показывают, что экспериментальное распределение стабильно не является гауссовским и болеев общего согласуется с гамма-распределением. С помощью экспериментально полученного гамма-распределения можно предсказать ту часть населения, которая имеет в N число раз большую радиоактивность, чем средняя активность для любого уровня радиоактивных осадков. Авторы испытали эту модель при четырехкратном увеличении активности с середины 1962 года и обнаружили, что можно точно предсказать существующее распределение радиоактивности цезия-137 между отдельными образцами, взятыми у населения.


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ANÁLISIS TEMPORAL Y DISTRIBUCIÓN DE FRECUENCIAS DEL CESIO-137 PROCEDENTE DE LA PRECIPITACIÓN RADIOACTIVA EN MUESTRAS DE TEJIDO MUSCULAR. Cuando las concentraciones de radioactividad artificial en el cuerpo son bajas, el efecto perjudicial recae sin duda en aquella parte de la población en la cual la concentración representa un múltiplo del término medio. Solamente puede evaluarse adecuadamente el riesgo que entraña la precipitación radiactiva si se conoce la distribución de frecuencias de la radioactividad en la población. Los intentos para determinar la forma de la curva de distribución, a partir de los datos de Kulo sobre la concentración del estroncio-90 en los huesos de los niños no han tenido mucho éxito debido al reducido tamaño de las muestras y a la falta de equilibrio en el hueso entre el estroncio-90 y el calcio. Para superar estas limitaciones, los autores han medido el contenido en cesio-137 de unas 900 muestras en músculos que fueron obtenidas en intervenciones post mortem entre enero de 1959 y agosto de 1963. El empleo del cesio-137 como monitor de los productos de fisión aseguró que todos los componentes del grupo, sea cual fuese su edad, estuvieran esencialmente en equilibrio con el ambiente radiactivo que les rodeaba al tiempo de su muerte.

El período de investigación coincide con la primera moratoria en los ensayos de armas nucleares y la reanudación de los mismos en gran escala durante el otoño de 1961. La concentración media de cesio-137 en las muestras permaneció relativamente constante a lo largo de 1959, disminuyó a la mitad durante 1960 y se mantuvo bastante estable hasta principios del verano de 1962. Desde mediados de este año, el nivel
CAESIUM-137 FALL-DÚT IN MUSCLE

1. INTRODUCTION

The inhomogeneity of fall-out body burdens has been a subject of scientific discussion and debate since 1956, when TURKESON and KULP [1] proposed a normal distribution for their data on strontium-90 calcium ratios in children's bone. Their viewpoint was opposed by both NEUMAN [2] and DAHL [3], who pointed out that the data were skewed toward the higher values and appeared to be better fitted by a log normal distribution. LIBBEY [4] endorsed the Gaussian model which has been used in LANGHAM and ANDERSON'S estimates of caesium-137 fall-out hazards [5]. The importance of this controversy lies in the asymmetry of the observed data. In such cases a much larger fraction of the population has several times the mean activity than would be the case for a normal distribution. Though both normal and log normal distributions have been tested against strontium-90 bone data [6], the results have been inconclusive because of small sample size and lack of strontium-90 calcium equilibrium in contemporary bone. Recently, SNYDER and COOK [7] have used a different approach to the problem. Instead of hypothesizing on the type of parent distribution, they have used a non-parametric analysis to establish confidence bands for an empirical cumulative distribution curve. Because each point on the cumulative curve is systematically dependent on the preceding values, a confidence band established in this manner is quite wide. However, by restricting the analysis to one point on the cumulative curve, they are able to determine the confidence limits at that point with reasonable precision.

We have tested each of the proposed frequency distributions against our data of caesium-137 in skeletal muscle and found neither the normal or log normal distributions to be acceptable models of the parent distribution. Instead we propose a gamma frequency distribution. This model adequately describes the observed data. Furthermore, it is relatively insensitive to changes in the overall level of radioactivity in the environment; and therefore can be used to predict maximum body burden variations under a variety of conditions. We have also analysed our data with two types of non-parametric statistics; one of these is the type of analysis used by SNYDER and COOK, the other a non-parametric test developed by W. WADSWORTH et al. [8]. The results of these analyses are compared to the parametric analysis using the gamma distribution and the confidence levels for each type of analysis compared.
2. EXPERIMENTAL DATA

To provide a sample population large enough to test the proposed distributions, we measured the caesium-137 content of 878 skeletal muscle samples from the same number of individuals. Since skeletal muscle contains approximately 80% [9] of the body caesium, the variation in caesium-137 content of the de-fatted muscle samples should be a reliable index of caesium-137 body burden variations. The muscle samples (90-140 g) were obtained from the thigh or lower abdomen during post-mortem operations performed at the Massachusetts General Hospital. Samples were not collected from patients who had received radioisotopes for medical purposes or died of highly infectious diseases. The muscle samples were dehydrated in a vacuum oven and packed in plastic test tubes for counting. The counting apparatus consisted of a 5-in x 5½-in sodium iodide (TI) well crystal surrounded by an 18-in x 18-in plastic scintillator. The plastic scintillator was operated in anti-coincidence with the sodium iodide crystal to suppress both cosmic ray background and Compton reactions in the sodium iodide. The crystals are shielded on the sides by 4-in lead and mercury and on the top by 7-in cast iron. A description of this apparatus has been published [10].

The gamma spectra of the samples were measured with a 256-channel pulse height analyser. For an average sample the counting error for the caesium peak was 15%. After counting, the samples were de-fatted in a 3-1 mixture of chloroform and ethyl alcohol and dried to constant weight at 102°C. Final counting data is expressed in picocuries/gram of de-fatted, dry tissue.

3. TIME VARIATION OF CAESIUM-137 BODY BURDENS

To determine how the average level of caesium-137 activity varied throughout the period of sample collection, the data was averaged in serial subsets of 25 samples each. The average sample activity of each subset is shown by the crosses in Fig. 1. The mean sample activity as a function of time, determined by fitting a least squares fourth order polynomial to the 878 data points, is shown by the solid curve.

Following the bomb test moratorium in the fall of 1958, the body burden of caesium-137, as reflected in samples collected throughout 1959, was relatively constant. Starting in early 1960 there was a gradual decrease in sample activity, which continued until January of 1961. It is believed that this decrease was due to the lesser amount of direct fall-out material in foodstuffs following the atmospheric clearance which took place during 1959. From 1 January 1961 to 1 June 1962, the mean levels of caesium-137 activity was constant and at a minimum. During this period, the average caesium-137 concentration in muscle was 0.47 ± 0.02 pc/g, dried, de-fatted. This average is based on 325 samples, and is probably close to the steady state value for the amount of fission product, 62 megatons [11]**, introduced

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* Increasing the order of the approximating polynomial did not significantly change this curve or the subsequent data analysis. 
** 30 megatons of the 92 expended before 1 January 1959 was deposited as "close in fall-out near the test site" [8].
into the environment prior to the test moratorium. Although atmospheric testing was resumed in September 1961, a rising trend in sample activity was not seen until the summer of 1962. The delay was probably due to a variety of factors, such as the altitude at which the nuclear debris was injected, the fact that most crops and fodder had been harvested by the fall of 1961, the time lag in foodstuff distribution and use. Since mid-1962, the increase in activity has been quite rapid (see Fig. 2). This increase will eventually be followed by another decrease, as in 1960. If the geographical distribution of the 101 megatons [12] of fission products from the last period of atmospheric testing is not too different from that of tests prior to 1961, the final mean steady state caesium-137 concentration in muscle will be about 1.2 pc/g (dry, de-fatted).

4. FREQUENCY DISTRIBUTION OF THE OBSERVED DATA

Because of the time variation in sample activity, it is necessary to normalize the data in terms of standard scores before determining their frequency distribution. This normalization was done by analysing the data in serial subsets of 50 samples each. The variance of each subset was calculated about a mean given by the polynomial in Fig. 1, and a histogram of the subset prepared in terms of relative standard deviation intervals, $s$. A grand histogram of the first 14 subsets prepared by summing the histograms in terms
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Fig. 2
Probability histogram of the first 670 samples plotted as a function of $s$, the relative standard deviation of the sample. For a normal distribution, the histogram would be symmetric about the mean sample.

Fig. 3
The solid curve is a histogram of the sample data scaled for comparison with the gamma distribution ($\alpha = 3.5$) shown by the dotted lines. The sample mean is at 2.12.

of $s$ is shown in Fig. 3. The asymmetry of this distribution is obvious; in particular the number of samples above the $+3s$ level, the lack of samples below the $-2s$ level, indicate that these data are not part of a normally distributed parent population. A chi-square test shows that there is essentially zero probability that this sample was derived from a normally distributed population ($X^2 = 200$ for 13 degrees of freedom).

The asymmetry of the histogram shown in Fig. 3 is typical of fall-out data. Since a logarithmic transformation removes most of the apparent asymmetry, it is always tempting to assume a log normal distribution for data of this type. Indeed, the distribution of our sample data looks normal after a log transformation. However, a chi-square test on the transformed data gives a probability of less than 1% that the parent population is log normal [13]. YAMAGATA [14] reported a log normal distribution for non-radioactive caesium-133 in 78 muscle samples. This finding is reasonable
since it was based on a visual analysis of a log transformed histogram rather than statistical tests. His results are particularly interesting in that he also measured the potassium content of the samples and showed that the caesium-133 potassium ratios were also log normal, i.e. skewed. This finding contradicts the reported distribution of potassium-40 caesium-137 ratios by LANGHAM and ANDERSON [15]. Like Yamagata, we find that the potassium distribution is much more symmetric than that of caesium. We have not investigated the distribution of caesium potassium ratios further since the concept of caesium potassium ratios has outlived its usefulness as a method of hazards evaluation [16].

Another simple frequency distribution that can be used to describe an asymmetric unimodel data population is the gamma distribution. It has the limits of zero and infinity and is expressed by the function

\[ P(x) = \frac{1}{\beta^{\alpha+1} \Gamma(\alpha+1)} x e^{-x/\beta} , \]

where \( P(x) \) is the probability density of a caesium-137 concentration of \( \text{x pc/g} \) and \( \alpha \) and \( \beta \) are the two parameters which describe a particular distribution. The parameter \( \beta \) serves mainly as a scale factor while \( \alpha \) determines the skewness of the distribution [17].

Values of \( \alpha \) for each of the 50 sample subjects have been calculated from the mean sample activity and subset variance [18]. The results, Table I, indicate that the values of \( \alpha \) are relatively constant and independent of the absolute level of sample activity. The solid curve in Fig. 3 is a histogram of the sample data scaled for comparison with a histogram of a gamma distributed parent population having the same \( \alpha \) (3.5). A chi-square test gives a probability of 0.25 that the data is from an infinite set having the same gamma distribution. In Table I, it is seen that the mean \( \alpha \) value for females is less than that for males and the range of \( \alpha \) values is reduced by a factor of two when the sexes are analysed separately. Although the increased skewness of the female data is of borderline significance, \( (t = 1.7)^* \), chi-square tests show that the data is more adequately described by an appropriate gamma distribution when each sex is considered separately. A chi-square test on the male data gives a 0.55 probability that it was taken from a parent population with \( \alpha = 3.9 \). The same test on the female data gives a 0.70 probability that it was taken from a parent population with \( \alpha = 3.3 \).

We believe the gamma distribution can serve as a useful model for the distribution of caesium-137 body burdens. It has reasonable limits and adequately describes the sample data over the range of observed values. Of particular importance is the observation that the average \( \alpha \) was relatively constant throughout a five-year period in which the mean sample activity varied by as much as 300%. This leads us to believe the gamma distribution can be used to predict what fraction of the population will have \( N \) times the mean activity, relatively independent of how this mean varies.

The Federal Radiation Council has suggested that a factor of three be used in determining permissible total population exposure risks to allow for variations in individual body burdens [19]. Applying this criteria to a

* Student's \( t \) test indicates that the difference in male-female means has a chance probability of about 0.15.
### Table I

**CALCULATED $a$ VALUES FOR SERIAL 50 SAMPLE SUBSETS**

<table>
<thead>
<tr>
<th></th>
<th>Both sexes and unknowns (878 samples)</th>
<th>Males (500 samples)</th>
<th>Females (345 samples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time (d)</td>
<td>$a$ Median time</td>
<td>$a$ Median time</td>
<td>$a$ Median time</td>
</tr>
<tr>
<td>131</td>
<td>3 6 878</td>
<td>3 6 165</td>
<td>3 6 286</td>
</tr>
<tr>
<td>292</td>
<td>4 3 966</td>
<td>3 5 441</td>
<td>3 5 538</td>
</tr>
<tr>
<td>428</td>
<td>4 5 1102</td>
<td>2 2 540</td>
<td>2 2 716</td>
</tr>
<tr>
<td>451</td>
<td>3 8 1345</td>
<td>1 2 668</td>
<td>1 2 859</td>
</tr>
<tr>
<td>528</td>
<td>2 7 1229</td>
<td>3 7 775</td>
<td>3 7 1109</td>
</tr>
<tr>
<td>638</td>
<td>3 7 1322</td>
<td>7 2 917</td>
<td>7 2 1254</td>
</tr>
<tr>
<td>692</td>
<td>5 6 1366</td>
<td>3 0 1109</td>
<td>3 1 1476</td>
</tr>
<tr>
<td>709</td>
<td>2 1 1483</td>
<td>2 0 1228</td>
<td>2 0 1576</td>
</tr>
<tr>
<td>801</td>
<td>2 4 1532</td>
<td>2 4 1358</td>
<td>2 4 1537</td>
</tr>
</tbody>
</table>

$\bar{a} = 3.5 \pm 0.35$

$\bar{a} = 3.9 \pm 0.33$

$\bar{a} = 3.3 \pm 0.20$
population having a normally distributed body burden with the same variance as our sample population, we calculated that approximately one person in 100,000 would have a body burden exceeding three times the mean. For a skewed distribution of body burdens, i.e., gamma distributed with an \( \alpha \) of 3.5, approximately 150 persons per 100,000 would exceed this criteria. A comparison of the probabilities for other multiples of the mean body burden are given in Table II. It is seen that the skewed distribution gives considerably larger probability fractions for values of \( N \) greater than 2.

**TABLE II**

**FRACTION OF THE POPULATION EXCEEDING \( N \) TIMES THE MEAN FOR GAMMA AND NORMAL FREQUENCY DISTRIBUTIONS**

<table>
<thead>
<tr>
<th></th>
<th>Gamma ( \alpha = 3.5 )</th>
<th>Normal ( \sigma = 0.47 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N = 2 )</td>
<td>( 3.5 \times 10^{-2} )</td>
<td>( 1.7 \times 10^{-2} )</td>
</tr>
<tr>
<td>( N = 3 )</td>
<td>( 1.5 \times 10^{-3} )</td>
<td>( 1.2 \times 10^{-5} )</td>
</tr>
<tr>
<td>( N = 4 )</td>
<td>( 4.0 \times 10^{-5} )</td>
<td>( 9 \times 10^{-11} )</td>
</tr>
<tr>
<td>( N = 6 )</td>
<td>( 1.9 \times 10^{-8} )</td>
<td>( 5 \times 10^{-16} )</td>
</tr>
<tr>
<td>( N = 8 )</td>
<td>( 6.2 \times 10^{-12} )</td>
<td>--</td>
</tr>
<tr>
<td>( N = 10 )</td>
<td>( 1.6 \times 10^{-15} )</td>
<td>--</td>
</tr>
</tbody>
</table>

5. CONFIDENCE LEVELS FOR PARAMETRIC AND NON-PARAMETRIC ANALYSES

We have calculated the 95% confidence level for the fraction of our sample which exceeds three times the mean activity by evaluating our data non-parametrically (no assumption as to the type of parent distribution) and parametrically by assuming the parent population is gamma distributed. The skewness of a gamma distribution is a function of the parameter \( \alpha \). As \( \alpha \) decreases, the fraction of the population in the upper tail increases. Based upon the standard deviation of the mean for \( \alpha = 3.5 \) (Table I), the 95% confidence interval for \( \alpha \) is between \( \alpha = 2.7 \) and \( \alpha = 4.3 \). If the true value of \( \alpha \) is 2.7, the fraction of the sample exceeding the mean by three or more is 0.003, compared with Table II.

We have calculated the same confidence level non-parametrically using the method outlined by Snyder and Cook [7]. If \( n \) samples are ranked in ascending order of activity and \( k \) of them have less than a pre-determined activity \( x_k \), the 95% confidence level, \( P_0 \), for the fraction of the sample having less activity than \( x_k \) is given by the binomial expression:

\[
\sum_{j=0}^{k} \frac{n!}{j! (n-j)!} P_0^j (1 - P_0)^{n-j} = 0.05
\]
Since \( P_0 \) is the lower limit of the 95% confidence interval, the fraction of the samples that can have greater activity at the same confidence level is \( 1 - P_0 \). It is important to note that the use of this analysis assumes that the sampling process is truly random and that the activity of the \( k \)th sample is fixed.

A more general non-parametric method [8], which does not use the inverse probability argument of Snyder and Cook, can be used to estimate \( R \), the mean number of samples that would exceed \( x_k \) in another sample of size \( N \). It is less subject to non-randomness in the sampling procedure than the previous method, since it assumes that the activity of the \( k \)th sample will be different in another ranked set of \( n \) samples. The probability that the \( k \)th sample is between \( x_k \) and \( x_k + dx_k \) is:

\[
A(x_k)dx_k = \frac{n!}{(k-1)! (n-k)!} \left[ \int_{-\infty}^{x_k} f(x) dx \right]^{k-1} \left[ \int_{x_k}^{\infty} f(x) dx \right]^{n-k} f(x_k) dx_k
\]

where \( f(x) \) is the unknown frequency distribution of the parent population. The probability that exactly \( R \) of another set of \( N \) samples will be greater than \( x_k \) is:

\[
B[R(x_k)] = C(N, R) \left[ \int_{-\infty}^{x_k} f(x) dx \right]^{N-R} \left[ \int_{x_k}^{\infty} f(x) dx \right]^R
\]

where \( C(N, R) \) is the binomial coefficient. The joint probability that \( x_k \) is between \( x_k \) and \( x_k + dx_k \) and that \( R \) of the \( N \) samples is greater than \( x_k \) is the product of these probabilities. By integrating this joint distribution over all values of \( x_k \) we get the total probability that exactly \( R \) of the samples have greater activity than \( x_k \) for all possible values of \( x_k \).

\[
P(R > x_k) = \int_{-\infty}^{+\infty} A(x_k)dx_k B(R(x_k))
\]

By substituting:

\[
u = \int_{-\infty}^{x_k} f(x) dx
\]

the integration over the parent frequency distribution is eliminated and the total probability \( R > x_k \) becomes:

\[
P(R > x_k) = \int_{0}^{1} u^{k-1} [1 - u]^{n-k} u^{N-R} (1 - u)^R C(N, R) k C(n, k) du
\]

This probability density can be integrated for a given \( R \) to find the probabili-
ty that exactly $R$ of the $N$ sample would exceed $x_k$. It is simpler to find the moment generating function for $P(R > x_k)$:

$$M(\theta)_{R>x_k} = kC(n, k) \int_0^1 u^{k-1} (1-u)^{n-k} \left[ u + (1+u)e^\theta \right]^N du$$

and take derivatives to find the mean and variance of $R$.

$$M'(\theta)_{R>x_k} = \frac{\mu_n^2}{R} = \frac{n-k+1}{n+1}N,$$

where $R$ is the mean number of samples that would exceed $x_k$ in another sample of size $N$.

$$M''(\theta)_{R>x_k} = \frac{\nu_2}{R} = N \left[ \frac{n-k+1}{n+1} + \frac{(N-1)(n-k+2)(n-k+1)}{(n+2)(n+1)} \right]$$

The variance of $\frac{\mu_n}{R}$ is found from this second moment.

$$\sigma^2 = \frac{\nu_2}{R^2} - \frac{\mu_n^2}{R^2}.$$ 

This variance can be used to set confidence limits on $R$ since in a large number of trials $R$ would be approximately normally distributed.

The results of the three analyses are compared in Table III. The agreement is quite close for the three methods. A gamma approximation to the parent population is admittedly a strong assumption. It has the compensating feature that its confidence interval is based on the total sample and is therefore not affected as much as a non-parametric analysis by sampling errors or chance contamination of a few samples. It also has an advantage

TABLE III

ESTIMATES OF FRACTIONS EXCEEDING THREE TIMES THE MEAN ACTIVITY AT A 95% CONFIDENCE LEVEL

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Type of analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.003</td>
<td>Parametric gamma $\alpha = 2.7$</td>
</tr>
<tr>
<td>0.006</td>
<td>Non-parametric SNYDER and COOK [7]</td>
</tr>
<tr>
<td>0.007</td>
<td>Non-parametric WADSWORTH and BRYAN [8]</td>
</tr>
<tr>
<td>0.002</td>
<td>Observed in our sample</td>
</tr>
</tbody>
</table>
in that it can be used to estimate confidence levels for larger amounts of activity than were observed in the sample population.

Since there are very few samples from the upper tail of the parent distribution, setting a confidence level on the number of persons having several times the mean body burden is admittedly a difficult statistical situation. However, estimates of these small probabilities are of interest simply because the number of persons exposed to fall-out is large.

ACKNOWLEDGEMENTS

We are indebted to Professor G. Wadsworth, Department of Mathematics, M.I.T., whose contributions to the statistical analysis were invaluable. Messrs S. Pizer and A. Callahan wrote the programme used in the machine analysis. We thank the Pathology Department, M.S.H., for supplying the tissue samples, and the United States Public Health Service for furnishing financial support under Grants Nos. Rad C-2187 and AM 05423-03.

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[17] Ibid., p. 88.
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THE ENHANCED RADIOCESIUM LEVELS OF PEOPLE IN NORTHERN SWEDEN

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Abstract — Résumé — Аннотация — Resumen

THE ENHANCED RADIOCESIUM LEVELS OF PEOPLE IN NORTHERN SWEDEN. After the discovery of the high caesium-137 body activity of Swedish Lapps early in 1961 measurements were performed on large groups of Lapps and other Swedes on a similar diet. In September, 1961 162 persons from an area close to the arctic circle were measured in a semi-portable whole-body counter. In the Lapp group caesium-137 levels ranging from 15 to 690 nc were found. At the same place a group of 157 persons were counted in April, 1962. At that time the caesium-137 range was 30 to 740 nc. During a five weeks' expedition to seven different centres in northern Sweden in April, 1963 a total number of 488 persons were studied by means of the same counter set up in a bus. The caesium-137 range for Lapps in the above mentioned area was then 50 to 900 nc. The average caesium-137 body activity of all the adult male reindeer breeders (78 persons) measured in April, 1963 was 461 nc. The maximum body activity found was 1340 nc caesium-137. Details are presented on the variation of caesium-137 in human beings with age, sex, occupation and diet as well as on the seasonal and geographical variations found. An increase in the average caesium-137 body activity has been observed from 1961 to 1963. For comparison, non-Lapps have also been counted. Almost all of them also show a substantially enhanced caesium-137 level if compared with persons in southern Sweden.

The radiation dose from caesium-137 is in many cases two to three times as large as the potassium-40 dose, the observed maximum giving a dose eight times that of the potassium dose.

CHARGE CORPORELLE DE RADIOCÉSIUM RELATIVEMENT ÉLEVÉE CHEZ LES HABITANTS DE LA SUÈDE SEPTENTRIONALE. Lorsqu'on eut découvert au début de 1961 que la charge corporelle de césium 137 était élevée chez les Lapons de Suède, on a fait des dosages sur des groupes importants de Lapons et d'autres habitants de la Suède qui suivent un régime alimentaire analogue. En septembre 1961, on a effectué des dosages sur 162 personnes d'une région située à proximité du cercle arctique au moyen d'un anthropogammamètre semi-portatif. Chez les Lapons, on a relevé des charges corporelles de césium 137 allant de 15 à 690 nc. En avril 1962, on a fait des dosages sur un autre groupe de 157 personnes de la même région. Les charges de césium 137 allaient alors de 30 à 740 nc. En avril 1963, une expédition qui, en cinq semaines, s'est rendue dans sept centres de la Suède septentrionale a fait des dosages sur un total de 488 personnes au moyen du même appareil monté sur un autobus. Cette fois-là, les charges de césium 137 chez les Lapons de cette région allaient de 50 à 900 nc. La charge corporelle moyenne de césium 137 pour tous les éleveurs de rennes - soit un groupe de 78 personnes - mesurée en avril 1963 s'élevait à 461 nc. La charge corporelle maximum était de 1340 nc. Le mémoire présente des détails sur les variations des charges de radiocésium chez l'homme selon l'âge, le sexe, l'occupation et le régime alimentaire, ainsi que sur les fluctuations saisonnières et géographiques qui ont été relevées. On a observé un accroissement de la charge corporelle moyenne de césium 137 de 1961 à 1963. Aux fins de comparaison, on a également fait des dosages sur des habitants des mêmes régions autres que lapons. Chez presque tous, la charge de césium 137 était sensiblement supérieure à celle qui a été trouvée chez les habitants de la Suède méridionale.

La dose de rayonnement due au radiocésium est, dans bien des cas, de deux à trois fois la dose qui provient du potassium 40, le maximum observé étant de huit fois cette dose.

ПОВЫШЕННОЕ СОДЕРЖАНИЕ РАДИОАКТИВНОГО ЦЕЗИЯ В ОРГАНИЗМЕ У ЖИТЕЛЕЙ СЕВЕРНОЙ ШВЕЦИИ. После обнаружения высокого содержания цезия-137 в организме у шведских лопарей в начале 1961 года было проведено обследование больших групп лопарей и других жителей Швеции, получающих такую же диету. В сентябре 1961 года обследовали 162 человека из района, примыкающего в Арктическом кругу; измерения производились с помощью полупереносного счетчика для измерения радиоактивности всего организма. В группе лопарей содержание цезия-137 находилось в пределах от 15 до 690 мккюр. В этом же районе в апреле 1962 года была обследована группа из 157 человек. В это время
уровень цезия-137 составлял 30—740 ммкюри. Во время 5-недельной экспедиции в 7 различных центрах северной Швеции в апреле 1963 года было обследовано 458 человек с помощью той же счетной установки, размещенной в автобусе. Уровень цезия-137 у лопарей в указанном районе в это время составлял 50—900 ммкюри. Среднее содержание цезия-137 у взрослых мужчин-оленеводов в апреле 1963 года составляло 461 ммкюри (группа из 78 человек). Максимальное содержание цезия-137 составляло 1340 ммкюри. Представлены подробные данные относительно колебаний содержания радиоактивного цезия у людей в зависимости от возраста, пола, профессии и диеты, а также от сезонных и географических показателей. Наблюдалось повышение среднего содержания цезия-137 в организме в течение 1961—1963 годов. Для сравнения были проведены измерения у шведов, живущих в тех же округах, что и лопари. Почти у всех было обнаружено значительное повышение содержания цезия-137 в организме по сравнению с жителями Южной Швеции.

Внутренняя доза, создаваемая радиоактивным цезием, обычно в 2—3 раза больше дозы Калия-40 при максимуме в 8 раз превышающем дозу Калия.

CARGAS DE RÁDIOCESIO ANORMALMENTE ELEVADAS EN LOS HABITANTES DEL NORTE DE SUECIA.

Después de descubrirse a principios de 1961 la elevada carga corporal de cesio-137 que tenían los laponés suecos, se han efectuado mediciones en grandes grupos de laponés y otros habitantes de Suecia que siguen un régimen alimenticio análogo. En septiembre de 1961 se examinaron 162 personas de una zona próxima al Círculo polar ártico con un antropogammametro semiportátil. En los laponés se registraron cargas de cesio-137 comprendidas entre 15 y 690 nc. En la misma región, se sometió a recuento en abril de 1962 a un grupo de 157 personas. En esta ocasión la carga de cesio-137 osciló entre 30 y 740 nc. En el curso de una expedición que en cinco semanas visitó a siete centros de Suecia septentrional en abril de 1963, se examinaron en total 458 personas con el mismo contador montado en un omnibus. Esta vez, la carga de cesio-137 de los laponés de la zona antes mencionada estuvo comprendida entre 50 y 900 nc. La carga media de cesio-137 en todos los criadores de renos (78 hombres adultos), medida en abril de 1963, fue de 461 nc. La carga corporal máxima observada fue de 1340 nc de cesio-137. Se facilitan detalles sobre la variación de la carga de cesio-137 en función de la edad, el sexo, el tipo de ocupación y el régimen alimenticio, así como sobre las variaciones estacionales y geográficas observadas. De 1961 a 1963 se ha advertido un aumento de la carga corporal media de cesio-137. Con fines comparativos, se sometió también a recuento a individuos no laponés. En casi todos ellos se observó una carga de cesio-137 muy elevada en comparación con la de los habitantes del sur de Suecia.

LA DOSIS DE IRRADIACIÓN DEBIDA AL CESIO-137 SUELE SER DOS O TRES VECES MAYOR QUE LA DEBIDA AL POTASIO-40...
2. INVESTIGATION No. 1

In September, 1961 a body-activity investigation was carried out at Jokkmokk in northern Sweden. One hundred and sixty-two subjects were counted by means of transportable whole-body counting equipment [6], and a rough estimate of the diet of meat, fish and milk was obtained from an interview of all subjects.

This investigation was planned before the nuclear weapon tests started in 1961 and was performed before the new global fallout reached Sweden. The results from these measurements therefore will serve as a reference base for the measurements performed later.

The subjects studied were invited to participate in the investigation by means of announcements on the radio and in the newspapers. The composition of the population sample and the body activities obtained can be seen in Table I. Efforts were made to get about the same number of Lapps and non-Lapps, males and females, and adults and children. With some effort we also succeeded in getting four vegetarians.

3. INVESTIGATION No. 2

Atmospheric nuclear weapon tests in the autumn of 1961 made it important to follow up the activity levels. A new study was undertaken at the same place in April, 1962. In this case 157 subjects were investigated. About the same sampling method was used as in the first investigation, but special efforts were made to secure a better representation in certain groups. However, it was difficult to get the same subjects again. The results of the second investigation (Table II) are therefore not fully comparable with the results of the first investigation. The results of the measurements of those subjects also measured in September, 1961 are shown in Table III. A diet investigation was also performed by an interview method. Some results of investigations Nos 1 and 2 were reported earlier [7].

4. INVESTIGATION No. 3

In April, 1963 a new more extensive investigation was performed. The whole-body counting equipment was mounted in a bus. Measurements were performed at Jokkmokk, but also at six other places in northern Sweden. These places were chosen since they are centres of Lapp communities with not too small a population. The places visited are shown on the map in Fig. 1; they are also listed in Table IV.

The subjects to be investigated were randomly selected from demographic tables, and they were invited in advance. From earlier investigations we learned that urban people had quite low body activities, in general below 30 nc. Therefore it was decided to compare the Lapps with non-Lapps, farmers and lumbermen. This group was sufficiently homogeneous and also to some extent had living conditions in common with Lapps.

Three hundred and ninety-eight Lapps were selected from a list made in 1958 [8]. Some of these people had died or moved away from the place.
<table>
<thead>
<tr>
<th>Group</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Number of subjects</th>
<th>Body activity of Cs137</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Average</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>uc/kg</td>
</tr>
<tr>
<td>Lapps</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reindeer -</td>
<td>M</td>
<td>20-65</td>
<td>28</td>
<td>336</td>
</tr>
<tr>
<td>Breeders</td>
<td>F</td>
<td>20-65</td>
<td>5</td>
<td>207</td>
</tr>
<tr>
<td>Non-reindeer</td>
<td>M</td>
<td>20-65</td>
<td>6</td>
<td>172</td>
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<tr>
<td>Breeders</td>
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<td>20-65</td>
<td>4</td>
<td>156</td>
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<td>Children</td>
<td>M</td>
<td>10-13</td>
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</tr>
<tr>
<td></td>
<td>M</td>
<td>14-19</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
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<td>F</td>
<td>10-13</td>
<td>16</td>
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<tr>
<td></td>
<td>F</td>
<td>14-19</td>
<td>14</td>
<td>92</td>
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<td>13</td>
<td>78</td>
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<td>Children</td>
<td>M</td>
<td>10-19</td>
<td>29</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>10-19</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>Vegetarians</td>
<td>Mixed</td>
<td>4</td>
<td>90</td>
<td>0.34</td>
</tr>
</tbody>
</table>

**Table I**

Cs137 Levels in Human Beings, Obtained by Whole-Body Counting at Jokkmokk (66.6°N, 19.9°E), Sweden in September, 1961

K. LIDÉN and Y. NAVERTSEN
<table>
<thead>
<tr>
<th>Group</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Number of subjects</th>
<th>Body activity of Cs$^{137}$</th>
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<tr>
<td></td>
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<td>Reindeer-</td>
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<td>495</td>
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<td></td>
<td></td>
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<td>nc/kg</td>
</tr>
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<td>nc/kg</td>
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<td>10-19</td>
<td>11</td>
<td>61</td>
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RADIOCAESIUM LEVELS IN N. SWEDEN 171
THE CHANGE OF THE Cs$^{137}$ LEVEL IN A CONTROL GROUP AT JOKKMOKK,
MEASURED IN SEPTEMBER, 1961 AND APRIL, 1962

<table>
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<tr>
<th>Group</th>
<th>Sex</th>
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<th>Number of subjects</th>
<th>Body activity of Cs$^{137}$</th>
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<td></td>
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<td>nc</td>
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<td>M</td>
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<td>416</td>
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<tr>
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<td>F</td>
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<tr>
<td>Reindeer breeders</td>
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<td>11-16</td>
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<td>20</td>
</tr>
</tbody>
</table>

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RADIOCAESIUM LEVELS IN N. SWEDEN

Fig. 1

Map of Sweden showing the area of special interest in this investigation

Approximate limit of area normally used for reindeer breeding

Approximate limit of area reserved for the reindeer herds of the Lapp communities being studied

The places listed in Table IV are indicated by capitals

If this number of subjects is omitted from the original list, 60 to 65% came to the investigation. Of 195 non-Lapps invited 68% came. Besides these

TABLE IV

PLACES VISITED BY THE MOBILE LABORATORY DURING THE INVESTIGATION OF BODY ACTIVITIES IN APRIL, 1963 (cf map in Fig. 1)

<table>
<thead>
<tr>
<th>Place</th>
<th>Code</th>
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<th>Longitude (°E)</th>
<th>Altitude above sea level (m)</th>
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<tbody>
<tr>
<td>Övre Soppero</td>
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<tr>
<td>Jukkas järvi</td>
<td>B</td>
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<td>20.5</td>
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<td>Pumu</td>
<td>C</td>
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<td>21.2</td>
<td>530</td>
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<tr>
<td>Jokkmokk</td>
<td>D</td>
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<td>19.8</td>
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<td>Tärnaby</td>
<td>E</td>
<td>65.7</td>
<td>15.3</td>
<td>440</td>
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<tr>
<td>Arvidsjaur</td>
<td>F</td>
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<td>G</td>
<td>62.5</td>
<td>12.5</td>
<td>580</td>
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</table>
selected subjects, for various reasons about 100 additional persons were investigated.

Parallel to the whole-body counting a dietary investigation was performed by an interview method. Samples of reindeer meat, fish and cow's milk were also collected for a gammaspectrometric assay.

This paper primarily contains results of the whole-body counting measurements. An evaluation of the diet investigation will be made elsewhere [9].

Tables V and VI give the body activity of groups of Lapps and non-Lapps in the seven different areas. The number of subjects is indicated in brackets and both the activity and the specific activity are given.

In Table VII the subjects from the different areas are put together to show age and sex dependence for Lapps and non-Lapps.

Table VIII compares the Jokkmokk results in 1962 and 1963 for a control group of 48 Lapps and seven non-Lapps.

5. DISCUSSION OF THE RESULTS

5.1. Annual variation due to change of diet

The increase found from September, 1961 to April, 1962 (Tables I to III) is assumed to be mostly a result of the annual variation of the diet. Dietary investigations and radio assays of food samples have shown that the primary intake of Cs$^{137}$ is through reindeer meat [3, 7, 9]. These studies also showed an annual variation of the intake, partly due to a variation of the amount of reindeer meat in the diet, and partly due to an annual variation of the specific activity of the reindeer meat, winter meat sometimes being about five times more active. The minimum value of the body activity of Lapps should appear in the autumn and the maximum late in the spring or beginning of the summer.

For most Lapps (a population of about 3000) reindeer meat constitutes a large part of the diet, often about 500 g/d. During the summer time reindeer meat is to some extent replaced by fresh-water fish.

For non-Lapps reindeer meat is more exclusively a winter constituent of the diet. But even during winter time the meat consumption is several times lower than for the Lapps. Many urban people seldom eat reindeer meat. In 1961 they had a body activity of less than 30 nc, i.e. about the same level as the vegetarians (Table I).

Non-Lapps engaged in hard manual labour eat somewhat more reindeer meat than urban people. Their body activity was about the same as for several Lapps.

When comparing the results from 1961 and 1962 in Tables I and II an increase was noticed for almost all the groups, for Lapps in general between 10 and 40%. For non-Lapps the spring values were 100 to 200% higher than the autumn values.

Since the groups were not composed exactly of the same subjects on both occasions, it was difficult to calculate a representative figure of the increase. However, 71 of those subjects measured in 1961 were also measured in April 1962 (Table III). An analysis of the group of 11 male reindeer breeders demonstrates the difficulty in assigning a figure for the annual variation. Three of the subjects actually decreased. The interview revealed
TABLE V

LAPP GROUPS FROM SEVEN DIFFERENT AREAS IN NORTHERN SWEDEN

The Cs$^{137}$ body activity (nc) and the specific body activity (nc/kg) in April 1963*

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20</td>
<td>M</td>
<td>166 (10)</td>
<td>82 (4)</td>
<td>155 (5)</td>
<td>194 (4)</td>
<td>110 (1)</td>
<td>355 (6)</td>
<td>233 (3)</td>
<td>260 (36)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.99</td>
<td>2.19</td>
<td>5.43</td>
<td>5.41</td>
<td>1.80</td>
<td>6.20</td>
<td>6.69</td>
<td>6.87</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>114 (10)</td>
<td>56 (3)</td>
<td>90 (5)</td>
<td>136 (12)</td>
<td>36 (1)</td>
<td>136 (3)</td>
<td>-</td>
<td>117 (33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.94</td>
<td>1.14</td>
<td>2.14</td>
<td>3.20</td>
<td>1.03</td>
<td>2.20</td>
<td>2.70</td>
<td>2.52</td>
</tr>
<tr>
<td>21-40</td>
<td>M</td>
<td>351 (3)</td>
<td>398 (1)</td>
<td>383 (5)</td>
<td>413 (5)</td>
<td>-</td>
<td>668 (6)</td>
<td>497 (10)</td>
<td>490 (34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.96</td>
<td>5.99</td>
<td>6.98</td>
<td>6.26</td>
<td>-</td>
<td>16.60</td>
<td>1.96</td>
<td>7.45</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>202 (4)</td>
<td>170 (3)</td>
<td>212 (4)</td>
<td>213 (8)</td>
<td>146 (3)</td>
<td>243 (5)</td>
<td>744 (3)</td>
<td>209 (20)</td>
</tr>
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<td></td>
<td></td>
<td>2.51</td>
<td>2.23</td>
<td>3.86</td>
<td>4.31</td>
<td>2.66</td>
<td>4.70</td>
<td>5.96</td>
<td>3.77</td>
</tr>
<tr>
<td>41-65</td>
<td>M</td>
<td>399 (6)</td>
<td>494 (6)</td>
<td>381 (1)</td>
<td>489 (11)</td>
<td>290 (3)</td>
<td>362 (10)</td>
<td>536 (7)</td>
<td>459 (44)</td>
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<td>7.47</td>
<td>6.97</td>
<td>7.78</td>
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<td>6.61</td>
<td>5.17</td>
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<td></td>
<td>F</td>
<td>297 (6)</td>
<td>134 (3)</td>
<td>-</td>
<td>583 (4)</td>
<td>226 (4)</td>
<td>170 (15)</td>
<td>286 (11)</td>
<td>207 (40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.78</td>
<td>2.40</td>
<td>4.76</td>
<td>3.46</td>
<td>3.06</td>
<td>4.74</td>
<td>3.94</td>
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</tr>
</tbody>
</table>

* The different areas are indicated by capitals according to Table IV. Figures in brackets indicate the number of randomly selected subjects.
<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>Average</th>
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<tr>
<td>13 - 66</td>
<td>M</td>
<td>260 (19)</td>
<td>335 (13)</td>
<td>322 (14)</td>
<td>411 (34)</td>
<td>244 (4)</td>
<td>496 (52)</td>
<td>483 (50)</td>
<td>399 (114)</td>
</tr>
<tr>
<td></td>
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<td>6.95</td>
<td>5.90</td>
<td>6.83</td>
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<td>7.09</td>
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</tr>
<tr>
<td></td>
<td>F</td>
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<td>167 (11)</td>
<td>308 (24)</td>
<td>277 (9)</td>
<td>164 (20)</td>
<td>277 (14)</td>
<td>191 (104)</td>
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<td>5.50</td>
<td>5.35</td>
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<td>5.40</td>
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<td>249 (23)</td>
<td>209 (48)</td>
<td>200 (13)</td>
<td>311 (42)</td>
<td>308 (34)</td>
<td>299 (318)</td>
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<td>4.83</td>
<td>3.32</td>
<td>5.18</td>
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<td>5.30</td>
<td>4.69</td>
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<td>186 (13)</td>
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<td>355 (34)</td>
<td>257 (110)</td>
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<td>5.34</td>
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<td>5.28</td>
<td>4.78</td>
<td>5.47</td>
<td>4.46</td>
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<td>Median radiation dose rad/a</td>
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<td>27</td>
<td>30</td>
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<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
<td>G</td>
<td>Average</td>
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<td>1.78</td>
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<td>2.05</td>
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<td>0.69</td>
<td>1.66</td>
<td>1.51</td>
<td>1.77</td>
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* The different areas are indicated by capitals according to Table IV. Figures in brackets indicate the number of randomly selected subjects.
<table>
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<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>Average</th>
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<td>100 ( 5)</td>
<td>194 ( 7)</td>
<td>150 (17)</td>
<td>102 ( 8)</td>
<td>110 ( 8)</td>
<td>118 ( 9)</td>
<td>158 ( 63)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>136 (10)</td>
<td>89 (10)</td>
<td>441 ( 6)</td>
<td>74 (10)</td>
<td>41 ( 5)</td>
<td>77 (11)</td>
<td>70 ( 9)</td>
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<td></td>
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<td>2.23</td>
<td>0.94</td>
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<td>1.40</td>
<td>1.66</td>
<td>1.50</td>
<td>2.30</td>
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<td>3.59</td>
<td>2.29</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>92 (15)</td>
<td>126 (18)</td>
<td>111 (30)</td>
<td>64 ( 8)</td>
<td>91 (19)</td>
<td>92 (17)</td>
<td>122 (133)</td>
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<td>0.66</td>
<td>1.27</td>
<td>1.24</td>
<td>1.80</td>
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<td>88 (13)</td>
<td>52 (13)</td>
<td>85 (30)</td>
<td>56 ( 8)</td>
<td>52 (10)</td>
<td>78 (17)</td>
<td>85 (133)</td>
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<td>3.14</td>
<td>0.77</td>
<td>1.87</td>
<td>0.60</td>
<td>0.90</td>
<td>0.98</td>
<td>1.47</td>
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<tr>
<td>Median radiation dose mrad/a</td>
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<td>6</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>
that they had been herding during the summer of 1961. During this time they had eaten a lot of dried meat, whereas during the winter they had a more mixed diet. Omitting these subjects the other eight increased by an average of 25%; the four subjects with the highest body activity increased 11% and the four with the lowest values increased 48%. It is probable that the average seasonal variation from autumn to spring for reindeer breeders is between 20 and 50%; for "Lapps, non-reindeer-breeders" and "Lapp children", the increase is about 10 to 20%.

5.2. Change due to new fall-out

Owing to the food-chains involved in this particular human contamination, a rather long delay exists between the entering of the fall-out in the biosphere and its appearance in man. Since the ground during the winter time is covered with snow, the accumulation in lichens is rather limited during this time. Reindeer slaughtered in the winter 1961/62 therefore contained little fall-out from the tests in the autumn of 1961. Most meat consumed during the spring and summer of 1962 came from reindeer slaughtered during the first months of 1962. Therefore it can be assumed that the 1961 fall-out to a rather small extent contributed to the body activity in man until the beginning of the autumn of 1962.

Investigations by SVENSSON and LIDÉN [10] show that the Cs$^{137}$ fall-out during this time increased the specific activity of lichens by about 30 to 40%. About the same increase could be expected to be found in Lapps from April, 1962 to April, 1963. The control group in Jokkmokk (Table VIII)
TABLE VIII

THE CHANGE OF THE $^{137}$Cs LEVEL IN A CONTROL GROUP
AT JOKKMOKK, SWEDEN, MEASURED IN APRIL, 1962
AND APRIL, 1963

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Subjects No.</th>
<th>$^{137}$Cs Level Increase (%)</th>
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</thead>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>1962</td>
</tr>
<tr>
<td>Lapps</td>
<td>11-13</td>
<td>M</td>
<td>5</td>
<td>3.15</td>
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<td></td>
<td>F</td>
<td>1</td>
<td>1.64</td>
</tr>
<tr>
<td></td>
<td>14-20</td>
<td>M</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>18</td>
<td>2.58</td>
</tr>
<tr>
<td></td>
<td>21-40</td>
<td>M</td>
<td>3</td>
<td>7.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>7</td>
<td>3.46</td>
</tr>
<tr>
<td></td>
<td>41-65</td>
<td>M</td>
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<td>6.91</td>
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<td></td>
<td></td>
<td>F</td>
<td>5</td>
<td>4.00</td>
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<tr>
<td>Average</td>
<td></td>
<td></td>
<td>48</td>
<td>4.02</td>
</tr>
<tr>
<td>Non-Lapps</td>
<td>33-56</td>
<td>M</td>
<td>5</td>
<td>2.88</td>
</tr>
<tr>
<td></td>
<td>42-49</td>
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<td>2.85</td>
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<tr>
<td>Average</td>
<td></td>
<td></td>
<td>7</td>
<td>2.87</td>
</tr>
</tbody>
</table>

showed an increase of that order of magnitude. The results from the whole groups from Jokkmokk (1962 and 1963) do not permit a comparison owing to the entirely different sampling methods.

5.3. Activity levels of Lapps and farmers in the whole area investigated in 1963

The results in Table V show a relatively constant $^{137}$Cs level for the whole area. For the Lapps the highest average values were found in the area (G), where also the maximum body activity of 1360 nc was found. The lowest average value was found in the central part of the whole area (E): From this area comparatively low meat activities have been reported [11], which judging from the interviews, partly could be due to the fact that the supply of grass pasture for reindeer was better here than in other areas.

At all the places studied several male reindeer breeders could not come to the investigation. It can be assumed that they had higher activities than the average obtained for adult Lapps. Values in the 10 nc/kg range are like-
ly to be frequent for them, judging from data obtained for subjects not belonging to the randomly selected groups. The highest rate of absence was found in the areas (A), (B) and (D). The low values found at (A) were therefore probably not really representative for that area.

For non-Lapps (Table VI) the highest values were found at (A). The diet interview also showed that reindeer meat was more frequently consumed here than in the other areas. The highest body activities (490 nc) among non-Lapps were found at (A) and (D).

In Table VII a marked age and sex dependence can be seen. For minors the sex ratio female to male is higher (0.7 to 0.8) than for adults (0.4 to 0.6). The low sex ratio for Lapps in the age range 17 - 20 is probably due to the fact that girls stay longer in school, whereas boys begin reindeer herding with a change in diet towards more consumption of reindeer meat. The age and sex trends are very similar for Lapps and non-Lapps.

6. THE RADIATION DOSE

The annual radiation dose from internally retained Cs\(^{137}\) can be calculated by assuming a homogeneous distribution \([12]\). In the case of the contamination of humans in northern Sweden we have to take into account the annual variation of the body activity. As mentioned earlier, the spring-to-autumn ratio is fairly well under control in the Jokkmokk area. Judging from the diet investigations the annual variation for the other areas is about the same, except for area (A), where the non-Lapp group is more like the Lapp group.

In Tables V and VI the annual radiation dose is given for the groups from different areas. The doses given are calculated by using data due to MIETTINEN et al. \([3]\) and assuming a body weight of 70 kg and a height of 170 cm. The doses are calculated for the central value (median) of each area. However, no correction is made for the annual variation of the body activity. Thus, an estimate of the annual dose can be obtained by multiplying the specific activity values given in this paper by eight.

The maximum radiation dose, calculated in this way, for a male Lapp was 151 mrad/a. The corresponding value for a female was 102 mrad/a.

7. PROGNOSIS

From measurements of the fall-out deposition and accumulation rate of Cs\(^{137}\) in lichens it is possible to make a rough estimate of the average group body activities to be expected in northern Sweden in the future.

The results of measurements of the specific activity of lichens in 1962 and 1963 \([10]\) indicate that the level of the adult Lapp groups may increase by as much as 40 to 50% from 1963 to 1964. If no further nuclear weapon tests are made, it is nevertheless probable that a substantial but somewhat smaller increase will also occur between 1964 and 1965. After that time a decrease can be anticipated.

On such premises we consider it important to continue the observation of these uniquely high contamination levels of Cs\(^{137}\) in human beings.
REFERENCES

THE BODY BURDEN OF CAESIUM-137 IN PEOPLE OF SOUTHERN FINLAND 1961-1963

E. HÄSÄNEN AND J. K. MIETTINEN
DEPARTMENT OF RADIOCHEMISTRY, UNIVERSITY OF HELSINKI, FINLAND

Abstract — Résumé — Аннотация — Resumen

BODY BURDEN OF CAESIUM-137 IN PEOPLE OF SOUTHERN FINLAND 1961-1963. In connection with the investigations of the caesium-137 body burden of Finnish Lapps several measurements of smaller groups of people living in Southern Finland were carried out.

In November 1961 eleven Helsinki inhabitants, five men and six women, 15 to 54 yr old, were counted for caesium-137 and potassium in Stockholm. None of these persons were laboratory workers, two were schoolboys. They were apparently healthy. Their diet was studied by the interview method. Ten of these people were counted again in the mobile whole-body counter of the Radiochemical Department of the University of Helsinki one year later. The average body burden of caesium-137 in men (5, average age 29) had increased from 8.4 nc in November 1961 to 18.4 nc in November 1962, in women (5, average age 34) from 2.9 nc to 8.7 nc. Potassium contents were the same within 2% (men 140 g, women 100 g).

For more detailed studies larger control groups were selected at the beginning of 1963 and counted four times, in February, May, August and October. For the group of men 25 privates of an infantry battalion (age 19, average weight 65 kg), for women 24 girl students of a household school (age 22, average weight 60 kg) were selected. In both cases the diet could be checked in detail and could be considered to be an average Finnish diet. In addition, the individual food consumption of each subject was studied by interview with the aid of weighed samples. Caesium-137 contents of both diets were determined for the time periods between the measurements.

In both groups the caesium-137 content remained about constant (men, 17.5 nc; women, 11.0 nc) until the end of June, when the caesium-137 content of milk and meat was approximately doubled within about one week. At the end of August the body burden of caesium-137 had increased in both groups to about 40% above the spring level. In the middle of October the men’s values had increased by 22%, the women’s values by 14% of the August level. The determination of the biological half-time of caesium-137 from the dietary intake is discussed.

CHARGE CORPORELLE DE CÉSIIU 137 CHEZ LES HABITANTS DE LA FINLANDE MÉRIDIONALE EN 1961-1963. Dans le cadre des recherches sur la charge corporelle de césium 137 chez les Lapons de Finlande, il a été procédé à plusieurs dosages sur de petits échantillons de la population résidant dans le sud de la Finlande.


Un an plus tard, dix de ces onze sujets ont fait de nouveau l’objet de dosages au moyen de l’anthropogammamètre mobile du Département de radiochimie de l’Université de Helsinki. On a constaté qu’entre novembre 1961 et novembre 1962, la charge corporelle moyenne de césium 137 était passée chez les cinq hommes (âge moyen 29 ans) de 8,4 à 18,4 nc et chez cinq femmes (âge moyen 34 ans) de 2,9 à 8,7 nc. Les variations de la teneur en potassium ne dépassaient pas 2%: cette teneur était de 140 g chez les hommes et de 100 g chez les femmes.

Aux fins d’une étude plus poussée, on a choisi au début de 1963 des échantillons plus nombreux, qui ont fait l’objet de dosages à quatre reprises: en février, mai, août et octobre de cette année. L’un des échantillons était constitué de 25 fantasins d’un même bataillon (âge 19 ans, poids moyen 65 kg) et l’autre par 24 étudiantes d’une école d’arts ménagers (âge 22 ans, poids moyen 60 kg). Dans les deux cas, il a été possible de contrôler minutieusement le régime alimentaire qui pouvait être considéré comme normal pour des Finlandais. En outre, on a étudié, au moyen de portions de poids connu, la consommation individuelle des diverses denrées alimentaires, sur laquelle on a demandé à chacun des sujets de donner oralement des renseignements. On a déterminé quelle était la teneur en césium 137 des produits alimentaires consommés par chaque groupe pendant les intervalles entre les dosages.
Pour les deux groupes, la charge de césium 137 est demeurée sensiblement constante (hommes 17,5 nc, femme 11 nc) jusqu'à fin juin. À partir de ce moment, la teneur du lait et de la viande en césium 137 a approximativement doublé en une huitaine de jours. À fin août, la charge corporelle de césium 137 avait augmenté, dans l'un comme dans l'autre échantillon, de 40% par rapport à ce qu'elle était au printemps. À la mi-octobre, on relevait chez les hommes une augmentation de 22% et chez les femmes une augmentation de 14% par rapport aux chiffres relevés en août.

La détermination de la période biologique du césium 137 d'après les quantités de produits alimentaires consommées fait l'objet de quelques observations.

CARGA CORPORAL DE CESIO-137 EN CIERTOS GRUPOS DEMOGRAFICOS DEL SUR DE FINLANDIA EN 1961-1963. Con motivo del estudio de la carga corporal de cesio-137 en los lapones de Finlandia se realizaron asimismo varias determinaciones en grupos demográficos más limitados residentes en el sur de Finlandia.

En noviembre de 1961 se sometió al recuento de cesio-137 y del potasio a un grupo de once habitantes de Helsinki (cinco hombres y seis mujeres, de edad comprendida entre 15 y 54 años). Nueve de ellos trabajaban en laboratorios y los dos restantes eran escolares. Todos gozaban aparentemente de buena salud. Para estudiar su régimen alimenticio, se recurrió al método de las entrevistas.

Un año más tarde se repitió el recuento de diez personas del grupo en el antropogammámetro móvil del Departamento de Radiología de la Universidad de Helsinki. La carga corporal media de cesio-137 en los cinco hombres (promedio de edades: 29 años) había aumentado de 20,4 nc en noviembre de 1961 a 26,4 nc en noviembre de 1962, mientras que en las cinco mujeres (promedio de edades: 34 años) de 2,9 nc a 8,7 nc. El contenido de potasio no acusó variaciones (dentro de un margen de 2%), manteniéndose en 140 g para los hombres y 100 g para las mujeres.

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A fin de efectuar estudios más detallados, a fines de 1963 se eligieron grupos testigo más numerosos y se sometieron al recuento cuatro veces, a saber, en febrero, marzo, agosto y octubre, respectivamente. El grupo masculino estaba compuesto por 25 soldados de un batallón de infantería (edad: 19 años; peso medio: 65 kg); el femenino por 24 estudiantes de economía doméstica (edad: 22 años; peso medio: 60 kg). En ambos casos, el régimen alimenticio pudo comprobarse en detalle: resultó ser el típico de la población de Finlandia. Además, se estudió el consumo individual de alimentos de cada sujeto, mediante entrevistas y recurren a muestras de peso conocido. Se determinaron los contenidos de cesio-137 de dos grupos correspondientes a los intervalos entre las mediciones.

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THE BODY BURDEN OF Cs\textsuperscript{137}

En ambos grupos, el contenido de cesio-137 permaneció casi constante (hombres: 17,5 nc; mujeres: 11 nc) hasta fin de junio, cuando la proporción de cesio-137 en la leche y la carne prácticamente se duplicó en un plazo de una semana. A fin de agosto, la carga corporal de cesio-137 había crecido casi 40% con respecto al valor registrado en la primavera; a mediados de octubre el contenido en los hombres había aumentado en un 22% y en las mujeres en un 14% con respecto a agosto. Los autores discuten los resultados de la determinación del semiperíodo biológico del cesio-137 absorbido con los alimentos.

1. SUBJECTS STUDIED

In connection with the investigations of the Cs\textsuperscript{137} body burden of Finnish Lapps (see the following paper) several measurements of smaller groups of people living in southern Finland were carried out.

The two first measurements were performed with eleven inhabitants of Helsinki, six women and five men, 15 to 54 yr old, who were counted for Cs\textsuperscript{137} and potassium in Stockholm in November 1961, and in Helsinki in November 1962. Nine of these persons were laboratory workers and two were schoolboys. They were apparently healthy and their diet and food consumption, which were checked by the interview method, were typical for city people and intellectual workers.

For more detailed studies larger "control groups" were selected at the beginning of 1963. Attempt was made to get these groups as homogeneous as possible regarding the age, diet, and physical activity. For the group of men 25 privates of an infantry battalion (age 19, average weight 65 kg), for that of women 24 girl students of a "household school" (a domestic science college) (age 22, average weight 60 kg), were selected. In both cases the diet was checked and could be considered to be an average Finnish diet. In addition, the individual food consumption of each female subject was determined by interviews with the aid of weighed samples. For the male subjects the study of individual diets was not possible, but their average food consumption could be determined from the food consumption records of the battalion. The Cs\textsuperscript{137} contents of all main food items were determined in each time period between the measurements in order to make possible calculations of the Cs\textsuperscript{137} intake.

2. WHOLE-BODY COUNTING

The second measurement of the smaller groups in November 1962 and the first measurement of the larger groups in February, 1963 were performed by the mobile counter (for a description of this counter and its calibration, see next paper), but the later measurements were performed in the iron room of this Department. This "room" has the same counting geometry and efficiency but a lower background than the mobile counter and it was calibrated in the same way as the latter. The calibrations of the two counters were cross-checked and the counting efficiency was checked periodically by phantom measurements. Intercalibration of our counters by "live" cross-countings with the whole-body counters of the International Atomic Energy Agency (Dr. R.A. Dudley) and Lund University (Dr. K. Lidén) proved that all these counters gave the same results within 4%.
One standard deviation of single measurements in the present study was 5 to 15% for Cs\textsuperscript{137}, 10% for potassium.

3. RESULTS OF WHOLE-BODY COUNTING

The results of the first two measurements are presented in Table I. As can be seen, the increase from November 1961 to November 1962 was about threefold in the female group and slightly more than twofold in the male group. This difference is partly due to the fact that in November 1961 the body burden of one of the male subjects was three times the average, due to elk-meat consumed, and increases the mean value of men in November 1961.

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Weight</th>
<th>Height</th>
<th>(PC Cs\textsuperscript{137})</th>
<th>(gK)</th>
<th>(PC Cs\textsuperscript{137}/gK)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women: Average</td>
<td>34</td>
<td>60</td>
<td>163</td>
<td>2.9</td>
<td>8.7</td>
<td>99</td>
</tr>
<tr>
<td>Men: Average</td>
<td>29</td>
<td>77</td>
<td>177</td>
<td>8.4</td>
<td>18.4</td>
<td>139</td>
</tr>
</tbody>
</table>

* Subjects measured in November 1961, at AB Atomenergi, Stockholm
Same subjects re-measured in November 1962, at the University of Helsinki, 5 women and 5 men.

The results of the measurements of the larger groups, 20 to 25 subjects in each, are presented in Table II. As can be seen from this Table, the women's body burden of Cs\textsuperscript{137} (PC/g K) increased by 65% and the men's by 89% from February to December 1963. The potassium contents remained unchanged in both groups (women 1.6; men 2.2 g K/kg). The results of all measurements are summarized in Fig. 1.

4. Cs\textsuperscript{137} IN MILK, BEEF AND TOTAL DIET

The results of Cs\textsuperscript{137} measurements in milk by two laboratories are presented in Fig. 2. As can be seen, the level of Cs\textsuperscript{137} in Helsinki milk (one-day samples) was relatively constant (about 100 PC/l) until the beginning of July when it increased by about 60% within a short time (about one week). This higher level was then maintained until the end of the year.

The results of analyses of average monthly samples from two powdered milk factories, Somero and Nastola, were obtained from the Institute of
TABLE II

BODY BURDEN OF Cs137 IN PEOPLE OF SOUTHERN FINLAND FROM FEBRUARY 1963 TO MARCH 1964

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cs137 (nc)</td>
<td>Cs137 (pc/gK)</td>
<td>Cs137 (pc/gK)</td>
<td>Cs137 (pc/gK)</td>
<td>Cs137 (nc)</td>
<td>Cs137 (pc/gK)</td>
</tr>
<tr>
<td>Women:</td>
<td></td>
<td></td>
<td>11.9</td>
<td>10.9</td>
<td>16.9</td>
<td>17.5</td>
<td>17.3</td>
<td>18.5</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td>22</td>
<td>60</td>
<td>164</td>
<td>112</td>
<td>112</td>
<td>114</td>
</tr>
<tr>
<td>Min.</td>
<td>6 8</td>
<td>70</td>
<td>75</td>
<td>10.7</td>
<td>13.7</td>
<td>13.7</td>
<td>14.2</td>
<td>14.7</td>
</tr>
<tr>
<td>Max.</td>
<td>17 3</td>
<td>146</td>
<td>171</td>
<td>39.6</td>
<td>52.4</td>
<td>56.1</td>
<td>28.4</td>
<td>27.7</td>
</tr>
<tr>
<td>Men:</td>
<td></td>
<td></td>
<td>16.4</td>
<td>13.2</td>
<td>13.2</td>
<td>28.4</td>
<td>22.4</td>
<td>20.4</td>
</tr>
<tr>
<td>Average</td>
<td>19.6</td>
<td>181</td>
<td>191</td>
<td>39.8</td>
<td>38.8</td>
<td>239</td>
<td>286</td>
<td>46.4</td>
</tr>
<tr>
<td>Min.</td>
<td>19.6</td>
<td>181</td>
<td>191</td>
<td>39.8</td>
<td>38.8</td>
<td>239</td>
<td>286</td>
<td>46.4</td>
</tr>
<tr>
<td>Max.</td>
<td></td>
<td></td>
<td>19.6</td>
<td>181</td>
<td>191</td>
<td>39.8</td>
<td>38.8</td>
<td>239</td>
</tr>
</tbody>
</table>

* 24 Students of Household School and 25 Privates of Infantry Battalion
Radiation Physics [1]. The monthly mean values from the Somero area (23.5°E, 60.5°N) are on the same level but show a less sharp maximum than the one-day samples from Helsinki, but those from the Nastola area (26.7°E, 61°N) are essentially higher. The average Helsinki levels marked in Fig. 2 were used in this study.

The Cs\textsuperscript{137} content of beef, too, was constant (550 pc/kg fresh weight) until July when it increased by about 80% (to 1000 pc/kg fresh weight).

Calculations of the Cs\textsuperscript{137} content in the total diet showed that the intake of Cs\textsuperscript{137} through milk and beef was 70% (46 + 24%) in the female group. In the male group it was 72% (47 + 25%) of the total intake.

After the increase of the activity level in July the total intake of Cs\textsuperscript{137} by the women was 240 pc/d per subject (=4 pc/kg body weight/d), that of the men 470 pc/d per subject (7.2 pc/kgd). However, the latter value is based on the battalion's food consumption lists and is uncorrected for losses in preparation and food left uneaten. Since these losses can be estimated to be about 15 to 25%, the food intake value for men may be as much as 25% too high. However, the error in the Cs\textsuperscript{137} intake is lower than this, about 15±5%, since milk, the main source of Cs\textsuperscript{137} in the diet, is usually consumed nearly quantitatively.
5. BIOLOGICAL HALF-TIME OF Cs\(^{137}\)

The sharp increase in the dietary intake of Cs\(^{137}\) in July made possible calculations of the approximate half-time of this nuclide in women and men.

The change from the lower to the higher level of Cs\(^{137}\) intake was assumed to have taken place on 10 July. The body contents of Cs\(^{137}\) were assumed to have remained unchanged from May until this date. For the calculations, Cs\(^{137}\) values (nc/kg body weight) of only those subjects (18 women, 16 men) who had been subjected to every measurement, were used. These values with the calculated standard deviation and its confidence interval are presented in Table III.

The mathematical equation used in the calculation was based on the following assumptions:

From 10 July onwards the subjects had a constant daily intake, \(a\), nc Cs\(^{137}\). Simultaneously Cs\(^{137}\) was excreted from the body at a rate \(k\), which is proportional to the body content \(A\).

The change in the Cs\(^{137}\) body content is

\[
\frac{dA}{dt} = \frac{a}{w} - kA \times dt,
\]

in which \(w\) = mean body weight in kg. The solution of Eq. (1) is

\[
A = A_0 + \left(\frac{a}{wk} - A_0\right)(1 - e^{-kt}),
\]

which gives the average Cs\(^{137}\) body content of the group at the time \(t\). In Eq. (2) \(k\) is unknown and was determined for both groups by the "best fit" to the observed values.

For the female group the body content (nc/kg) is

\[
A_{\text{fem}} = 0.309 - 0.129 \times e^{-0.0129 t},
\]

and for the male group

\[
A_{\text{male}} = 0.527 - 0.257 \times e^{-0.0136 t}.
\]

Cs\(^{137}\) body content (nc/kg body weight) in control groups of 16 men (age 19) and 18 women (age 22)

The same subjects in all measurements. For calculation of the theoretical curves, see text.
<table>
<thead>
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<tbody>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of measurements (n)</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Mean (x)</td>
<td>0.268</td>
<td>0.297</td>
<td>0.382</td>
<td>0.383</td>
<td>0.304</td>
</tr>
<tr>
<td>σ of single measurement (s)</td>
<td>0.040</td>
<td>0.055</td>
<td>0.045</td>
<td>0.048</td>
<td>0.055</td>
</tr>
<tr>
<td>σ of mean (σ)</td>
<td>0.009</td>
<td>0.013</td>
<td>0.011</td>
<td>0.011</td>
<td>0.013</td>
</tr>
<tr>
<td>95% conf. interv. of x</td>
<td>0.160-0.590</td>
<td>0.220-0.374</td>
<td>0.259-0.394</td>
<td>0.238-0.394</td>
<td>0.276-0.391</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of measurements (n)</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Mean (x)</td>
<td>0.270</td>
<td>0.385</td>
<td>0.468</td>
<td>0.479</td>
<td>0.479</td>
</tr>
<tr>
<td>σ of single measurement (s)</td>
<td>0.056</td>
<td>0.050</td>
<td>0.057</td>
<td>0.057</td>
<td>0.056</td>
</tr>
<tr>
<td>σ of mean (σ)</td>
<td>0.014</td>
<td>0.013</td>
<td>0.014</td>
<td>0.014</td>
<td>0.013</td>
</tr>
<tr>
<td>95% conf. interv. of x</td>
<td>0.240-0.500</td>
<td>0.354-0.413</td>
<td>0.428-0.496</td>
<td>0.428-0.530</td>
<td>0.428-0.530</td>
</tr>
</tbody>
</table>

* 18 Students of Jarvenpaa Household School and 16 Privates of Infantry Battalion same subjects in each measurement
The theoretical curves are presented in Fig. 3, with the measured values and their 95% confidence limits indicated by bars.

The "apparent half-time" of the Cs\textsuperscript{137} uptake thus obtained is 51 d for the men and 54 d for the women.

We know, however, that about 10% of the daily Cs\textsuperscript{137} intake has a very high excretion rate with a half-time of about 1 d [2, 3]. If we take this into account and use Eq. (3) (for the derivation of this equation (see ref. [3]),

\[ A = A_0 e^{-k_1 t} + \frac{(1-p)a}{wk_1} [1 - e^{-k_1 t}], \]

in which

\[ k_1 = \text{the slow biological fractional excretion rate of Cs}^{137} \text{ d}^{-1} \]

\[ p = \text{fraction of the daily intake being excreted at the fast excretion rate}, \]

we get for the long half-time components: 60 d for women and 55 d for men.

We also know (see section 4) that the men's Cs\textsuperscript{137} intake calculated from food consumption lists is estimated to be 15 ± 5% too high. When this correction is made we get 64 d for men. Thus, the half-times for the "slow component" obtained in this investigation are

- women 60 ± 9 d,
- men 64 ± 16 d.

The errors given include both those of the Cs\textsuperscript{137} intake values, which were considered to be ±10% for women and ±15% for men (nutritional chemist's estimate) and those of the average values of the Cs\textsuperscript{137} body burdens, which were ±5% (68% conf. interv.) for both groups.

The above values are in excellent agreement with the value of 68 d obtained by Lidén and Naversten for nine Swedish Lapps [3], p. 33 and with the values of 65 ± 10 d for large groups (33 women, 50 men) of Finnish Lapps [3]. They are also in satisfactory agreement with those obtained by us for six adult subjects from Helsinki, who took orally 300 to 400 nc Cs\textsuperscript{137} and were then measured periodically for six months in 1962. For these subjects the following half-times for the "slow component" were obtained:

- women (mean age 35): 56, 53 and 42, mean 50 d;
- men (mean age 40): 53, 81 and 93, mean 77 d.

The latter groups are too small to give statistically significant results, as biological half-times of Cs\textsuperscript{137} in individuals differ greatly. We have observed in the present study that the Cs\textsuperscript{137} body content in the steady state in one of two girls of the same age, weight and dietary Cs\textsuperscript{137}-intake may be 40% higher than in the other, and other authors have made similar observations (e.g. [4]). RUNDO [5] gives as the standard deviation ±35% for the biological half-time of Cs\textsuperscript{137} in man.

However, the present groups as well as those of the Finnish Lapps measured earlier [3] are large enough to give statistically significant results, and all the above half-times are shorter than most obtained outside Scandinavia (for a recent review see RUNDO [6]). Rundo, for instance, gives as the average for adults in England 105 d ± 35% [5]. HUYCKE and OBERHAUSEN from Landstuhl, Germany, give a mean half-time of 140 d.
for persons older than 22 yr [4]. Half-times longer than 80 d are definitely impossible for the large groups we have measured. Therefore, it seems that in the people of northern countries Cs$^{137}$ has a shorter biological half-time than elsewhere. This may be due to differences in the diet.

ACKNOWLEDGEMENTS

We gratefully acknowledge a grant from the Finnish Atomic Energy Commission by which this investigation was made possible. We also wish to thank Miss Aili Jokelainen for the dietary data, Mr. O. Castren for Cs$^{137}$ values of the monthly milk samples, Dr. Esko Kaila for aid in the mathematical calculations, and Mr. I.Ó. Anderson for the first whole-body measurements of the smaller control groups in Stockholm. We are much indebted to Mrs. A. Tare, Director of the Jarvenpaa Domestic Science College, and to Major General P. Somer, M.C., Surgeon General, Finnish Defence Forces, for aid given in selection of the large control groups.

REFERENCES

MEASUREMENTS OF CAESIUM-137 IN FINNISH LAPPS IN 1962-1964 BY A MOBILE WHOLE-BODY COUNTER

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Abstract — Résumé — Аннотация — Resumen

MEASUREMENTS OF CAESIUM-137 IN FINNISH LAPPS IN 1962-1964 BY A MOBILE WHOLE-BODY COUNTER. The construction, calibration and use in-field investigations of a mobile whole-body counter of the type developed by K. Lidén et al. in Sweden are described.

The lead shield of the present system (2 t) is located in the middle of a covered heavy truck. The subject is surrounded by a 4-cm thick lead coffin, the NaI(Tl) crystal (5 in. diam. x 3 in) being protected from the other directions than the coffin by 8 cm of lead. The instrumentation consists of a 512-channel analyser, printer, x, y-recorder, and stabilizer, which are kept in shock- and dust-proof boxes during transport. The truck is provided with a thermostated heating system and contains two dressing cubicles.

The system was calibrated for caesium-137 by two methods:

1. By administering per os a precisely known amount (200 to 300 nCi) caesium-137 to several subjects and determining the counting efficiency after 3 to 6 d. The excreted portion of caesium-137 was determined by collecting and analysing the faeces and urine.

2. By counting a plastic phantom filled with 70 kg of a solution containing 1552 nCi caesium-137. The first method gave a 4.6% higher efficiency than the second. The efficiency obtained by the first method was adopted as the true calibration. This was also checked by three inter-calibration measurements with two other whole-body counting laboratories. The agreement was good (within 1 to 4%).

For potassium a preliminary calibration was made by the use of the phantom. The efficiency is 2.51 cpm/nCi caesium-137 (0.60-0.72 MeV, 20 channels), and 0.145 cpm/g K (1.38-1.55 MeV, 30 channels). When the truck is parked on rock, the corresponding background counts with a 70 kg sugar phantom are 77 cpm and 58 cpm, respectively. On sandy soil the background is about half of that on rock.

With this mobile counter three field investigations were carried out in Finnish Lapland. In May 1962 218 Lapps, statistically representative groups from the three Finnish Lapp countries, Inari, Karesuanto and Utsjoki, were counted. This study included also dietary and medical investigations. Both in September 1962 and in March 1963 about 100 Lapps were counted.

The first measurement of caesium-137 in Finnish Lapland was carried out in the Inari county in October 1961 by the Swedish counter. The average body burden of the most important group, reindeer breeders, men (age 20 to 50 yr), was, in the four measurements:

- October 1961 274 nc (33 subjects),
- May 1962 508 nc (20 subjects),
- September 1962 307 nc (9 subjects),
- March 1963 646 nc (10 subjects).

In other groups the body burden was considerably lower and the seasonal variations slightly different. The results of the four investigations are compared and discussed with reference to the results of the dietary and medical investigations.
300 μc) de césium 137 et en déterminant l’efficacité de comptage après trois à six jours. On a recueilli et analysé les matières fécales et l’urine pour déterminer la fraction excrétée de césium 137.

2. En effectuant le comptage sur un fantôme en matière plastique qui renfermait 70 kg d’une solution contenant 1852 nc de césium 137.

Avec la première méthode, l’efficacité de comptage a été de 4,6% plus élevée qu’avec la seconde. La première méthode a été adoptée comme donnant un étalonnage exact. Cette opération a également fait l’objet d’un contrôle par comparaison inter-laboratoires de trois mesures d’étalonnage faites avec deux autres anthropogammamètres. La concordance était bonne (de 1 à 4%). Pour le potassium, on a fait un étalonnage préliminaire à l’aide du fantôme.

L’efficacité est de 2,51 cpm/nc de césium 137 (0,60 - 0,72 MeV, 20 canaux) et 0,145 cpm/g de potassium (1,38 - 1,55 MeV, 30 canaux). Lorsque le camion stationne sur un sol pierreux, les bruits de fond correspondaient, avec un fantôme en sucre de 70 kg, à 77 et 58 cpm respectivement. Sur un sol sablonneux, les bruits de fond atteignent environ la moitié de ces dernières chiffres.


Précédemment, une première enquête sur la charge corporelle de césium 137 chez les Lapons de Finlande avait été faite en octobre 1961 dans le district d’Inari au moyen de l’appareil suédois. Les quatre enquêtes ont donné les résultats suivants relatifs à la charge corporelle moyenne pour le groupe le plus important, celui des élevage :

- octobre 1961 - 274 nc (33 sujets), mai 1962 - 508 nc (20 sujets);

Pour d’autres groupes, la charge corporelle était sensiblement moins élevée et les fluctuations saisonnières différaient légèrement. L’auteur compare les résultats des quatre enquêtes et les examine par rapport à ceux des recherches sur l’alimentation et la santé.
DETERMINACIÓN DEL CESIO-137 EN LAPONES FINLANDESES, EN 1962-1964, MEDIANTE UN ANTROPOGAMMAMÉTRO MÓVIL. El autor describe la construcción y calibración de un antropogammamétero móvil, del tipo ideado en Suecia por K. Lidén y colaboradores, así como su aplicación en las investigaciones en el terreno.

El blindaje de plomo de este aparato (peso: 2 t) se encuentra colocado en el centro de un pesado camión cerrado; el sujeto está rodeado por un cajón de plomo de 4 cm de espesor, quedando protegido el cristal de NaI(Tl) (de 12,5 cm de diámetro por 7,5 cm de altura) por un espesor de 8 cm de plomo en todas las direcciones, salvo la del cajón. El instrumental está integrado por un analizador de 512 canales, un impresor, un registrador en coordenadas cartesianas y un estabilizador, que se guardan para el transporte en cajas herméticas a prueba de choques. El camión posee un circuito de calefacción con termostato y dos pequeños vestuarios.

A fin de calibrar el sistema para las determinaciones de cesio-137, se aplican dos métodos:

1. Se administra por vía oral una cantidad exactamente conocida de cesio-137 (200 a 300 nc) a varios sujetos y se determina la eficiencia de recuento al cabo de 3 a 6 d. Se determina la porción excretada de cesio-137 recogiendo y analizando las heces y la orina.

2. Se somete al recuento un maniquí de material plástico relleno con 70 kg de una solución que contiene 1552 nc de cesio-137.

Con el primer método se obtuvo una eficiencia 4,6% mayor que con el segundo. Se adoptó como calibración real la obtenida mediante el primer método. Además, se controló su valor por medio de tres mediciones de intercalibración con otros dos laboratorios móviles de antropogammametría. La concordancia es satisfactoria (diferencias menores que 1 a 4%). Para el potasio se empezó por efectuar una calibración preliminar usando el maniquí.

La eficiencia es 2,51 cuentas/min por nc de cesio-137 (0,60 a 0,72 MeV, 20 canales) y 0,145 cuentas/min por g de K (1,38 a 1,55 MeV, 30 canales). Si se estaciona el camión sobre un suelo rocoso, las actividades de fondo correspondientes, con un maniquí relleno de 70 kg de azúcar, son 77 cuentas/min y 58 cuentas/min, respectivamente. Sobre un suelo arenoso, la actividad de fondo es aproximadamente la mitad de las anteriores.

Con este contador móvil se llevaron a cabo tres campañas de mediciones en la Laponia finlandesa. En mayo de 1962 se sometieron al recuento 218 lapones de grupos demográficos estadísticamente representativos de los tres condados lapones finlandeses de Inari, Karesuando y Utsjoki. El estudio comprendía investigaciones dietéticas y clínicas. En septiembre de 1962 y marzo de 1963 se efectuó la determinación de la radiactividad en otros 100 lapones, aproximadamente.

La primera determinación del cesio-137 en los lapones finlandeses se efectuó en el condado de Inari en octubre de 1961, con el contador sueco. La carga corporal media del grupo más importante, formado por criadores de renos (hombres de edad comprendida entre 20 y 50 años), evaluada en las cuatro mediciones fue:

- en octubre de 1961, 274 nc (33 sujetos);
- en mayo de 1962, 508 nc (20 sujetos);
- en septiembre de 1962, 307 mmk guru (5 sujetos);
- en marzo de 1963, 648 mmk guru (10 sujetos).

En otros grupos, la carga corporal fue mucho menor y las variaciones estacionales fueron algo diferentes. El autor compara los datos obtenidos en las cuatro investigaciones y los examina relacionándolos con los resultados de los estudios dietéticos y clínicos.

1. INTRODUCTION

Analyses of strontium-90 and caesium-137 in plant and animal samples from northern Norway and Finland revealed during 1958-1960 an efficient radionuclide "food chain" leading from lichens through reindeer to man (for a recent review, see [1]). Since reindeer meat constitutes a staple diet in
the sub-arctic regions of Scandinavia, elevated body burdens of these nuclides especially in Lapps, the main consumers of reindeer meat, could be assumed [1].

The first direct measurements of caesium-137 body burdens in Lapps were performed by K. Lidén by whole-body counting at Lund, Sweden, in the spring of 1961 [2]. The average caesium-137 body burden of the three Lapps measured, about 300 nc, was approximately forty times higher than the general population average. Spurred by this important result Lidén and his associates developed in the summer of 1961 a semi-portable whole-body counter [3] with which they counted 170 people in the Swedish Lapland during September, 1961 [4]. One month later 180 people were counted at Inari, Finland, with the same equipment, as a joint Finnish-Swedish project. Full results of the latter survey have been published [5]; they include also an investigation of the diet and the determination of its caesium-137 content for the population groups studied. The results obtained in Sweden and Finland were rather similar and fully confirmed those of Lidén's first measurements [2]. In Finland the male reindeer-breeding Lapps contained on the average 245 nc caesium-137, about 30 times the Helsinki average, while females and children had an average of 122 and 51 nc, respectively. From the dietary and whole-body data, a biological half-time of 65 d for adult Lapps was calculated. It could be shown, too, that the Lapps' caesium-137 body burden undergoes a large seasonal variation, the measured October values representing the annual minimum level.

Prompted by the new period of nuclear weapon tests a mobile whole-body counter installed in a covered truck was constructed in our laboratory during the winter 1961-1962 by a grant obtained from the Finnish Atomic Energy Commission. One hundred and seventy adult subjects and 44 children of 10 to 14 yr, representing the whole Finnish Lapp population, were selected by a random sampling method and measured by the mobile counter in May, 1962. A smaller number of the same subjects were re-measured in September, 1962, March 1963, and April 1964. The main investigation in May, 1962 also included detailed dietary, medical and clinical studies, of which partial results have been published [6, 7]. The full results of this investigation will soon be published. This paper contains a description of the mobile counter and its calibration, together with partial results of the four whole-body measurements.

2. DESCRIPTION OF THE MOBILE WHOLE-BODY COUNTER

The Lidén counter [3] with Argonne Chair geometry was chosen as the starting point for the development of our truck-installed system. This geometry has the advantages of higher efficiency and smaller dimensions compared with the bed geometry. The lead shield (2 t) of our counter is located in the middle of a covered heavy truck (Hanomag Kurier diesel, Fig. 1). The subject is surrounded by a 4-cm-thick lead coffin, the NaI(Tl) crystal (5 in diam, X3 in) being protected from other directions than the coffin by 8 cm of lead (Fig. 2). The instrumentation consists of a 512-channel analyzer, stabilizer, high voltage set, printer, and x,y-recorder, which are kept in shock- and dust-proof boxes during transport. The truck is provided with a thermostatic heating system and contains two dressing cubicles.
When the subject in disposable paper pyjamas enters the coffin, one lead wall and the crystal with its 3σ lead shield are rolled aside (Fig. 2). The sliding wall and crystal are then rolled back and locked. During the measurement photons from outside the shield cannot hit the crystal unless they have either penetrated the lead shield or been scattered and thus reduced in energy. The temperature is kept constant within ±1°C. The drift is less than three channels per 24 h. The Lapps are routinely measured for 10 min at the energy range 0.08 - 1.60 MeV using 256 channels.
The counter was calibrated for caesium-137 by two methods:
(1) Administering orally a precisely known amount (200 to 300 nc) of caesium-137 to several subjects and determining the counting efficiency after 3 to 6 d. The excreted portion of caesium-137 was determined by collecting and analysing the faeces and urine;
(2) Counting a plastic phantom (Fig. 3) filled with 70 kg of water containing 1552 nc caesium-137.

Aliquots of the above caesium-137 solutions were compared with an "absolute' standard" of the Radiochemical Centre, Amersham, in a well counter.

The first method gave a 4.6% higher efficiency than the phantom calibration. The efficiency obtained in vivo was adopted as the true calibration.

For potassium the counter was calibrated by the following method: 1 μc potassium-42 (from an absolute standard of the Radiochemical Centre, Amersham) was administered orally to four subjects; the urine was collected for 10 to 15 h and counted for potassium-42; the subject was then counted and corrections made for the potassium-42 excreted in urine. This gave the in vivo efficiency for potassium-42. The "in phantom" efficiencies were then determined for natural potassium and potassium-42. From the values obtained the efficiency in vivo for natural potassium is obtained in the following way:

\[
\text{Eff. } K_{\text{in vivo}} = \text{Eff. } K_{\text{phantom}} \times \frac{\text{Eff. } K^{42}_{\text{in vivo}}}{\text{Eff. } K^{42}_{\text{phantom}}}
\]

The efficiency of the mobile counter is 2.51 ± 0.05 cpm (1σ) per nc caesium-137 (0.60-0.72 MeV, 20 channels) and 0.145 ± 0.004 (1σ) cpm per 1 g K (1.38-1.55 MeV, 30 channels), measured by the above method. The phantom filled with a solution of natural potassium gave a 2% lower value.
When the truck is parked on rock, the corresponding background counts with
a 70 kg sugar phantom are 77 and 58 cpm for the energy ranges of the photo­
peaks of caesium-137 and potassium, respectively. Intercalibration measure­
ments with our iron room (see preceding paper) were in good agreement
(within 2%).

A typical Lapp spectrum and several background spectra are presented
in Fig. 4. When taking all non-systematic errors into account one sigma is
in a single 10-min measurement for a 100 nc caesium-137 body burden ±4 nc,
and for a body content of 100 g K, ± 23 g K. The systematic error of cali­
bration should not exceed 2% for caesium-137 and 3% for K (1σ). Corrections
for weights differing from 70 kg are performed as in [5].

![Gamma spectra obtained by the mobile whole-body counter](image)

**Fig. 4**

1. Background spectrum when the truck is standing
   on rocky ground, without sugar phantom
   (Helsinki)
2. Background spectrum on rocky ground with
   a 70 kg sugar phantom (Helsinki)
3. Background spectrum on sandy soil with the
   sugar phantom (Inari)
4. Net spectrum of a subject with ca. 380 nc Cs
   and ca. 135 g K.

### 4. SELECTION OF SUBJECTS

The study was carried out in the three Finnish Lapp counties, Enontekiö,
Inari and Utsjoki (Fig. 5). The adult subjects, 20 to 50 yr of age, were
selected from church registers by a random sampling method and personal
invitations were sent by mail two weeks in advance. The ratio of men to
women invited was 2:1. All invited subjects did not attend the investigation, non-attendance being for three main reasons: (1) The invitation had not reached the subject due to slow mail transport (12 to 20%); (2) The subject was prevented from attending by sickness, or due to children, etc. (3-14%); (3) The subject was not willing to come (0 to 6%).

In the different groups the subjects who arrived comprised 50 to 88% of those invited. If the subjects who had not received the invitation are excluded, the average attendance was about 85%. This good result was obtained only by diligently fetching to the study all the subjects whose location was known. An aeroplane was hired and made several flights to the mountains where the reindeer breeders were known to live. Altogether, 172 adults and 44 children were studied. All children of 10 to 14 yr of age whose family members had been invited were taken to the study from the local schools.

The whole-body counting was repeated in September, 1962, March 1963 and April 1964 at Inari and in March 1963 also at Enontekiö. Invitations were sent to the same subjects who were originally selected in the spring of 1962. About 100 adults arrived at each of the later studies, including several who could not attend the first study. No children were measured in April 1964 as many of those who had been measured earlier had left the school.

5. RESULTS AND DISCUSSION

Concise results of the four whole-body measurements are presented in Tables I and II. The results for several minor groups, for example, the Utsjoki Lapps in the three last measurements, and those of subjects who could not be justly included in the occupational and dietary groups chosen, are not included in these Tables.

When the results of the main investigation (May, 1962) from Tables I and II are compared, it can be seen that the reindeer breeding Lapps in regions 1 and 2 (Fig. 5), Enontekiö and Inari, have about similar body burdens. The Inari Lapps are settled, the Enontekiö Lapps are nomadic in summer, and both have similarly high reindeer meat consumption, the adult males eating about 20 kg per person per month in winter [5, 6]. The Utsjoki Lapps—
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Enontekiö (Region 1)</th>
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<td></td>
<td>Reindeer breeders, same in 1962 and 1963</td>
<td>25-50</td>
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</tr>
<tr>
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<td>Reindeer breeders, same in 1962 and 1963</td>
<td>23-47</td>
</tr>
</tbody>
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**TABLE 1**

**Ca^{137} Body Burden of Lapps in the Enontekiö and Utsjoki Counties, Finland in May 1962 and March 1963**
TABLE II

BODY BURDEN OF Cs$^{137}$ IN LAPPS AT INARI, AND IN A CONTROL GROUP IN HELSINKI, FINLAND, FROM OCTOBER 1961 TO APRIL 1964 *

<table>
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<td>Males:</td>
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<tr>
<td>Reindeer breeders</td>
<td>272</td>
<td>498</td>
<td>307</td>
<td>646</td>
<td>1105</td>
<td>(+30)</td>
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<td>(Number of subjects)</td>
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<td>(20)</td>
<td>(9)</td>
<td>(10)</td>
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<td>189</td>
<td>404</td>
<td>863</td>
<td>(+25)</td>
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<td>fishers</td>
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<td>(16)</td>
<td>(4)</td>
<td>(2)</td>
<td>(11)</td>
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<tr>
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<td>187</td>
<td>132</td>
<td>205</td>
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<td>-</td>
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<td>Adult males:</td>
<td>8.4</td>
<td>~8</td>
<td>17.9</td>
<td>16.4</td>
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<td>(+105)</td>
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<td>(10)</td>
<td>(2)</td>
<td>(4)</td>
<td>(6)</td>
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<td>128</td>
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<td>(+80)</td>
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<tr>
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<td>70</td>
<td>82</td>
<td>-</td>
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<td>Adult females</td>
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<td>9.3</td>
<td>111.5</td>
<td>18.6</td>
<td>(+188)</td>
<td>0.204</td>
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*Age group 20-50 yr, adults, and 10-14 yr, pupils.
CAESIUM-137 IN FINNISH LAPPS

(region 3, Fig. 5) have about 40% lower caesium-137 body burden than the Lapps of regions 1 and 2. This is due to their lower reindeer meat and fish consumption [7]; in addition, the bulk of fish consumed at Utsjoki is salmon and cod from the Arctic Ocean, which have an extremely low caesium-137 content [8].

The changes of the caesium-137 body burdens of Inari Lapps can be followed from October, 1961 to March 1964 (Table II). In the first study the seasonal change of the caesium-137 body burden was calculated on the basis of the dietary data and 65 d half-time [Fig. 9 of ref. 5]. The calculated values for 15 May, 1962 were 630, 230 and 100 nc for men, women and boys of the reindeer-breeding Lapps. The values measured between 12 May and 15 May, 1962 were 498, 237 and 83 nc, respectively.

The agreement is satisfactory since the groups are rather different. That of October, 1961 (selected by a cluster sampling method) contained only full-time reindeer breeders, while that of May, 1962 (randomly selected from church registers) also contained "part-time breeders", owners of small herds, who also have a second occupation and consume less reindeer meat. If the seasonal variation is overlooked, there was no significant increase in the caesium-137 values until September, 1962. The fallout from the tests of the autumn of 1961 came down mainly in May-June, 1962, but since the reindeer does not eat lichen in summer this fallout did not reach the reindeer Lapps before winter, 1962. In March, 1963 there was already a significant increase in the caesium-137 body burdens compared with the May, 1962 values. If the whole groups are compared, the increase in the male reindeer breeders was 30% (from 498 to 646 nc). If the same ten subjects only are compared, it was 34%, from 483 to 646 nc (not given in Table II). The fallout from the "dirty" tests in 1962 reached the Lapps during last winter. The present level (April, 1964) in the different Lapp groups is from 120 to 360% higher than in the spring of 1962. As can be seen from Table II the increase is higher in the control groups of Helsinki inhabitants who do not consume reindeer meat regularly. This is understandable as lichens and reindeer meat remained relatively radioactive throughout the test moratorium.

In the last column of Table II the measured values per gram potassium are also given. As the counting error of potassium determinations with a 10-min counting time is large, these ratios are much less accurate than the total body values of caesium-137. One sigma of the mean potassium content for 10 subjects having 150 g potassium per subject is about ±5%, that for a group of five subjects about ±7% (counting error alone).

Caesium-137 total body values for the year 1962 for Swedish Lapps [4] and Alaskan Eskimos [9] have been published. The average for 35 male reindeer breeders at Jokkmokk, Sweden, was 435 nc in April and that of one group of Eskimos, at Anaktavuk Pass, in the summer of 1962, 474 nc, compared with 498 nc at Inari in May. The maximum values were even closer, Finland and Alaska 790, Sweden 740 nc.

Thus the situation seems to be very similar in Scandinavia and Alaska. In April, 1964 the highest individual caesium-137 values in Inari were 2.66 μc for males and 1.01 μc for females. The first of these is very close to the MPBB value of the ICRP, 3 μc in individuals of the general population [10]. The present average caesium-137 body burden for adult Finnish Lapps is
890 nc for males and 400 nc for females. The corresponding total body radiation doses are approximately 80 and 35 mrem/yr, respectively, with due allowance in both cases for the lower body burdens in summer. These are quite significant values; especially as the very same population evidently has an average body burden of the natural radionuclides RaD and RaF about ten times higher than normal (cf., e.g., ref. [1]). The radioactive contamination of the sub-arctic populations must therefore be studied quite thoroughly.

ACKNOWLEDGEMENTS

This investigation was financed by a grant from the Finnish Atomic Energy Commission. Mr. O. Autio and Mr. R. Monni of the Finnish Cable Works (manufacturers of the multichannel analyser) gave valuable aid in the planning of the mobile counter and its electronics. Contributions by Miss Aili Jokelainen in the dietary studies and by Mr. E. Hästinen in the numerous whole-body measurements, are gratefully acknowledged. Many other persons gave valuable aid in the four field investigations: They will be given credit in the final reports of these studies.

REFERENCES

[1] MIETTINEN, J. K., "Radioactive food chains in arctic regions", in press
P. WENGER: I should like to contribute to Dr. Miettinen's review of these papers by illustrating the results of studies which we have conducted at the Institut du Radium et Centre de Radioactivité Médicale in Geneva. Figure 1D shows concentrations of caesium-137 in the human body. Curve 5 refers to a 37-yr-old woman and Curve 2 to a woman aged 20. The three other curves refer to men. The man represented by Curve 1 eats a substantial amount of cheese.

Figure 2D shows concentrations of caesium-137 in milk and was derived from weekly measurements taken between June and December 1963. The general pattern is similar to that described by Mr. Jeanmaire in his paper on two cases of varying caesium-137 content in individuals.*

C.R. HILL: I would like to make two comments on Dr. Miettinen's paper, "Measurements of caesium-137 in Finnish Lapps in 1962-1964 by a mobile whole-body counter". First, Dr. Miettinen said the levels of polonium-210 and lead-210 were not measured but only calculated. In the paper on total counting and spectroscopy in the assessment of alpha radioactivity in human tissues** Professor Mayneord presented one value which we were able to measure of polonium-210 in the bone of a Canadian eskimo. This was something like one hundred times the normal level and it might therefore be interesting if somebody took further measurements to determine what these dose rates are.

Second, it would be interesting to measure plutonium levels in Laplanders because high results would indicate that plutonium was being absorbed through the gut. On the other hand, if the results were at about the same level as we find in the more general population, this would presumably correspond to absorption through the lung.

J.K. MIETTINEN: I agree completely with Dr. Hill.

E. POCHIN: With regard to the same paper, one reason that is sometimes overlooked for quoting caesium-137 body contents as "per gram of potassium" is that the dose rate in fat-free body tissues correlates much better with caesium per gram of potassium than with caesium per kilogram of body weight, because much of the variation in the potassium content per kilogram of body weight is due to variations in fat tissue, which contains little caesium or potassium.

K. LIDÉN: Do the spectra shown in Figs. 2 and 3 of the paper by Dr. Pellerin, "Premiers résultats d'une étude systématique des contaminations internes consécutives aux retombées radioactives" refer to humans?

J.P. MORONI: Yes. The spectrum shown in Fig. 2 was derived from a sample of 100 persons and is fairly typical of the distribution we found in this sample, in that it shows traces of fission products of medium half-life. In fact about 50 of these persons showed more or less clear traces of ruthenium-103, zirconium-95 and niobium-95.

*JEANMAIRE, L., "Note à sujet de deux types de contamination humaine par le $^{137}$Cs", these Proceedings.

**MAYNEORD, W.V. and HILL, C.R., "Total counting and spectroscopy in the assessment of alpha radioactivity in human tissues", these Proceedings.
Figure 3 on the other hand, illustrates a special case, that of a man who services the engines of long-range jet aircraft. Since large amounts of air pass through these engines there is a high risk of radioactive contamination. I would point out, however, that the levels shown for ruthenium-103,
zirconium-95 and niobium-95 are well below the maximum levels permitted in workers.

K. LIDÉN: Was the case illustrated by Fig. 3 one of internal contamination or was it superficial?

J. P. MORONI: I could not state positively that contamination was only internal. In spite of various precautions, in particular regular showers and the wearing of special clothes when measurements were being taken, there undoubtedly remained slight external contamination.

K. LIDÉN: It is remarkable that we did not see a spectrum of this type in our studies.

A. BURNER: I would like to comment on Dr. Moroni's remarks about the contamination of jet aircraft engines.

We have carried out studies of this problem and have found no contamination of any significance in jet engine intakes. The levels were measurable immediately after the onset of testing, but were not high enough to require protective measures such as the prohibition of direct handling.

P. KAMATH: We have monitored about 25 Convair jet engines during overhaul in India and found a considerable amount of surface contamination giving spectra similar to that shown in Fig. 3.

J. RUNDO: Since early 1962 we have been following the levels of very small amounts of zirconium-95 and niobium-95 in human lungs, and we have seen the levels increase and decrease more or less in step with the concentration of these fission products in the air. The lung contents have never exceeded about 600 pc (total gamma-ray activity). On the other hand, we have frequently observed substantial amounts of fission products in ordinary clothing, at levels of activity comparable with those shown in Fig. 3. But since our subjects always shower and change into clean clothes which have been stored in plastic bags, we have never observed any interference from short-lived fission products which was external to the human body.
RADIUM AND RADON
(Sessions 10 and 11)
PHYSICAL MEASUREMENTS AND CLINICAL FINDINGS OF PERSONS WITH RADIUM BURDENS

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Abstract — Résumé — Аннотация — Resumen

PHYSICAL MEASUREMENTS AND CLINICAL FINDINGS OF PERSONS WITH RADIUM BURDENS. Results of physical measurements and some clinical findings of persons with radium burdens are reported and discussed. Ten workers of the dial painting industry, two chemists, who have been working for between 10 and 20 yr in the radium industry, one technician, who has been working for over 20 yr with high-emanation radium preparations and one person with high radium intake of rather unknown history were measured in a whole-body counter for evaluation of the body burdens of radium-226 and radium-228 + actinium-228. In some cases the radon concentration of expired air was also measured. For four of the measured persons the radium-226 burden is of the order of the maximum permissible amount (MPA : $10^{-7}$ c) or more. In one case the burden amounts to more than three times the MPA, $(3.4 \times 10^{-7}$ c), in another case to more than 100 times the MPA $(160 \times 10^{-7}$ c). In one case the radium-228 + actinium-228 burden exceeds the MPA $(6 \times 10^{-8}$ c in bone). The measured radon concentrations in the expired air were used to calculate the excretion rate of radon. The average was 67%. Clinical findings with some of the measured persons are related to the measured body burdens. The patient with the high body burden of $160 \times 10^{-7}$ c radium-226 shows heavy bone changes leading to spontaneous bone fractures. The blood picture shows a decrease in the number of erythrocytes and a low haemoglobin content but puncture of the sternum indicates normal haematopoiesis. It seems that the low number of erythrocytes is caused by chronic nephropathia, the reason for which might be an additional intake of uranium because uranium was found in the urine by gamma spectroscopy. The results are discussed with respect to the MPA of radium-226 recommended by the International Commission on Radiological Protection.

1) Work performed under the auspices of the Bundesminister fur Wissenschaftliche Forschung of the Federal Republic of Germany
In connection with a research project studying the effects of body burdens of long-living bone-seeking radionuclides in man, investigations with a large number of persons were performed in our institute. First results of this research work, especially concerning the measurements of thorotrast patients, were reported in 1961 by MUTH and OBERHAUSEN [1]. Two other papers presented at this Symposium give further results of our investigations with thorotrast patients [2,3].

In this paper the physical measurements of persons with radium burdens are reported. Clinical findings, known in some cases, are discussed in relation to the results of the physical measurements.
METHODS OF MEASUREMENT.

(1) In all cases the body burdens of $\text{Ra}^{226}$ and $\text{Ra}^{228} + \text{Ac}^{228}$ respectively were determined by measurement with a whole-body counter. We had the opportunity to use the 2 $\pi$-walk-in human counter with liquid scintillator of the United States Medical Research Unit Landstuhl/Pfalz, which was developed by ANDERSON and co-workers [4] in Los Alamos. In this counter we installed additionally an 8 in $\times$ 4 in NaI(Tl) crystal [5, 6]. Figure 1 shows the two possibilities of measurement with this equipment. The person to be measured stands upright in the counter during measurement with the liquid scintillator and sits in front of the crystal (chair arrangement, [7]) when measured with the crystal connected to a multichannel analyser to obtain a gamma-ray spectrum. The tank of the liquid scintillator is in the shape of a half cylinder; therefore a geometry of nearly 2 $\pi$ is obtained. About 13% of the surface of the tank is covered by six photomultiplier tubes with a diameter of 16 in. The counter volume and the liquid scintillator are shielded with 7.5 cm lead and 0.6 cm steel against the environmental and cosmic radiation.

(2) The radon concentration ($\text{Em}^{222}$) of expired air was measured by a sensitive equipment using dual ionization chambers in compensation and an electrometer [8].

(3) In some cases the $\text{Ra}^{226}$ content in excretions was measured using the

* We thank Dr. Ch. O. Onstead and Dr. E. J. Huycke, the former and the present heads of this American Research Unit for their kind help and many important discussions.
emanation method after appropriate processing of samples of urine and faeces.

(4) The Po\textsuperscript{210} and RaD (Pb\textsuperscript{210}) content of samples of urine and faeces was measured using the method described by SULTZER and HURSH [9]. The alpha-rays emitted by the Po\textsuperscript{210} plated on the silver foils were measured by scintillation counting. The first plating gives the Po\textsuperscript{210} content, a later plating gives the RaD (Pb\textsuperscript{210}) content by measuring the Po\textsuperscript{210} built up in the time between the two platings.

RESULTS OF PHYSICAL MEASUREMENTS AND CLINICAL FINDINGS

(1) Table I gives the results of measurements of nine persons working with radioactive luminous paints. Some of these persons worked in industrial

<table>
<thead>
<tr>
<th>Case</th>
<th>Ra\textsuperscript{226} (10\textsuperscript{-8} c)</th>
<th>Ra\textsuperscript{226} + Ac\textsuperscript{228} (10\textsuperscript{-8} c)</th>
<th>Ra\textsuperscript{226} in 24 h sample urine (% of total body burden)</th>
<th>Ra\textsuperscript{226} in 24 h sample faeces (% of total body burden)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt; 0.5</td>
<td>&lt; 0.3</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>&lt; 0.5</td>
<td>&lt; 0.3</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>1.6</td>
<td>&lt; 0.3</td>
<td>0.001 (2% of total excretion)</td>
<td>0.05 (98% of total excretion)</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.3</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>6</td>
<td>0.6</td>
<td>&lt; 0.3</td>
<td>0.005 (1.5%)</td>
<td>0.3 (98.5%)</td>
</tr>
<tr>
<td>7</td>
<td>&lt; 0.5</td>
<td>&lt; 0.3</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>8</td>
<td>0.6</td>
<td>&lt; 0.3</td>
<td>0.001 (17%)</td>
<td>0.005 (83%)</td>
</tr>
<tr>
<td>9</td>
<td>0.6</td>
<td>&lt; 0.3</td>
<td>0.007 (7%)</td>
<td>0.009 (93%)</td>
</tr>
<tr>
<td>11</td>
<td>2.5</td>
<td>0.3</td>
<td>0.004 (5%)</td>
<td>0.008 (95%)</td>
</tr>
</tbody>
</table>

* The activity was less than the lower limit of detection of 5 \times 10\textsuperscript{-9} c.

** The activity was less than the lower limit of detection of 3 \times 10\textsuperscript{-9} c.
laboratories, others in their own home under inadequate safety conditions. In spite of this in none of these cases was the maximum permissible amount exceeded or even reached. (Maximum permissible body burden for Ra\(^{226}\) = \(10^{-7}\) c and for Ra\(^{228}\) + Ac\(^{228}\) = \(6 \times 10^{-8}\) c; bone being the critical organ.)

The Ra\(^{226}\) body burden was determined by whole-body counting assuming that two-thirds of the radon built up in the body was expired. The radon concentration in expired-air was also measured, and in cases 4 and 11 the true elimination rate of radon could be estimated as 67% and 68%.

In four cases the Ra\(^{226}\) burden was below the detectable amount of \(5 \times 10^{-9}\) c. Three other persons had Ra\(^{226}\) burdens of about 500-1000 times the normal Ra\(^{226}\) content of \(10^{-11}\) to \(10^{-10}\) c. The largest value for Ra\(^{226}\) found in this group was one-quarter of the maximum permissible body burden (case 11). All Ra\(^{228}\) + Ac\(^{228}\) values are more than 20 times lower than the maximum permissible body burden.

None of these nine persons showed any sign or symptom of radiation damage. In all cases the blood picture was normal.

(2) Table II gives the results of three chemists and one technical assistant who worked for 10-20 yr in the radium industry, mainly with unsealed sources.

In case 12 a radium burden of about one-sixth the maximum permissible body burden was determined; in case 13 the maximum permissible body burden was just reached. Case 10 has a burden of about twice the maximum permissible amount. In case 3 six measurements with the whole-body counter were done in the period from 1959 to 1964. In this case the maximum permissible body burden is exceeded by a factor 2-5.

Cases 3, 10 and 12 are chemists who worked for many years in the radium industry. In cases 10 and 12, having worked temporarily with high-activity solutions of mesothorium in the production of luminous paint, mesothorium (Ra\(^{228}\) + Ac\(^{228}\)) was also detectable by whole-body counting. In case 10 the body burden of both Ra\(^{228}\) + Ac\(^{228}\) and Ra\(^{226}\) exceed the maximum permissible body burden. Here too the measurements of samples of urine and faeces show that the excretion in the faeces is more than 90% of the total excretion. This is in good agreement with former references [10, 11]. Some errors of our measured daily excretion rates might be caused by the difficulties in obtaining accurate 24-h samples.

The results of the first four measurements of case 3 show good consistency. The measurement in 1963 showed a higher amount of Ra\(^{226}\) in the body. During the period from 1961 to 1963 the chemist had worked more intensively with higher concentrations of unsealed sources of different radionuclides, especially with Ra\(^{226}\). With the first measurements in the whole-body counter, amounts of Cs\(^{137}\) were also detected. These were far below the maximum permissible amount (30 µc Cs\(^{137}\) per total body), but much larger than the average values which were obtained from the general population at that time. The Cs\(^{137}\) amounts of case 3 were: August 1959 = 196 nc and April 1960 = 60 nc. From these values an effective half-life for Cs\(^{137}\) in man of \(\text{T}_{\text{eff}}\) = 144 d can be estimated. This is in good agreement with the value of 140 d given by the ICRP [12]. In April, 1963 the chemist (case 3) retired from the radiochemical industry and from working with radionuclides. When he was measured in March, 1964, he had not worked with radioactive substances for more than one year. The last measured value of Ra\(^{226}\) body burden was nearly twice less than the previous measurements. Therefore
<table>
<thead>
<tr>
<th>Case</th>
<th>Date</th>
<th>Ra(^{226}) (10(^{-4}) c)</th>
<th>Ra(^{228}) + Ac(^{228}) (10(^{-5}) c)</th>
<th>Ra(^{228}) in 24 h sample urine (% of total body burden)</th>
<th>Date</th>
<th>Ra(^{228}) in 24 h sample faeces (% of total body burden)</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>7.8.59</td>
<td>34</td>
<td>2</td>
<td>0.0097 (1.9%)</td>
<td>11.8</td>
<td>0.45 (88.0%)</td>
<td>11.8</td>
</tr>
<tr>
<td>13</td>
<td>21.7.60</td>
<td>34</td>
<td></td>
<td>0.0003 (11%)</td>
<td>21.7.60</td>
<td>0.004 (99%)</td>
<td>21.7.60</td>
</tr>
<tr>
<td>10</td>
<td>2.6.61</td>
<td>34</td>
<td></td>
<td>0.0055 (1% )</td>
<td>2.6.61</td>
<td>0.9 (99%)</td>
<td>2.6.61</td>
</tr>
<tr>
<td>3</td>
<td>1.3.63</td>
<td>34</td>
<td></td>
<td>0.0095 (0.4%)</td>
<td>1.3.63</td>
<td>3.0 (99.7%)</td>
<td>1.3.63</td>
</tr>
<tr>
<td>5.2.64</td>
<td>34</td>
<td></td>
<td>0.0095 (0.9%)</td>
<td>5.2.64</td>
<td>23.2.61 (99.7%)</td>
<td>23.2.61</td>
<td></td>
</tr>
</tbody>
</table>

TABLE II
MEASUREMENTS OF RADIUM (Ra\(^{226}\)), MESOTHORIUM (Ra\(^{228}\) + Ac\(^{228}\)) AND RADON IN FOUR WORKERS OF INDUSTRIAL RADIOCHEMICAL LABORATORIES

H.MUTH AND E. OBERHAUSEN
it must be assumed that the higher values had been caused by Ra\(^{226}\) which was incorporated into the body during the last months of work in the laboratory. The same situation may be true in cases 10, 12 and 13 in Table II because these persons were working daily with radioactive substances at the time of whole-body counting. The same explanation may be given for the fact that the excretion coefficients \(f\) (average daily Ra\(^{226}\) excretion in the

### TABLE III

**COEFFICIENTS OF DAILY Ra\(^{226}\) EXCRETION**

<table>
<thead>
<tr>
<th>Case</th>
<th>(f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>(1.8 \times 10^{-2})**</td>
</tr>
<tr>
<td>4</td>
<td>(4.7 \times 10^{-4})</td>
</tr>
<tr>
<td>6</td>
<td>(3.1 \times 10^{-1})</td>
</tr>
<tr>
<td>8</td>
<td>(4.9 \times 10^{-3})</td>
</tr>
<tr>
<td>9</td>
<td>(8.8 \times 10^{-3})</td>
</tr>
<tr>
<td>10</td>
<td>(8.9 \times 10^{-1})</td>
</tr>
<tr>
<td>11</td>
<td>(8.9 \times 10^{-2})</td>
</tr>
<tr>
<td>12</td>
<td>(5.3 \times 10^{-3})</td>
</tr>
<tr>
<td>13</td>
<td>(3.8 \times 10^{-3})</td>
</tr>
</tbody>
</table>

* \(f\) = excretion coefficients.

** samples of 1 January, and 25 February, 1961 related to \(3.3 \times 10^{-7}\) c Ra\(^{226}\) total body burden.

faeces divided by the total Ra\(^{226}\) amount in the body) given in Table III are much higher than the coefficients given in the literature for old radium poisoning cases. NORRIS et al. [11] give a value of \(8 \times 10^{-5}\) as an average of 10 cases of old radium poisoning and LUCAS et al. [13] a value of \(7 \times 10^{-5}\).

In several cases, in addition to determination of Ra\(^{226}\) body burden by whole-body counting, the radon concentration in breath was measured, and the radon elimination rate was calculated. The resulting average is 66.5%, in good agreement with former references [11, 14].

(3) Case 14 is a 58 yr-old female who had been working from 1922 to 1957 in a pharmaceutical firm which produced drugs containing radioactive substances, especially Ra\(^{226}\). In 1955 a spontaneous fracture of the right femur occurred, which did not heal under normal treatment. Later, on extensive bone lesions, especially in the skull, the spine, the pelvis and the femurs were found by X-ray. However malignant degeneration has not as yet been established. Additionally, the patient suffers from a recurrent nephritis, and an anaemia with haemoglobin values of about 50%. Since the bone marrow obtained by sternal puncture gave no valid pathological result, it is assumed that the anaemia is secondarily caused by the nephritis. More recently (in 1962) for the first time radiation damage of the skeleton was suspected. In
1963 we were able to study this case. Measurements of the patient in the whole-body counter and of samples of urine and faeces were performed.

RESULTS

1. Whole-body counting on 5 April, 1963:
   
   16.5 µC \( \text{Ra}^{226} \) mesothorium was not detectable.

2. Measurement of a urine sample of 17 April, 1963:
   
   \[ \text{Ra}^{226} = 8.7 \times 10^{-12} \text{c per daily excretion} \]
   \[ \text{Po}^{210} = 2.5 \times 10^{-11} \text{c per daily excretion} \]
   \[ \text{Po}^{210} \text{ is in radioactive equilibrium with RaD (Pb}^{210}) \]

3. Measurement of a sample of faeces of 17 April, 1963:
   
   \[ \text{Ra}^{226} = 3.4 \times 10^{-10} \text{c per daily excretion} \]

4. Measurement of faeces collected quantitatively over one week in May 1963:
   
   \[ \text{Ra}^{226} = 2.5 \times 10^{-10} \text{c per daily excretion} \]
   \[ \text{Po}^{210} = 1.3 \times 10^{-10} \text{c per daily excretion} \]
   \[ \text{RaD (Pb}^{210}) = 0.9 \times 10^{-10} \text{c per daily excretion} \]

In this case of chronic radium poisoning the coefficient of the daily \( \text{Ra}^{226} \) excretion is \( 1.6 \times 10^{-5} \). This value is smaller by the factor 4-5 than those given by Norris et al. [11] and LUCAS et al. [13], but the order of magnitude is the same. Under the supposition that the power function given for the radium retention by Norris, Speckman and Gustafson is valid, we could estimate the date of incorporation by means of the total-body burden and the daily excretion of \( \text{Ra}^{226} \). If we suppose one single incorporation, we get the following equation for the "excretion coefficient":

\[
\frac{dR_t}{dt} = bxt^{-1} = 0.52xt^{-1} \quad \text{when } t > 1.
\]

(\( R_t \) = retention, i.e. that fraction of the total incorporated amount which is still in the body, \( t \) is given in days.)

This equation applied to case 14 leads to a value of \( t = 94 \text{ yr} \). Since it is impossible that the incorporation is older than 40 yr at the most, this value is at least twice too high. This example therefore shows that the applied function for the retention is not valid in all cases. In our case probably the conditions are changed because of disturbed mineral metabolism resulting from the nephritis. There is no doubt that the high body burden of \( \text{Ra}^{226} \) is the cause of the skeletal damage in case 14. Additional depositions of uranium must be taken into account because uranium was determined qualitatively in urine by gamma-ray spectroscopy. Quantitative measurements are provided. It may be possible that the nephritis is caused by the incorporated uranium. Unfortunately up to now it was impossible to determine either the exact date or the circumstances of the incorporation, in spite of extensive inquiry.
In six cases with radium burdens the Po\textsuperscript{210} content of urine was also determined. The results are given in Table IV. In four cases the ratio Po\textsuperscript{210} per daily excretion per Ra\textsuperscript{226} total body burden is in the order of magnitude of 10\textsuperscript{-4}. In case 3 this ratio is about one order of magnitude higher.

**TABLE IV**

Ra\textsuperscript{226} BODY BURDEN AND DAILY EXCRETION OF Po\textsuperscript{210} IN URINE

<table>
<thead>
<tr>
<th>Case</th>
<th>Ra\textsuperscript{226} total body burden ( (\text{c}) )</th>
<th>Po\textsuperscript{210}/24 h in urine</th>
<th>( \frac{\text{Po}	extsuperscript{210}/24 \text{ h}}{\text{Ra}	extsuperscript{226}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>( 3.3 \times 10^{-7} )</td>
<td>( 3.5 \times 10^{-10} )</td>
<td>( 1.1 \times 10^{-3} )</td>
</tr>
<tr>
<td></td>
<td>(average) ( (\text{Po}\textsuperscript{210} = 3.5 \times 10^{-13}) )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>( 1.8 \times 10^{-7} )</td>
<td>( 2.2 \times 10^{-11} )</td>
<td>( 1.2 \times 10^{-4} )</td>
</tr>
<tr>
<td>11</td>
<td>( 2.5 \times 10^{-8} )</td>
<td>( 5.3 \times 10^{-12} )</td>
<td>( 2.1 \times 10^{-4} )</td>
</tr>
<tr>
<td>12</td>
<td>( 1.8 \times 10^{-8} )</td>
<td>( 2.2 \times 10^{-12} )</td>
<td>( 1.2 \times 10^{-4} )</td>
</tr>
<tr>
<td>13</td>
<td>( 9.6 \times 10^{-9} )</td>
<td>( 7.0 \times 10^{-12} )</td>
<td>( 7.3 \times 10^{-5} )</td>
</tr>
<tr>
<td>14</td>
<td>( 1.6 \times 10^{-6} )</td>
<td>( 2.5 \times 10^{-11} )</td>
<td>( 1.5 \times 10^{-6} )</td>
</tr>
</tbody>
</table>

and in case 14 about two orders of magnitude lower. The relatively high value in case 3 is probably caused by high concentrations of radon in the air of the laboratories where the chemist was working for many years. By this reason the deposited RaD (Pb\textsuperscript{210}) and Po\textsuperscript{210} is caused not only by decay of the Ra\textsuperscript{226} in the body but also by direct uptake of radon and, above all, its short-living decay products with air. In this connection a paper should be mentioned concerning a case of radium poisoning which led to death and which occurred in the same firm. (MUTH and SCHRAUB [15].) In this case a large deposition of Po\textsuperscript{210} was established which was much higher than the deposited amounts of Ra\textsuperscript{226} and Th\textsuperscript{228} + Ra\textsuperscript{224} (radiothorium + thorium X). In cases 10, 11, 12 and 13 of Table IV it may also be assumed that radon and its decay products were inhaled additionally. In case 14, where an old radium deposition is present, an additional radon inhalation is certainly not to be assumed. For this reason the Po\textsuperscript{210} and Pb\textsuperscript{210} can only be caused by decay of Ra\textsuperscript{226} in the body, and therefore the ratio Po\textsuperscript{210} per daily excretion per Ra\textsuperscript{226} body burden is about two orders of magnitude lower than in the cases with additional radon inhalation.

For comparison with the values of Po\textsuperscript{210} measured in cases of radium poisoning, the value of normally excreted natural Po\textsuperscript{210} will be given. The average of nine normal persons was \( 1.8 \times 10^{-12} \) c Po\textsuperscript{210} per daily excretion with urine [16]. In case 14 Po\textsuperscript{210} and Pb\textsuperscript{210} were in radioactive equilibrium in the urine, but in the faeces different values were found. There was more Po\textsuperscript{210} than Pb\textsuperscript{210}.

LUCAS et al. [13] were able to determine the Ra\textsuperscript{226} content and the Pb\textsuperscript{210} content in bone samples in addition to whole-body counting in a case of
chronic radium poisoning. They obtained a constant value of $\text{Pb}^{210}/\text{Ra}^{226}$ of $0.28 \pm 0.01$. In case 14 we had no opportunity to measure bone samples, but under the supposition that the ratio of 0.28 is also valid, we would get a total-body burden of $4.6 \times 10^{10}$ c $\text{Pb}^{210}$. The daily excretion coefficient (daily excretion of $\text{Pb}^{210}$ in faeces divided by total-body burden of $\text{Pb}^{210}$) for $\text{Pb}^{210}$ then would be $2.0 \times 10^{-5}$. This is in the same order of magnitude which was found for $\text{Ra}^{226}$ in this case ($1.6 \times 10^{-5}$). (See also HOLTZMAN [17].)

(5) At last I want to mention an example of the incorporation of several different radionuclides. This man, a physicist, is working in industrial laboratories where radium as well as artificial radioactive nuclides are handled. Figure 2 shows the gamma-ray spectrum of this physicist (case 15) recorded with the 8 in × 4 in NaI(Tl) crystal in connection with a multichannel analyser in the whole-body counter. There can be no doubt of a $\text{Cs}^{137}$ and a $\text{Co}^{60}$ incorporation. The $\text{Cs}^{137}$ peak of 0.66 MeV and the two peaks of $\text{Co}^{60}$ (1.17 MeV and 1.33 MeV) are clearly shown. A body burden of 91 nc $\text{Cs}^{137}$ and 21 nc $\text{Co}^{60}$ was calculated. The gamma-ray spectrum also shows gamma rays of higher energies than 1.7 MeV; therefore an additional incorporation of $\text{Ra}^{226}$ or $\text{Th}^{228}$ was suspected which would have been higher than the maximum permissible body burden. By measurements of breath no thoron could be detected, and the measured radon concentration was due to only $1 \times 10^{-8}$ c $\text{Ra}^{226}$. We found that the gamma rays of the higher energies were the result of the $\text{Co}^{60}$ sum peak. Cobalt-60 was mainly deposited in the lungs; hence in the chair position the geometry of measurement was extremely good, and the sum peak occurred relatively often. By measuring the bremsstrahlung with the liquid scintillator in the whole-body counter, a body burden of about 60 c $\text{Sr}^{90} + \text{Y}^{90}$ could be detected. The $\text{Ra}^{226}$ burden is one-tenth of the maximum
permissible body burden, the burdens of Cs$^{137}$, Co$^{60}$ and Sr$^{90}$ are less than 1/100 of the maximum permissible amounts. Similar results were found for other persons working with several different radionuclides. This example shows that it is necessary to determine the body burdens of these persons with several methods to prevent errors.

In conclusion I may say that the reported results can perhaps be interpreted so that there may be no urgent need to lower the basic reference of 0.1 $\mu$C of Ra$^{226}$ recommended by ICRP.

REFERENCES


[17] HOLTZMAN, R.B., "RaD (PhB) in the human skeleton: Estimates of the exponent of the retention function, the skeletal content, and the dose rate in high-radium people", Radiology, N.Y. 89 (1963) 122-123.

DISCUSSION

B. GODFREY: You describe two methods of whole-body counting, using the 2π liquid scintillator and the single crystal counter. Have you measured
any cases by both methods and, if so, were any differences noted between the measurements?

H. MUTH: The radionuclides were identified by gamma-spectrometry using the crystal. Quantitative determination was done with the 2π liquid scintillation counter.

C. E. MILLER: Have you found any patients whose radon content in the breath was considerably more than 70% of their total body content, say 80%, as might be expected if they had ingested the radium recently?

H. MUTH: No. The range was 60-70% and the average was about 67%.

L. BENGTSSON: You say you detected as little as 60 nanocuries of strontium-90 in a case of heavy contamination with gamma-emitters. Could you tell us what energy range was used for the liquid scintillation measurements, how long the measurement times were and how you performed the correction for the gamma-emitters?

H. MUTH: Perhaps I could pass this question to my colleague, Dr. Oberhausen.

E. OBERHAUSEN: The energy range used was 50-100 keV. The amounts of gamma emitters are measured in higher energy bands and from these measurements the contribution in the 50-100 keV channel is calculated. To evaluate this contribution we made measurements with phantoms, taking body weight and height into consideration. Measurements on 20 persons have shown that we can predict the contribution of potassium-40 and caesium-137 in the 50-100 keV channel with a standard deviation of 1.5%.

J. WEBER: Can you give any explanation for the low body burden that is found in the dial painters? We also noted this in the Netherlands with dial painters who were working in extremely bad conditions.

H. MUTH: An explanation might be that the radioactive material used was in a chemical form insoluble in water. Some of these people had surprisingly high contamination on their clothes so we don’t think they had taken much care to avoid incorporation.

R. I. MOORE: In your oral presentation you mentioned that one patient might have had a nephropathy as a result of uranium poisoning. This is interesting, and I wonder if you could comment further on this.

H. MUTH: You are speaking of Case 14. I can give no information other than what is in the paper. Since we found no mention, in the literature, of nephritis caused by radium poisoning, we thought it might be due to uranium poisoning. That is all.

C. J. MALETSKOS: In one of the cases which you measured over a period of several years, the radium-226 burden remains at 30-35×10⁻⁸ c, then jumps up to about 55×10⁻⁸ c and then drops to about 20×10⁻⁸ c. I believe the fractional radon loss through the breath remained at about 67% during this time. If this is so, can you explain the constancy of the breath radon loss in the face of the variable radium burden?

H. MUTH: No changes in the fractional radon loss through breath have been observed. However, the accuracy of our radon breath measurements is within ±10%, so small changes are not excluded.

P. R. KAMATH: Can you please tell us the thorium-228 content in the luminous paint and, secondly, referring to your Table II, could you give us some measurements of radium-224?
I raise these points because the damage due to short-lived, strong alpha-emitting daughters of radium-224 such as radon-220 and polonium-216 could be very significant. We have analysed some luminous compounds and have found a very high radium-224 content. We think radium-224 is an important parameter in these considerations, when radium-224 parents are present.

H. MUTH: Perhaps I may ask Dr. Oberhausen to answer this question.

E. OBERHAUSEN: In the Federal Republic of Germany, according to our information, luminous paints containing products of the thorium series have not been used since 1945. I am sorry that I have at the moment no information concerning the thorium concentrations in luminous paints previously used.

The values of radium-228 in Table II are derived from whole-body counting, assuming radium-228 to be in equilibrium with its daughters. This assumption may be right within 10%.
QUANTITATIVE EVALUATION OF DOSE-RESPONSE RELATIONSHIPS IN HUMAN BEINGS WITH SKELETAL BURDENS OF RADIUM-226 AND RADIUM-228

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Abstract — Résumé — Аннотация — Resumen

QUANTITATIVE EVALUATION OF DOSE-RESPONSE RELATIONSHIPS IN HUMAN BEINGS WITH SKELETAL BURDENS OF RADIUM-226 AND RADIUM-228. The 361 subjects with skeletal burdens of radium-226 and radium-228 studied in this laboratory now represent a large enough sample to allow the quantitative evaluation of the relationship between biological response and internal radiation dose. This report describes the procedures and preliminary results for such an analysis.

The biological responses consist of a variety of clinical results such as X-ray scores, tumours, fractures, urinalysis, haematology, blood chemistry, and protein electrophoresis. The internal radiation dose is calculated and expressed as the retained body burden in microcuries of minimum pure radium-226 equivalent (MPRE), cumulative rads, and cumulative rad-years.

The first step in the analysis determines whether a relationship exists between a clinical parameter and the radiation dose. The determination is carried out by applying a contingency test, by means of which the actual data are compared with a postulated model of independence between the two variables.

If no independence is found then some relationship is presumed to exist and a quantitative description of the dependence is obtained. Least-squares curve fitting procedures are used to derive the coefficients and the standard deviations of the coefficients of a power series. Such an expression provides an empirical quantitative description of the results along with a measure of their variability, is useful for impartial comparison with results from other laboratories, but implies no biophysical mechanism.

The clinical results on these subjects are compared with results from control subjects with normal radium burdens, whether or not there is a dependence on radiation dose.

Preliminary results indicate that the X-ray score shows the strongest and clearest correlation with internal radiation dose.

There are definite indications of non-skeletal effects at higher burdens, particularly in lymphocyte count and sedimentation rate, which are similar to those obtained in the dog experiments at Utah. Further analysis is indicated.

No clinically significant signs or symptoms are observed at MPRE < 0.5 μc. In the region 10^{-3} to 10^{-1} μc MPRE the clinical data are in the normal range.
carrés pour calculer les coefficients et les écarts types des coefficients d’un développement en série. Une telle expression fournit une description quantitative empirique des résultats en même temps qu’une mesure de leur variabilité, elle est utile pour une comparaison impartiale avec les résultats des autres laboratoires, mais n’implique aucun mécanisme biophysique.

Les auteurs ont comparé les résultats cliniques obtenus sur ces sujets avec les résultats obtenus sur des sujets témoins ayant des charges normales de radium, qu’il y ait ou non variation en fonction de la dose. Les résultats préliminaires indiquent que les radiogrammes révèlent la corrélation la plus marquée avec la dose due à la contamination interne.

Pour des charges élevées, on a relevé des indications certaines d’effets sur des parties de l’organisme autres que le squelette, notamment sur le sang (numération lymphocytaire et vitesse de sédimentation); ces effets sont semblables à ceux qui ont été observés lors d’expériences faites sur des chiens dans l’Utah. Les auteurs estiment qu’il convient de poursuivre les analyses.

Aucun signe ni symptôme clinique important n’a été observé pour un équivalent minimum de radium 226 pur inférieur à 0,5 μC. Lorsque l’équivalent minimum de radium 226 pur se situe entre 10^{-5} et 10^{-4} μC, les données cliniques ne dépassent pas les limites de la normale.

**EVALUACIÓN CUANTITATIVA DE LAS RELACIONES DOSIS-RESPUESTA EN SERES HUMANOS CON CARGAS DE RADIO-226 Y RADIO-228 EN EL ESQUELETO.** El grupo de 361 sujetos con cargas de radio-226 y radio-228 en el esqueleto, estudiado por los autores, constituye una muestra suficientemente grande para permitir la evaluación cuantitativa de las relaciones existentes entre la respuesta biológica y la dosis de radiación interna. En la memoria se describen los procedimientos de estudio aplicados y los resultados preliminares obtenidos.

Las respuestas biológicas constan de una variedad de datos cínicos tales como cuadros radiográficos resultados de exámenes de tumores y fracturas, análisis de orina, pruebas hematológicas y hematoquímicas y...
electroforesis de las proteínas. La dosis debida a la irradiación interna se expresa por la carga corporal retenida en microcuries de equivalente mínimo de radio-226 puro en rad acumulativos y en rad-aflos acumulativos.

El primer paso del análisis consiste en comprobar si existe o no alguna relación entre un parámetro clínico dado y la dosis de irradiación. Esta determinación se efectúa recurriendo a una prueba de contingencia, que permite comparar los datos efectivos con un modelo de independencia entre ambas variables, que se considera posible.

Si no se comprueba tal independencia, se da por sentado que existe una relación y se obtiene una descripción cuantitativa de la ley de dependencia. Se aplican procedimientos de ajuste por cuadrados mínimos a fin de deducir los coeficientes y las desviaciones estándar de los coeficientes de un desarrollo en serie. Tal expresión proporciona una descripción cuantitativa de carácter empírico de los resultados, así como una medida de su variabilidad, y sirve para comparar objetivamente los resultados con los obtenidos en otros laboratorios, pero no supone la intervención de mecanismos biofísicos.

Los resultados del examen clínico de estos sujetos se comparan con los datos obtenidos en testigos con cargas normales de radio, haya o no relación de dependencia con la dosis de irradiación.

Los resultados preliminares indican que los cuadros radiográficos son los que presentan una correlación acusada y neta con la dosis de irradiación interna.

Hay claros indicios de efectos fuera del esqueleto para cargas más elevadas, sobre todo en el recuento de linfocitos y en la velocidad de sedimentación, que son análogos a los obtenidos en los experimentos realizados con perros en Utah. Se indican otros datos de los análisis.

Para un equivalente mínimo de radio-226 puro < 0,5 μc, no se observan señales o síntomas clínicos significativos. En el intervalo de 10⁻³ a 10⁻¹ μc, los datos clínicos presentan valores normales.

INTRODUCTION

About 30 yr have elapsed since this laboratory initiated studies on the toxicity of radium in human beings. During the early years a number of subjects were studied who came to the attention of the laboratory because of the symptoms which these subjects showed. Methods were developed to assess, non-destructively, the Ra²²⁶ body burden of these persons for correlation with the clinical findings. In 1941 the maximum permissible body burden of 0.1 μc Ra²²⁶ was established [1], and it remains as an acceptable value to this day. The decision for this value was based on the observation that osteogenic sarcoma or other major clinical manifestations had not been found in subjects with body burdens less than 1.5 μc Ra²²⁶ and on the use of a factor of 10 as a margin of safety.

In the last two decades, considerable improvements have been made in the methods of determining not only the Ra²²⁶ burdens but also the Ra²²⁸ (MsTh) burdens and in the sensitivity for determining these isotopes and their daughter products. During this time significant efforts were made to find additional cases, and starting in 1957 a large number of subjects were located by search and history, rather than by symptom, and studied. The Argonne National Laboratory and the New Jersey State Department of Health have been carrying out similar investigations in the United States while several groups in Europe are also working in this field. To date a number of summaries on radium toxicity in human beings have appeared [2 - 6].

Our laboratory is reporting in this paper on 361 subjects who have been exposed to the internal deposition of Ra²²⁶ and Ra²²⁸ (MsTh). With such a large number of subjects available, quantitative relationships can be sought between clinical results and internal radiation dose. This paper describes
the procedures for and the results of a quantitative evaluation of the dose-
response relationships for each of the clinical and exposure history para-
eters amenable to numerical analysis.

MATERIALS

Subjects studied

The 361 subjects reported here are a heterogeneous group. Two-thirds
of the subjects are dial painters, some of whom were exposed to Ra\textsuperscript{226} alone
and others who were exposed to a mixture of Ra\textsuperscript{226} and Ra\textsuperscript{228}. The remainder
are persons exposed as a result of laboratory work, or by ingestion or in-
jection of radioactive materials. Table I shows a breakdown of Ra\textsuperscript{226} and

<table>
<thead>
<tr>
<th>TABLE I</th>
</tr>
</thead>
<tbody>
<tr>
<td>BREAKDOWN OF Ra\textsuperscript{226} AND Ra\textsuperscript{228} CASES BY TYPE OF EXPOSURE</td>
</tr>
<tr>
<td>(1915—1930)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dial Painters</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plant No. 1</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>150*</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>11</td>
<td>24*</td>
</tr>
<tr>
<td>12</td>
<td>12 238</td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
<tr>
<td>Radithor</td>
<td>12</td>
</tr>
<tr>
<td>Medical ingested</td>
<td>12</td>
</tr>
<tr>
<td>Medical injected</td>
<td>12</td>
</tr>
<tr>
<td>Chemical or physical laboratory</td>
<td>82</td>
</tr>
<tr>
<td>Industrial accidents</td>
<td>3</td>
</tr>
<tr>
<td>Relatives of dial painters</td>
<td>2 123</td>
</tr>
<tr>
<td>Total 361</td>
<td></td>
</tr>
</tbody>
</table>

Male = 88, female = 273
Found by search = 299; by symptom = 62
* One dial painter in each plant was also exposed to thorotrast.

Ra\textsuperscript{228} cases by type of exposure. Most of the cases studied earlier (pre-1957)
came to our attention because of the symptoms they had developed, while
the majority of the cases studied more recently were investigated after being
found by search.
The main exposure period of dial painters was from 1918 to 1925, although a few started work as early as 1915. Fourteen of the cases are the original ones examined by Martland [2, 7].

Physical measurements

Over the years, a number of methods have been used for determining the body burdens of persons exposed to internally-deposited radioactive materials. Basically, all these methods fall into two categories: (1) determination of the gamma-ray output of the body from the daughter products of that fraction of the radon and thoron which does not leave the body; and (2) determination of the radon and thoron in the breath for that fraction of the radon and thoron which is expired. Techniques for measurement are summarized in Table II. This Table also shows the varied instrumentation which has been used since the 1930's.

TABLE II

METHODS AND INSTRUMENTATION FOR DETERMINING BODY BURDENS OF Ra^{226}, Ra^{228} AND Ra^{228}

<table>
<thead>
<tr>
<th>Methods</th>
<th>Instrumentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-body</td>
<td>Electroscope</td>
</tr>
<tr>
<td>(RaC + ThC\textsuperscript{7})</td>
<td>Double ion chamber</td>
</tr>
<tr>
<td></td>
<td>Single ion chamber</td>
</tr>
<tr>
<td></td>
<td>Quartz fibre electrometer</td>
</tr>
<tr>
<td></td>
<td>Vibrating reed electrometer</td>
</tr>
<tr>
<td></td>
<td>Vacuum tube electrometer</td>
</tr>
<tr>
<td>Breath</td>
<td>Geiger–Müller counters</td>
</tr>
<tr>
<td>(Rn + Tn)</td>
<td>Scintillation counters</td>
</tr>
<tr>
<td></td>
<td>NaI(Tl)</td>
</tr>
<tr>
<td>Sample</td>
<td>Bones</td>
</tr>
<tr>
<td>(RaC, ThC\textsuperscript{7}, Rn + Tn de-emanation)</td>
<td>ZnS(Ag)</td>
</tr>
</tbody>
</table>

An effort has been made to re-measure as many of our previously studied cases as possible with the newer techniques. Three hundred and thirty (330) subjects have been measured or re-measured since 1958. A breakdown of the physical measurements carried out on all the subjects is given in Table III.

The accuracy with which the body burden (and from this the internal radiation dose) is determined can vary over a wide range depending on the number and kinds of physical measurements which have been made. The most accurate information comes from a meter-arc measurement made in a whole-body counter using an NaI(Tl) scintillation crystal and an exhaled breath measurement taken with a spirometer. Reliable information is also obtained from the chair measurement in the whole-body counter and from a spirometer breath measurement. The best accuracy of such measurements
### TABLE III

**DISTRIBUTION OF SUBJECTS BY TYPE OF MEASUREMENT**

<table>
<thead>
<tr>
<th>Principal Method</th>
<th>Subjects No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Chair alone</td>
<td>2</td>
</tr>
<tr>
<td>*Chair + meter-arc</td>
<td>3</td>
</tr>
<tr>
<td>*Chair + Rn flask</td>
<td>6</td>
</tr>
<tr>
<td>*Chair + Rn tank</td>
<td>197</td>
</tr>
<tr>
<td>*Chair + Tn</td>
<td>1</td>
</tr>
<tr>
<td>*Chair + sample γ</td>
<td>1</td>
</tr>
<tr>
<td>*Chair + sample other</td>
<td>3</td>
</tr>
<tr>
<td>Rn flask only</td>
<td>100</td>
</tr>
<tr>
<td>Rn flask + sample γ</td>
<td>2</td>
</tr>
<tr>
<td>Rn flask + sample other</td>
<td>3</td>
</tr>
<tr>
<td>*Rn tank air only</td>
<td>4</td>
</tr>
<tr>
<td>*Rn tank air + Tn</td>
<td>3</td>
</tr>
<tr>
<td>*Rn flask + Tn</td>
<td>1</td>
</tr>
<tr>
<td>Whole-body other + Ta</td>
<td>1</td>
</tr>
<tr>
<td>Sample γ</td>
<td>16</td>
</tr>
<tr>
<td>Sample γ + sample other</td>
<td>4</td>
</tr>
<tr>
<td>Sample other</td>
<td>10</td>
</tr>
<tr>
<td>Whole skeleton</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>361</strong></td>
</tr>
</tbody>
</table>

* Subject came to MIT for measurement.
+ For most cases in this category several additional measurements were made, particularly breath Tn and, in some cases, meter-arc.

is estimated to be ±10% for cases with high body burdens of radium [8]. The error may become as large as a factor of 2-3 when the body burden is determined only from a bone or tooth sample [9]. For the contingency analysis described later in the paper, uncertainties of factors of 2 or 3 are expected to have little effect on the results since the test divides irradiation doses or body burdens by orders of magnitude.

Since 1962, this laboratory has been devoting its efforts to studying subjects with body burdens greater than 0.02 μc minimum pure radium equivalent (MPRE, defined later). Most subjects are first measured in their homes by the radon flask technique to estimate their body burden. During the past year an effort has been initiated to study cases with high radium burdens by the investigation of exhumed bodies.
Inter-laboratory comparisons on the determination of Ra$^{226}$ body burdens have been carried out in collaboration with the group at the Argonne National Laboratory. On the whole, the results show reasonably good agreement for total radium burden ($\pm$ 10-15%), but a discrepancy continues to exist in the fraction of radon expired through the breath ($\sim$ 60% for MIT and $\sim$ 70% for ANL).

**Clinical measurements**

Whenever possible, a subject is brought to our laboratory for physical measurements of body burden. At the same time a determination of the clinical status of the person is undertaken. A case history is obtained in which the medical status of the individual is determined and a history of the exposure to radium is recorded. Laboratory analyses (urinalysis, haematology, blood chemistry including protein electrophoresis) are carried out. A standard physical examination is done, with the pelvic examination omitted unless desired by female subjects. Finally, a comprehensive radiological skeletal survey is made of the whole body.

For the cases studied at this laboratory since 1958, consistency has been maintained by having all subjects examined by the same physician of this team, Dr. Samuel D. Clark. All laboratory analyses are carried out by the same clinical laboratory*, the reliability of which has been established by the MIT Medical Department. Accuracy of analyses by this clinical laboratory is $\pm$ 5% for chemical analyses and $\pm$ 10% for counts obtained microscopically. The biological variations between individuals may be as high as $\pm$ 30%. The X-rays have been taken and read by the same radiologist of this team, Dr. John E. Gary.

Dr. Robert J. Hasterlik and Dr. Asher J. Finkel of the Argonne National Laboratory, and Dr. John E. Gary [10] have developed a technique for expressing the qualitative observations on the X-rays of subjects by a numerical expression, or X-ray score. On the basis of inter-laboratory comparisons between MIT and Argonne and on re-readings by our radiologist of earlier X-ray films, the accuracy is estimated as $\pm$ 1-2 score units for a single X-ray film for greater than 90% of the time and $\pm$ 2-3 score units for the scoring of a set of some 25 films per subject for greater than 90% of the time. In practice, the highest X-ray scores recorded are $\sim$ 50; the lowest found are 0; then percentage errors may be as high as $\pm$ 100% at the low scores to $\pm$ a few percent at the higher scores.

About 60% of the cases reported here have been studied clinically by the methods described. Information on the remaining cases has come from physicians on the MIT team prior to 1958, from the subject's own physician, or from hospital records. In some cases the clinical data are intrinsically good but may be open to question because a subject may have a cold or other mild disorder or the person may be terminal.

**Bias in the data**

As a first approach in this analysis, all the data have been used, giving equal weight to all the information. With the inclusion of all data there is no variable in which all the subjects are represented.

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* Commonwealth Clinical Laboratory, Boston, Massachusetts.
In order to assess the accuracy and consistency of the data, the distribution of each variable about its mean has been investigated. While there is not a priori reason why all the variables should be distributed according to the normal law, this analysis affords a convenient procedure for finding questionable points which are far removed from the mean value. This procedure does not recognize potential errors in the values if they are close to the mean.

The principal bias in the data is that many of those cases with high body burdens, which provide information where effects with dose may be expected to show up most significantly, have been studied under less-than-ideal conditions. For example, only 6 of the 20 cases with the highest MPRE body burdens have come to the laboratory and none have undergone the standard medical procedure described. Most of the clinical data for these cases has been obtained from hospital records and can be assumed to be inconsistent with the medical data obtained since 1958.

A further difficulty of data from high burden cases is that these subjects came to the attention of our laboratory because of symptoms. These persons were ill, and went to their physicians who deduced the possibility of radium poisoning. The subjects were then brought to our laboratory for study or a post-mortem bone sample was made available for determining the body burden. A few "symptom" cases have also been found at lower body burdens. This "symptom" group is differentiated from the remaining or "search" group. "Search" cases were found mainly through employment records or by word of mouth.

METHOD

General plan

In making an evaluation of the dose-response relationships, the object has been to make a quantitative determination of which parameters depend on internal radiation dose or body burden. The procedure that has been followed is shown in Fig. 1.

The clinical and exposure data which are amenable to calculation are extracted for each subject. The radiation dose is determined in terms of microcurie equivalents of Ra\textsuperscript{226} (MPRE), cumulative rad (CR), and cumulative rad-years (CRY). All appropriate data are placed on IBM cards for machine computation.

The information contained in these cards is summarized in Table IV. A contingency test is made to determine whether a variable is independent of radiation dose or not. If the variable is independent, the value is compared with values obtained from normal populations to determine how closely the sample represents a normal population. If no independence is found, a dependence is presumed to exist. As above, the value of the variable at low doses is compared with values from normal populations. When appropriate, an empirical expression is developed describing the dependence on dose and providing a measure of the uncertainty involved.
**Checking of data**

Data representing 70 items per subject have been transferred to IBM cards. The entries on the cards were taken directly from original records. Minor errors in transcription were found and corrected. The information

**TABLE IV**

VARIABLES IN COMPUTER ANALYSIS OF Ra$^{226}$ AND Ra$^{228}$ TOXICITY RESULTS

<table>
<thead>
<tr>
<th>Card</th>
<th>Variables</th>
<th>Items No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Ra and MsTh burdens</td>
<td>15</td>
</tr>
<tr>
<td>B</td>
<td>Vital statistics</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Clinical results</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Dental results</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>Urinalysis</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Haematology</td>
<td>11</td>
</tr>
<tr>
<td>D</td>
<td>Blood chemistry</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Protein electrophoresis</td>
<td>7</td>
</tr>
<tr>
<td>E</td>
<td>Cumulative rad</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Cumulative rad-year</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td>70</td>
</tr>
</tbody>
</table>
on the cards was transferred to magnetic tape, and this one reel of tape has been used for all further calculations*.

**Expression of absorbed dose**

Historically, the radiation dose from internally-deposited radium has been expressed as microcuries of retained or fixed Ra\textsuperscript{226}. This unit has been used in this study to express the radiation dose because of its simplicity and convenience. However, since a portion of our subjects have burdens of Ra\textsuperscript{228} in addition to Ra\textsuperscript{226}, a unit taking into account the effects of both has been adopted. The body burden for these cases is expressed as a pure Ra\textsuperscript{226} equivalent. The Ra\textsuperscript{226} burden and the Ra\textsuperscript{226} equivalent of Ra\textsuperscript{228} are added together to give the effective burden. Since Ra\textsuperscript{228} has a long-lived daughter, Th\textsuperscript{228}, which may be taken up from the gastrointestinal tract independently of the Ra\textsuperscript{228} absorption, and which, if absorbed, would be significantly more toxic on a microcurie basis than the Ra\textsuperscript{226} or Ra\textsuperscript{228}, the concept of minimum pure radium equivalent (MPRE) has been used**.

The calculation of MPRE is illustrated in Fig. 2. The present Ra\textsuperscript{228}/Ra\textsuperscript{226} ratio is determined by measurements of Ra\textsuperscript{228} and Ra\textsuperscript{226} on the subject. The decay of Ra\textsuperscript{226} to time of exposure is calculated using a half-period of 5.7 yr for Ra\textsuperscript{228} [13, 14], rather than the long-accepted value of 6.7 yr [15]. The ratio of Ra\textsuperscript{228}/Ra\textsuperscript{226} in terms of rad/µc is taken as 1.5. This value represents the best estimate of the number of microcuries of Ra\textsuperscript{228} which are dosimetrically equivalent to 1 µc Ra\textsuperscript{228} many years after exposure, both on the basis of cumulative rads and of cumulative rad-years. Figure 3 shows the dosimetric relationship of Ra\textsuperscript{226} and Ra\textsuperscript{228} as a function of time. The value of 1.5 is compatible, within the biological errors and the theoretical uncertainties, with either hypothesis some 40 yr after exposure. The theoretical calculations leading to these curves are described later in this section.

Since most of the subjects with Ra\textsuperscript{228} burdens worked as dial painters in Waterbury, Conn., it is possible to estimate an MPRE for these cases even when the amount of Ra\textsuperscript{228} is below detectability. This is done indirectly, having established within ± 50%, the Ra\textsuperscript{228}/Ra\textsuperscript{226} activity ratio to be found in such dial painters and in the paints they used.

MPRE's were not considered acceptable for this analysis when radon breath samples were not accompanied by flasks for room background and when, in a few cases, contradictory results were obtained either on re-measurement of the same sample or on measurements of several samples. There are a few cases in which MPRE could not be calculated, when Ra\textsuperscript{228} was presumed to be present, since the Ra\textsuperscript{228}/Ra\textsuperscript{226} ratio is not known by measurement or by any other estimate.

From a radiobiological point of view, radiation dose units are more appropriate and cumulative rads and cumulative rad-years have been used. Dose calculations have been carried out using the retention functions of NORRIS et al. [16].

---

* Computations were carried out at the MIT Computation Center and at the Cooperative Computing Laboratory of MIT.

** Experiments in this laboratory, now nearing completion, are designed to determine the extent to which Th\textsuperscript{228} may be important in the dosimetry of subjects with Ra\textsuperscript{228} burdens [11, 12].
DOSE-RESPONSE RELATIONSHIPS SKELETAL BURDENS $^{226}$Ra, $^{228}$Ra

ILLUSTRATION FOR DIAL PAINTERS FROM WATERBURY, CONN.

MPRE = $[1 + (0.063)(100)(1.5)] = 10.5 \mu c$ Ra

Fig. 2

Definition of minimum pure radium equivalent

Each of the curves is the ratio of the $^{228}$Ra dose unit/\mu c to the $^{226}$Ra dose unit/\mu c. These ratios are derived from curves similar to those in Figs. 4 and 5 but on the basis of injected microcuries instead of current microcuries as used in those figures. An average value of 1.5 at ~50 yr after initial exposure is assumed for purposes of calculating MPRE.

$$R_{Ra} = \text{At}^b = (0.54)t^{-0.52}$$
$$R_{Rn} = (0.021)t^{-0.28}$$

where $R$ = fractional retention and $t$ = time since exposure in days. For the shorter-lived $^{228}$Ra, a quadratic expression has been used to describe the retention of radium during the first day, according to the method of REYNOLDS [17]. The following assumptions are made for the dose calculation:

1. For $^{226}$Ra
   (a) Radon daughters not exhaled remain in bone.
2. For Ra\(^{226}\)
   (a) Thoron exhalation loss is negligible.
   (b) Translocation of Th\(^{228}\) from bone is negligible.
   (c) Ingested Th\(^{228}\) is not absorbed by the body.

With the above assumptions, the average dose-rate to the entire skeleton can be calculated as a function of time for Ra\(^{226}\) and Ra\(^{228}\), assuming a standard man with a skeletal mass of 7000 g and a standard woman with a skeletal mass of 5000 g (the latter being the estimated average value for our female subjects). Integration of the daily dose-rate leads to the average skeletal dose in rads accumulated from the date of exposure to some subsequent date.

An alternative hypothesis is the cumulative rad-year. Cumulative rad-year has been defined as the sum of the products of rads received in each year multiplied by the number of years between that year and time of examination, as suggested by AUB et al. [2]. This model, based on the work of BRUES et al. [18], indicates that early doses are of greater significance than later ones because more time is available in which the effects may present themselves. We have used the integral form of this definition:

\[
\text{CRY} = \int_0^T R(t) (T - t) \, dt
\]

where \( R(t) \) = dose-rate and \( T \) is the interval between administration and time of examination.

The dose calculations for cumulative rads and cumulative rad-years are shown in Figs. 4 and 5, calculated on the basis of a currently observed microcurie of Ra\(^{226}\) and Ra\(^{228}\). The curves of Fig. 3 are calculated from data similar to Figs. 4 and 5 but calculated on a basis of an injected microcurie.

The above calculations are based on the assumption that the radium administration was instantaneous. This is a good approximation for most dial painters. The duration of exposure for dial painters is usually short compared with the interval between employment and measurement. Calculations have been made to determine the effect of exposure period on the cumulative radiation dose and a typical illustration is shown in Fig. 6. For these calculations it is assumed that the administration rate is constant over the exposure period. It is surprising that, in general, exposure period does not have a large effect on the cumulative dose when the interval from midpoint of exposure, for exposures less than 5 yr, to time of measurement is greater than 30 yr. Corrections for this effect amounting to less than 2% were not made. It was necessary to apply this correction to only three cases with a maximum correction of about 10%.

Contingency test

In making the test for dependence of parameters with radiation dose, two other assumptions are made in addition to all those enumerated above and in addition to the comments on the quality and consistency of the data. First, it is assumed that the biological effects of Ra\(^{226}\) and Ra\(^{228}\) are proportional to the alpha-ray energies absorbed. Second, the assumption is
The curves show the internal radiation dose to the bones from the alpha rays of Ra$^{226}$ and its daughters based on the present body burden of the subject. The calculations are based on the retention functions of Norris et al. [16]. The radiation dose unit, rad-year, is defined in the text. The calculations include the production of Po$^{210}$ from the long-lived Pb$^{210}$.

made that the population is homogeneous with respect to present age and to age at exposure. The extent to which this assumption may be valid is shown by the following statistics:

<table>
<thead>
<tr>
<th>Average date of birth</th>
<th>1902 ± 11 *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average date of administration</td>
<td>1922 ± 9</td>
</tr>
<tr>
<td>Average age at administration</td>
<td>24 ± 9 yr</td>
</tr>
<tr>
<td>Average date of measurement or re-measurement</td>
<td>1959 ± 4 yr</td>
</tr>
</tbody>
</table>

The most commonly used test for determining the independence between two variables is the contingency test. This test is used extensively in genetic and pharmacological studies and is described in most books on statistics (see [19] for example). Briefly, the test postulates independence between two variables in question and then checks the closeness of fit between the model of independence and the actual data. If the model fits, there is no dependence. If it does not fit, a dependence is presumed to exist and further investigation is warranted. The closeness of fit is determined quantitatively by the standard $\chi^2$ test.

* One standard deviation.
Fig. 5

The curves show the internal radiation dose to the bones from the alpha rays of Ra\textsuperscript{228} and its daughters based on the present body burden of the subject. The calculations are based on the retention functions of Norris et al. [16] and on other assumptions described in the text.

The radiation dose unit, rad·year, is defined in the text.

A half-period of 5.7 yr for Ra\textsuperscript{228} has been used in these calculations.

A contingency test is made by first dividing the two variables into convenient ranges and then forming a table whose elements are the numbers of subjects falling in the intersection of two ranges. The Table is generally in the form of a rectangular matrix with each range designated by the indices i and j:

\[
\begin{array}{cccc}
X_{11} & \ldots & X_{1j} & \ldots & X_{1m} \\
X_{i1} & \ldots & X_{ij} & \ldots & X_{im} \\
X_{n1} & \ldots & X_{nj} & \ldots & X_{nm} \\
\end{array}
\]

Here \(X_{ij}\) represents the number of cases in range i of one variable and range j of the other. \(Y_i\) is the row total of the i'th row, and \(Z_j\) is the column total of the j'th column. There is a total of N cases. The number of degrees of freedom is \((m - 1) \times (n - 1)\).

If the variables are independent, the probability of a case falling into
element $ij$ is equal to the product of its probability of being in row $i$ and the probability of its being in column $j$. This probability is:

$$p_{ij} = \frac{Y_i}{N} \times \frac{Z_j}{N}$$

and the expected number of cases in element $ij$ is then $Np_{ij} = \frac{Y_i Z_j}{N}$. The approximation is necessary because $N$ is finite.

$$G = \sum \sum \left( \frac{(X_{ij} - Y_i Z_j/N)^2}{Y_i Z_j/N} \right) = N \sum \sum \left( \frac{X_{ij}^2}{Y_i Z_j} - N \right)$$

is calculated and is assumed to be an approximation to $\chi^2$. The closeness of fit between the data and the predicted values is obtained by estimating the probability of a greater deviation from the independence model by assuming $G \approx \chi^2$ and taking $F$, the number of degrees of freedom, into consideration. A numerical illustration of the contingency test is given in Table V.

The contingency test programme developed for this analysis, called CHI and written in FORTRAN, splits each variable into five ranges. A $5 \times 5$ matrix is made from the data. The ranges are in orders of magnitude for dosage parameters and are of equal size for other parameters. The output of the programme includes a listing of the variables, the matrix generated from the data, the expected matrix, and $G = \chi^2$ with an interpretation.

The normal interpretation of a contingency test is to assume that a $P(>\chi^2) > 0.01$ or $0.02$ indicates an independence between the two variables. To be on the safe side in these calculations, the cut-off has been taken at $P(>\chi^2) > 0.05$ in order not to miss any potential dependences. This programme has been checked by hand calculation. At present it does not weigh the data.

A difficulty in the use of the contingency test arises from the fact that the experimental matrix is a discrete or integer distribution, while $\chi^2$ and the calculated matrix are continuous. The application of this test to situations where all expectations, i.e., the number of cases per element, are less than 5 becomes risky. There are many occasions in the present analysis where the elements are not only less than 5 but even 0. The use of the contingency test as described for the analysis of the data, then, is open to some question. It is not clear whether the test rejects significant dependences because of these low expectations. However, from the results obtained, as discussed in the results section, there is reason to believe that the present test is satisfactory.*

**Determination of empirical expression**

Having determined if there is a dependence, it is useful to provide a quantitative description of this dependence with radiation dose. As a first

* A discussion by FREEMAN and HALTON [20] has just been found on an "exact" treatment of contingency. Its applicability and usefulness to our requirements are being investigated.
TABLE V

ILLUSTRATION OF CONTINGENCY TEST

<table>
<thead>
<tr>
<th></th>
<th>Hct₁</th>
<th>Hct₂</th>
<th>Totals</th>
<th>Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>MPRE₁</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>3</td>
<td>8</td>
<td>0.471</td>
</tr>
<tr>
<td>Matrix</td>
<td>MPRE₂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>2</td>
<td>9</td>
<td>0.529</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Fraction</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Calculated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>expected</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>matrix</td>
<td>5.65</td>
<td>2.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G = 0.48 X²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>χ² for 1% level = 6.64</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F = (2-1)(2-1) = 1,∶∶P = ~ 0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results of statistical analyses

Table VI summarizes the results of the contingency test between 56 case history and clinical parameters and the three dosage parameters. Dependencies are found for 25 parameters and for 13 of these parameters the dependence occurs for all three dose variables. Twenty parameters show
### Table VI

**Results of Contingency Test**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MPRE (µc)</th>
<th>CR</th>
<th>CTR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brush tipping</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>No. of exposures</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Age at 1st exposure</td>
<td>X</td>
<td>0</td>
<td>XX</td>
</tr>
<tr>
<td>Year of 1st exposure</td>
<td>0</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Duration of all exposures</td>
<td>XX</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dead or alive</td>
<td>X</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Year of birth</td>
<td>X</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Year of death</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sex</td>
<td>XX</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No. of marriages</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No. of normal children</td>
<td>0</td>
<td>X</td>
<td>0</td>
</tr>
<tr>
<td>No. of still-births</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sterility</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Search or symptom</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>General health</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Weight</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Height</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blood pressure, systolic</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MPRE (µc)</th>
<th>CR</th>
<th>CTR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse</td>
<td>X</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>X-ray score</td>
<td>XX</td>
<td>XX</td>
<td>X</td>
</tr>
<tr>
<td>Osteogenic sarcoma</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Carcinoma of paranasal sinuses</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Spontaneous fractures</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>No. of teeth remaining</td>
<td>X</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Dental condition</td>
<td>XX</td>
<td>XX</td>
<td>XX</td>
</tr>
<tr>
<td>Urinalysis -- sp. grav. albumin</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sugar</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urinalysis -- epith/hpf</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rbc/hpf</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wbc/hpf</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bacteria</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mucus</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Haematology -- white blood cells</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polymorphonuclear neut.</td>
<td>0</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Parameter</td>
<td>MPRE (µg)</td>
<td>CR</td>
<td>CRY</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------</td>
<td>----</td>
<td>-----</td>
</tr>
<tr>
<td><strong>Haematology -- white blood cells</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>XX</td>
<td>XX</td>
<td>X</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Basophils</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sedimentation rate</td>
<td>XX</td>
<td>XX</td>
<td>0</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>0</td>
<td>XX</td>
<td>0</td>
</tr>
<tr>
<td>Sugar</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MPRE (µg)</th>
<th>CR</th>
<th>CRY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinton</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Calcium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein electrophoresis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Albmin</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total globulin</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Alpha 1</td>
<td>0</td>
<td>0</td>
<td>X</td>
</tr>
<tr>
<td>Alpha 2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Beta</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gamma</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* The average number of cases considered in each test is ~190.
  
  → no dependence
  
  XX = dependence at 95% level
  
  X = dependence at 99% level
  
  - = not checked, too few cases for reliable calculation
a dependence on MPRE, 20 on CR, and 16 on CRY. There is no great dominance, therefore, of one dose variable over the other two. Since this is so and because of its simplicity and past usage, MPRE will be used, whenever possible, in the following discussion.

Comments on several of the items are given below:

**Brush tipping**

In the case history, dial painters are asked to estimate the extent to which they tipped brushes. Since brush tipping is considered the source of ingested radium, the body burden would be expected to be related to the extent of tipping, as found.

**Age at first exposure**

In this series, higher burdens are found in persons who were older at first exposure. No simple explanation is offered at this time.

**Year of first exposure**

Brush tipping for dial painters was more prevalent before ~1926 and working conditions were more carefully controlled from 1926 on. Thus, higher body burdens would be expected in those subjects who worked earlier, as the results indicate. Internal therapeutic use of radium terminated about 1935.

**Year of birth**

It is not clear why a higher body burden should occur at an earlier year of birth. In the case of dial painters, those born earlier would probably have worked at an earlier date when working conditions were poorer.

**Sex**

Dial painters were almost always women and injection cases were mostly women so that few men appear in the high body burden region.

**Marriages, children, and still-births**

Dependence is not found with respect to the number of normal children, still-births, or sterility, in eight out of nine tests. A relationship with burden is not expected and the one positive test may be false.

**Discovery: search or symptom**

This item has been discussed earlier in the text and is confirmed quantitatively here. Most of the cases with high body burdens were ill and were therefore discovered by symptom rather than by search.
General health

This item grades the general health of each living subject at the time of the last examination as poor, fair, or good. A dependence is found showing poorer health with the higher body burdens.

Reasonable explanations can be given for most of the dependences thus far discussed. Such results generate confidence in the contingency test even though it was open to some question because numbers less than five were present in some of the matrix elements. On this basis, the dependences found in the remaining items can be presumed to exist and would or may warrant further investigation.

X-ray score, tumours, and fractures

The dependence of X-ray score, osteogenic sarcomas, carcinomas of the paranasal sinuses and mastoids, and spontaneous fractures has been deduced previously directly from the data and confirmed by the quantitative analysis. The dependence of X-ray score, which includes sarcomas, carcinomas, and fractures is the strongest of any of the clinical parameters studied.

Number of teeth and dental condition

The number of teeth found decreases and the condition of the teeth and jaws becomes poorer as the body burden increases.

The effects on bones and teeth have been recognized in all previous work and are confirmed by the quantitative study. The primary effect of radium fixed in the body is to produce changes in the skeletal tissue where it is located. Microscopic studies of sections of the paranasal sinuses show that the cells are within the range of alpha rays emitted from the underlying bone. Thus the carcinomas found in these soft tissues are regarded as produced by direct alpha-particle irradiation arising in the adjoining bone.

Previous to this study, in qualitative perusals of the data, it had been concluded that significant changes in urinalysis, haematology, blood chemistry, and protein electrophoresis did not take place as the body burden increased. The present quantitative analysis indicates that some changes in these clinical laboratory parameters probably take place and warrant further study. These are urine albumin, polymorphonuclear and lymphocyte counts, morphology of red blood cells, sedimentation rate, and blood urea nitrogen. Changes in the $a_1$ globulin are questionable. Of these parameters, dependence with burden has been found for polymorphonuclear and lymphocyte counts and sedimentation rate in dogs injected with Ra$^{226}$ and Ra$^{228}$ as reported by DOUGHERTY [21]. The blood urea nitrogen is found to increase with cumulative rads. The dog data [22] show a slight decrease at the higher Ra$^{226}$ burdens and a definite increase at the higher Th$^{228}$ burdens. The change in the morphology of the red blood cells and the finding of increased albumin in the urine with increasing dose are new possibilities. The conclusions for these two parameters are doubtful, however, because a small fraction of the cases show abnormal morphology in the red cells or a positive test for urine albumin making the application of the contingency test questionable.
This figure shows the calculated increase in the internal radiation dose, expressed as cumulative rad-years (CRY), due to an extended administration of Ra\(^{228}\) as compared with a single administration leading to the same current microcurie. The rate of administration over the exposure period is assumed to be constant. The corrections required at times long after administration (~40 yr) become relatively small. This curve is a typical illustration and the results for Ra\(^{226}\) and for cumulative rads (CR) are similar. The values shown for Ra\(^{228}\) represent the greatest changes at ~40 yr and corrections, ≤ 10%, were made for three cases. For all other cases the corrections were ≤ 2% and were not made.

In addition, both tests are subjective and relatively less reliable than other laboratory tests. For albumin tests there is always the difficulty of getting clean voided urine specimens from women.

The relationship of some of the clinical parameters with body burden are shown in Figs. 7 - 11. The X-ray score is shown in Fig. 7. Either no or minimal changes are observed up to ~0.5 μc MPRE; the score then rises and reaches maximum values of ~45-50. The third-order power fit is

$$\text{X-ray score} = (0.40 \pm 0.32) + (6.4 \pm 0.3) (MPRE) + (-0.37 \pm 0.03) (MPRE)^2 + (0.0051 \pm 0.005) (MPRE)^3.$$  

The shape of this curve at the very high MPRE's is untrustworthy because of the few points involved. An argument can be made that the X-ray score would not continue to increase and would level off. These high scores have
X-ray score, the numerical expression of the subjective interpretation of some 25 films of the whole body, shows the strongest and clearest dependence of any of the clinical parameters with MPRE. The X-ray observations include bone necrosis (radiolucent and radiopaque areas), abnormal trabecular pattern, dental abnormalities, spontaneous fractures, osteogenic sarcomas, and carcinomas of the paranasal sinuses and mastoids. Finite scores are observed above ~0.5 μc MPRE. Below this MPRE the score is zero. A radiological investigation of 120 normal subjects from the Boston area, matched for age with the subjects under study, has shown small scores in 16 persons leading to an average score of ~0.2 ± 0.4 as a result of age alone. The shape of the curve at MPRE > 10 μc is not well known and a peak is not necessarily implied. Numerals indicate numbers of subjects at each position; for example, there are 12 points at 10⁻³ MPRE.

already led to death and persons at even higher MPRE's would die long before many more skeletal changes could be produced. The curve could conceivably come down again at the high MPRE's by a further extension of this argument; namely, that death would occur from non-skeletal causes long before the skeletal changes could develop. Thus, at MPRE's > 10, the shape of the curve is still unknown. At the low MPRE's the X-ray score is zero. Measurements of X-ray score on 120 normal individuals with an age distribution similar to these subjects has yielded a small but finite X-ray score of ~0.2 ± 0.4. The effects of aging do produce in some persons small skeletal changes similar to those observed in subjects exposed to radium. The average X-ray score for such subjects is essentially zero from 10⁻³ to 10⁻¹ μc MPRE. Thus, even if the two populations are not exactly the same the scores of the exposed subjects at MPRE's < 0.5 μc are essentially similar to those of a normal population and serve as an internal base for comparison at the higher MPRE's.

Figures 8 and 9 show the differential lymphocyte and polymorphonuclear counts, the former dependent on MPRE and the latter possibly dependent. The lymphocyte differential drops while the polymorphonuclear differential rises with MPRE. The reason for these changes lies in the fact that the absolute lymphocyte count has dropped from an average of ~2880 to ~1660 from burdens ~10⁻³ MPRE to the highest burdens. The polymorphonuclear count, on the other hand, remains constant at ~5800. Thus, the change in these differentials with MPRE is due only to changes in the lymphocyte count. Since the change in the lymphocyte differential is real, the change in the polymorphonuclear is also real, but the relative change is not large
The figure shows the differential lymphocyte count decreasing with increasing body burden. The decrease in this count is due to the decrease in the absolute lymphocyte count from an average of ~2880 at low MPRE to ~1660 at high MPRE.

The absolute polymorphonuclear count remains constant over this MPRE range.

The relation of the differential lymphocyte count to MPRE is similar to that found in the dog experiments at Utah. The values between $10^{-3}$ and $10^{-1}$ μc MPRE are in the normal range and have a normal scatter.

Most values at MPRE > ~5 μc are from subjects who were terminal or near terminal.

The accuracy of the curve beyond ~5 μc MPRE is dubious because the blood counts of many of these subjects may have been distorted by terminal illness. The empirical expressions for these parameters are

\[
\text{lymphocyte count (\%) } = (37.6 \pm 0.8) + (-3.1 \pm 0.8) (\text{MPRE}) + (0.22 \pm 0.08) (\text{MPRE})^2 + (-0.0039 \pm 0.0015) (\text{MPRE})^3
\]

\[
\text{polymorphonuclear neutrophile count(\%) } = (58.6 \pm 0.8) + (3.1 \pm 0.9) (\text{MPRE}) + (-0.22 \pm 0.09) (\text{MPRE})^2 + (0.0040 \pm 0.0016) (\text{MPRE})^3.
\]

As in the case of X-ray score the shapes of these curves at high MPRE are not meaningful because of the very few points available. According to the Utah dog data [22] these differentials vary with time after exposure. The results shown in Figs. 8 and 9 represent the situation for the human being at ~40 yr after initial exposure.

Figure 10 shows the relationship of sedimentation rate with MPRE. The values at the lower three decades are within the normal range and noticeable departure takes place only above MPRE about 0.5 μc. Again, the shape of
In spite of the fact that the contingency test indicates independence with MPRE, the figure shows the differential polymorphonuclear count increasing with increasing burden.

The absolute polymorphonuclear count remains constant at \( \sim 8000 \).

The relative change in this count is the reflection of the decrease in the absolute lymphocyte count, but the change is not large enough to result in a dependence.

The values between \( 10^3 \) and \( 10^4 \) \( \mu \)c MPRE are in the normal range and have a normal scatter.

Most values at MPRE \( \sim 5 \mu \)c are from subjects who were terminal or near terminal.

the curve at high MPRE may not be meaningful. The values for sedimentation rate at the lower decades of MPRE are in the normal range.

Figure 11 shows the results on haematocrit as an illustration of a parameter which is not dependent on MPRE. These haematocrits are essentially all in the normal range. In the human being at these MPRE's no change is observed even though changes in haematocrit are known to occur in the high level dogs exposed to Ra\(^{226}\) and Ra\(^{228}\) in the experiments at UTAH [22].

All the other clinical parameters which show no dependence with MPRE have values which are in the range of normal populations investigated by the clinical laboratory.

CONCLUSIONS

An analysis is carried out on the unweighed data obtained from human beings with internal body burdens of Ra\(^{226}\) and Ra\(^{228}\). Contingency test procedures are described for determining the relationship between case history parameters, clinical parameters, and internal radiation dose expressed as minimum pure radium equivalent (MPRE), cumulative rads, and cumulative rad-years. The present analysis indicates the following conclusions:

1. X-ray score, the numerical expression of the comprehensive radiological skeletal survey of the whole body, shows the strongest and clearest dependence on radium burden of all the clinical parameters studied.
The figure shows the sedimentation rate increasing with increasing burden. This trend is similar to that found in the dog experiments at Utah. The values between $10^{-3}$ and $10^{-1}$ µc MPRE are in the normal range for women consistent with the fact that the study contains three times more women than men. Numerals indicate number of subjects at each position.

This figure is a typical illustration of a clinical parameter which has been found to have no significant relationship to MPRE. The values between MPRE = $10^{-3}$ and $10^{-1}$ µc are in the range of normally accepted values and have a normal scatter. Most values at MPRE $\approx 5$ µc are from subjects who were terminal or near terminal. Numerals indicate number of subjects at each position.
2. There are indications of non-skeletal effects at the higher burdens. Changes in lymphocyte count and sedimentation rate are the more important of these effects. The reliability of the data at the high burdens requires further analysis of the data. The changes observed are similar to those found in the dog experiments at Utah.

3. No clinically significant signs or symptoms are observed at MPRE < 0.5 μc. In the region 10^{-3} to 10^{-1} μc MPRE the clinical data are in the normal range.

4. The analysis indicates no great dominance of one radiation dose variable over the other two. Since this is so, and because of its simplicity and past usage, the continued use of MPRE is suggested for the present.

5. The procedure of analysis is applicable to the continued analysis of our data and is applicable to the analysis of pooled data from other laboratories.

ACKNOWLEDGEMENTS

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REFERENCES

DISCUSSION

B. RAJEWSKY: It is interesting that the new data give us the same order of magnitude for the minimum body-burden-producing detectable effects as was estimated 30 yr ago on the basis of American and German data.

C. J. MALETSKOS: The radium cases available to Professor R. D. Evans and his associates in 1940, when the US maximum permissible body burden of radium was first set, did not show any detectable effects below 1.5 µg. A safety factor of 10 was applied, and the value of 0.1 µg resulted. Subsequent studies with more refined techniques at various laboratories have revealed detectable effects down to about 0.5 µg but not below, and the maximum permissible body burden of 0.1 µg still stands.

W.S. JEE: I am not sure that I understood your statement about the dependence of radium burden on the year of birth of the dial painter. It is commonly agreed that the uptake of radium is higher in young individuals. I would expect a higher uptake of radium in the diffuse component, in other words an increase in the diffuse-to-uniform ratio, and also a higher uptake due to the greater number of hotspot sites (incidence of hotspots) in young people. Dr. Harold Frost in the Henry Ford Hospital, Detroit, Michigan, has shown conclusively that at age 13 one has considerably more (factor of 5) remodelling sites than at age 35. If the remodelling sites correspond to hotspot deposits, then a higher uptake of radium in young individuals should be observed. I hope you will make an attempt to check these speculations in your planned study of terminal bone.

C. J. MALETSKOS: I agree with what you say in regard to the relatively larger radium deposition in younger persons. However, we are not discussing the age of the subjects at exposure but the year of birth of these subjects, points in time, such as 1901 versus 1909.

It is found that the people who are oldest have the highest burdens, and this result is opposite to what one might expect, as you just implied. Since
we are working with data which will have to be scrutinized in greater detail and since the interpretation of statistical manipulations can be tricky, we are being very careful in the deductions we make about the results of our data analysis at this time.

C.E. MILLER: The changes observed in the skeletal X-rays of radium patients become more marked, and thus the X-ray score increases, with increasing time after exposure. A plot of X-ray score versus body content of radium should, therefore, contain data only for patients who have had the radium in their bodies for the same length of time. The data obtained on exhumed bodies should not be plotted with data obtained recently on living persons.

C.J. MALETSKOS: You are correct. However, points for only two exhumed subjects are included in the plot of X-ray score versus MPRE (see Fig. 5). But we do consider, as a first approximation, that the time of observation is essentially the same for all subjects, namely about 35-40 yr after administration. The extent to which this is not true is indicated in the text, in the section entitled "Contingency test".
ОПРЕДЕЛЕНИЕ ИНТЕГРАЛЬНЫХ ДОЗОВЫХ НАГРУЗОК НА КОСТНУЮ ТКАНЬ ЗА СЧЕТ ИНКОРПОРИРОВАННОГО РАДИЯ-226

В. М. МАЛЫХИН и В. П. ШАМОВ
НАУЧНО-ИССЛЕДОВАТЕЛЬСКИЙ ИНСТИТУТ РАДИАЦИОННОЙ ГИГИЕНЫ МИНИСТЕРСТВА ЗДРАВООХРАНЕНИЯ РСФСР, ЛЕНИНГРАД СССР

Abstract — Résumé — Аннотация — Resumen

CALCULATION OF TOTAL BURDEN TO BONE TISSUE THROUGH INCORPORATION OF RADIUM-226.

The paper deals with a calculational method of determining body burden due to radium-226. The activity of the excreta and the time of contact with radium constitute the starting data. The results of the paper can thus be used by a wide circle of radiobiologists not possessing special apparatus for determining radium burden by exhaled radon or by measurement of the \( \gamma \)-activity of its daughter products with the aid of large counters.

The paper gives values of the effective excretion constant \( \lambda_{\text{eff}} \) for contact times \( t_1 = 2, 4, 6, 8 \) and \( 10 \) yr and elapsed times after contact \( t_2 - t_1 = 2, 4, 6, 8 \) and \( 10 \) yr. These values are obtained on the basis of an exponential excretion model and uniform uptake of radium by the body over the period of contact. Using the values of \( \lambda_{\text{eff}} \) it is possible to determine the radium content of the skeleton from the excreta activity. On the basis of these same model assumptions, an analytical expression is obtained for the dose to the skeleton for the whole time since start of contact. For the sake of convenience the results are presented as a graph of the dose coefficient \( K_D \), which is equal to a dose of 1 pc Ra/day in the excreta. The magnitude of the dose is determined by simply multiplying the activity of the excreta by the calculated dose coefficient \( K_D \).

ДЕТЕРМИНАЦИЯ ЧИСЛОВОЙ ЧАСТИ РАДИУМА-226 НА ОРГАНИЗМ ПО СОКРУШЕНИЮ РАДИОЭЛЕМЕНТА. Работа посвящена расчетному методу определения нагрузки на организм от радия-226. Исходными данными являются активность выделений и время контакта с радием. В таком виде результаты работ становятся доступными для широкого круга радиобиологов, не обладающих специальной аппаратурой для определения содержания радиоэлемента по выдыхаемому радиону или по измерению \( \gamma \)-активности его дофинейших продуктов. Результаты расчета позволяют определить содержание Ra в скелете на основе конкретных условий экспонирования организма.
представлений получено аналитическое выражение для дозы на скелет за все время от начала контакта.

Для удобства использования результаты представлены в виде графика дозового коэффициента $K_d$, равного дозе на 1 мккюр радио/сутки в выделениях. Величина дозы определяется простым умножением активности выделений на расчетный дозовый коэффициент $K_d$.

При нормировании радиоактивных изотопов, депонирующихся в костной ткани, предельно допустимые количества этих изотопов определяются путем непосредственного сравнения с нагрузкой радия-226. Выбор радия-226 в качестве стандарта для облучения костной ткани обусловлен тем обстоятельством, что человечество имело достаточный опыт работы с данным изотопом. В силу вышеуказанного консультативный комитет национального бюро стандартов [1] впервые установил предельно допустимое содержание радия-226 для профессиональных рабочих на уровне 0,1 мкг радия. Практически весь радий концентрируется в костной ткани и 0,1 мкг радия вместе с его дочерними продуктами распада создает мощность дозы на костную ткань равную 30 бэр/год. Это значение мощности дозы получено для коэффициента эманации радона из костной ткани, принятого равным 0,7 [2].

Однако поскольку рядом исследователей наблюдалось значительные изменения в костях пациентов при содержании радия-226 на уровне предельно допустимой нагрузки [3] равной 0,1 мкг (есть основания полагать, что при увеличении срока наблюдения указанные изменения будут более выражены или будут встречаться с большей вероятностью), - по-видимому, сама допустимая нагрузка или те дозы, при которых наблюдался изменения, определены недостаточно точно. Таким образом, проблему допустимой дозовой нагрузки необходимо тщательно изучать с тем, чтобы по мере накопления дополнительных данных о хроническом действии радиация уточнять основной параметр дозовой нагрузки на костную ткань.

Однако при анализе заболеваемости у той категории лиц, которая в прошлом работала с солями радия, встречается немало трудностей, связанных с тем, что по прошествии ряда лет трудно определить фактически полученную дозу за счет инкорпорированного радио.

В то же время определение поглощенной дозы за все время непосредственного контакта с радием и время прошедшее после прекращения контакта представляет особый интерес именно у данной категории лиц, так
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как дает возможность численно связать наблюдаемые отдаленные последствия с интегральной дозой на костную ткань и тем самым установить корреляцию между поглощенной дозой и наблюдаемым эффектом. Установление же численных корреляций между поглощенной дозой и наблюдаемым эффектом является тем краеугольным камнем, на котором строятся все рассуждения как с точки зрения обоснования ПДУ, так и с точки зрения нормирования радиоактивных изотопов во внешней среде.

В настоящем сообщении делается попытка дать аналитическое выражение для поглощенных доз за все время носительства радио как по фактическому содержанию радио на момент наблюдения, так и по активности выделения, которая определяется спустя некоторое время после прекращения контакта с радио.

Для определения количества радио-226, находящегося на данный момент времени в костной ткани человека возможны следующие пути:

а) определение радио-226 по \( \gamma \)-активности продуктов распада на кристаллических счетчиках методом \textit{in vivo} [4];

б) определение радио-226 по содержанию радио в выдыхаемом воздухе* [5];

в) определение радио-226 по содержанию его в выделениях**.

В практическом здравоохранении наиболее часто применяется последний метод, так как первые два метода требуют сложной аппаратуры, которая пока еще не нашла широкого распространения.

В силу вышеуказанных причин в данном сообщении основное внимание уделено косвенному методу определения содержания радио-226 в человеческом организме (последний из указанных методов). В качестве рабочей модели, характеризующей динамику выведения радио-226 из человеческого организма, принята степенная модель со следующими численными значениями коэффициентов: \( A = 0,54; n = 0,52 \) дней радио-226 [6]:

\[
q(t) = Qf_1 A t^{-n}.
\]

Конечной целью является корректная оценка величины интегральной дозы на костную ткань. Эта оценка должна основываться на наиболее реальном варианте динамики поступления радио-226 в организм. Для оценки величины дозы необходимо знать текущее содержание радио-226 в костной ткани на протяжении от начала контакта \( t = 0 \) до момента наблюдения \( t = t_2 \).

Если исходить из величины содержания радио-226 на момент \( t_2 \), то в зависимости от динамики поступления будет меняться кривая содержания радио от времени и соответственно дозе. Схематически это ясно из рис.1, где \( t_1 \) — длительность контакта с радио; \( t_2 \) — момент наблюдения (определения содержания радио в организме или выделениях); \( q(t) \) — текущее содержание радио в костной ткани; \( t \) — время, отсчитываемое от начала контакта.

* Методы а) и б) предполагают знание коэффициента эманации радона из костной ткани, который по последним данным равен 0,7 [2].

** Последний метод предполагает, что модель, описывающая выведение радио из организма, известна.
Величина дозы пропорциональна площади под кривой \( q(t) \). В зависимости от предположения о времени поступления радия в организм (при одинаковом содержании радия на момент наблюдения \( q(t_2) \) величина дозы будет разной. Крайние пределы получаются из предположений, что радий попал в начале периода контакта и в конце периода контакта.

Еще большее различие дозы получается в том случае, если исходить из заданной активности в выделениях. В этом случае в зависимости от предположения о динамике поступления радио-226 (равномерное, однократное в начале срока или в конце) кривая текущего содержания радио отличается еще больше. Дело в том, что по степенной модели величина "эффективной постоянной" выведения \( \lambda_{\text{эфф}} \) зависит от динамики поступления. Она равна:

\[
\lambda_{\text{эфф}} = -\frac{1}{q} \frac{dq}{dt} = \frac{n}{t} \text{ для случая поступления в начале контакта;}
\]

\[
\lambda_{\text{эфф}} = \frac{n}{t_2 - t_1} \text{ для случая поступления в конце срока контакта [4].}
\]

При равномерном поступлении в течение \( 0 \div t_1 \) для момента наблюдения \( \lambda_{\text{эфф}} \) выражается следующим образом:

\[
\lambda_{\text{эфф}}(t_2) = \frac{(n - 1)[t_2^n - (t_2 - t_1)^n]}{t_2(t_2 - t_1)[t_2^{n-1} - (t_2 - t_1)^{n-1}]}.
\]

В последнем случае (равномерного поступления) \( \lambda_{\text{эфф}} \) имеет промежуточное значение. Рассчитанные значения величины \( \lambda_{\text{эфф}} \) для всех трех случаев даны в табл.1 для разных длительностей контакта \( t_1 \) и времени от начала контакта до момента наблюдения \( t_2 \).

Величина \( \lambda_{\text{эфф}} \) уменьшается с ростом времени прошедшего после поступления радио в организме. Поэтому при одном и том же содержании радио в выделениях количество в организме будет разным в зависимости от времени поступления его в организм.

Если в выделениях имеется, например \( q_+ = 1 \) мкмкг/сут., причем радий поступал в ранние сроки контакта, то содержание его в ор-
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Таблица 1

<table>
<thead>
<tr>
<th>$t_1$ (годы)</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>$3,6 \cdot 10^{-4}$</td>
<td>$2,4 \cdot 10^{-4}$</td>
<td>$1,8 \cdot 10^{-4}$</td>
<td>$1,4 \cdot 10^{-4}$</td>
<td>$1,2 \cdot 10^{-4}$</td>
</tr>
<tr>
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<td>$2,5 \cdot 10^{-4}$</td>
<td>$1,9 \cdot 10^{-4}$</td>
<td>$1,4 \cdot 10^{-4}$</td>
<td>$1,2 \cdot 10^{-4}$</td>
</tr>
<tr>
<td>6</td>
<td>$3,6 \cdot 10^{-4}$</td>
<td>$2,3 \cdot 10^{-4}$</td>
<td>$1,7 \cdot 10^{-4}$</td>
<td>$1,4 \cdot 10^{-4}$</td>
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</tr>
<tr>
<td>8</td>
<td>$3,2 \cdot 10^{-4}$</td>
<td>$2,0 \cdot 10^{-4}$</td>
<td>$1,6 \cdot 10^{-4}$</td>
<td>$1,3 \cdot 10^{-4}$</td>
<td>$1,1 \cdot 10^{-4}$</td>
</tr>
<tr>
<td>10</td>
<td>$2,9 \cdot 10^{-4}$</td>
<td>$1,9 \cdot 10^{-4}$</td>
<td>$1,5 \cdot 10^{-4}$</td>
<td>$1,2 \cdot 10^{-4}$</td>
<td>$1,0 \cdot 10^{-4}$</td>
</tr>
</tbody>
</table>

Математически это определяется величиной $\lambda_{\text{эфф}}$ для момента наблюдения, так как содержание в организме $q(t_2)$ равно:

$$q(t_2) = \frac{1}{\lambda_{\text{эфф}}} \left( \frac{dq}{dt} \right)_{t_2} = \frac{1}{\lambda_{\text{эфф}}} \cdot q_1(t_2).$$

Кривые текущего содержания радия в организме при одном и том же количестве в выделениях на момент $t_2$ для разной динамики поступления схематично изображены на рис. 2.

Ход зависимости $q(t)$ показывает большую разницу в величине дозы для различной динамики поступления.

В работе проанализированы три случая поступления:
1) равномерное на протяжении времени контакта от 0 до $t_1$;
2) концентрирование в начале контакта при $t = 0$;
3) концентрированное поступление в конце срока контакта (при $t = t_1$).

В соответствии с расчетом по степенной модели получены указанные выше величины $\lambda_{\text{эфф}}$.

Приведенные в табл. 1 величины $\lambda_{\text{эфф}}$ следует использовать для оценки величины содержания радия в организме по активности выделений ($q_1$ мккмкюри/сут.):

$$q(t_2) = q_1 \text{ мккмкюри радия/сут.} \cdot \lambda_{\text{эфф}}^{-1}/\text{сут.}.$$
Рис. 2
Ход кривых текущего содержания радия-226 в организме для различной динамики поступления. Кривые дают содержание q(t) на единицу активности в выделениях.

Расчеты по той же степенной модели для перечисленных трех случаев дают выражения для текущего содержания в организме. Это содержание q(t2) может быть выражено двумя способами:
1) через постоянные модели n; A; f1 и скорость поступления q1 следующим образом:
   a) \[ q(t2) = \frac{qf_1A}{1-n} \left[ t_{2}^{1-n} - (t_2-t_1)^{1-n} \right] \]
   для равномерного поступления,
   где f1 — коэффициент перехода активности из ЖКТ в кровь; A — доля поступления из крови в костную ткань через единицу времени и выводящаяся из организма по степенному закону с указанными коэффициентами A и n;
   б) \[ q(t2) = Q \cdot f_1A \cdot t_2^{-n} \]
   для поступления в начале контакта количества Q;
   в) \[ q(t2) = Q \cdot f_1A(t_2 - t_1)^{-n} \]
   для поступления в конце контакта;
2) через активность выделений в момент наблюдения (q1(t2)):
   a) \[ q(t2) = \frac{q_1 \cdot t_2^{n}(t_2-t_1)^{n}}{(1-n)[t_{2}^{1-n} - (t_2-t_1)^{1-n}]} \cdot \left[ t_{2}^{1-n} - (t_2-t_1)^{1-n} \right] ; \]
   б) \[ q(t2) = \frac{1}{n} \cdot q_1 \cdot t_2 ; \]
   в) \[ q(t2) = \frac{1}{n} \cdot q_1 \cdot (t_2 - t_1) . \]

Однако содержание радия в организме представляет лишь косвенный интерес, так как более существенной характеристикой является интегральная доза, полученная к моменту наблюдения. Именно она дает возможность в совокупности с клиническими данными сделать содержательные выводы:
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Величина дозы получается умножением текущего содержания \( q(t) \) мккюри на мощность дозы \((\text{бэр}*/\text{сут. на 1 мккюри})\) и интегрированием по времени:

\[
D = \int_{0}^{t_2} q(t) \cdot P_1 \cdot dt.
\]

После того, как получено аналитическое выражение для текущего содержания радия в костной ткани, доза получается простым путем преобразования последнего выражения.

Для простоты и удобства пользования получены графики для величины дозового коэффициента \( K_D \). Так мы называем величину интегральной дозы, рассчитанной на 1 мккюри радия/сут. в выделениях. На рис.3 представлен дозовый коэффициент для различных сроков контакта \( t_1 \), времени наблюдения \( t_2 \). Величина дозы получается простым умножением \( K_D \) для принятых \( t_1 \) и \( t_2 \) на среднюю суточную активность выделения \( q_1 \) в мккюри:

\[
D = K_D \cdot q_1.
\]

Для трех рассмотренных случаев \( K_D \) выражается так:

а) \( K_D = \frac{8.05 \cdot 10^{-7} \cdot t_2^n}{(t_2^2 - (t_2 - t_1)^n)(1 - n)} \left\{ \frac{1}{2 - n} \left[ t_2^{2\cdot n} - (t_2 - t_1)^{2\cdot n} \right] - t_1 \right\} \);

б) \( K_D = 8.05 \cdot 10^{-7} \cdot t_2^2 \cdot \frac{1}{n(1 - n)} \);

* бэр — биологический эквивалент рада.
в) \( K_D = 8.05 \times 10^{-7} \cdot (t_2 - t_1)^2 \cdot \frac{1}{n(1 - n)} \).

\( K_D \) для случаев б) и в) представлен одним общим графиком рис. 4, где под \( t \) надо понимать время с предполагаемого момента концентрированного поступления в организм.

![График](image)

Дозовый коэффициент \( K_{1D} \) для однократного поступления радиоисотопа в организм в момент \( t = 0 \). (\( K_{1D} \) равен интегральной дозе на \( q_1 = 1 \) ммккюр радиоисотопа/сут. в момент \( t_2 \)).

Цифры около стрелок дают крайние возможные значения дозы на единицу активности выделений для времени контакта \( t_1 = 6 \) лет и времени наблюдения 6 лет после окончания контакта \( (t_2 - t_1 = 6 \) лет).

Несомненно, что более корректным методом определения интегральной дозы является метод основанный на прямом определении содержания радиоисотопа на момент обследования. Данный метод свободен от дополнительных погрешностей, связанных с определением той части радиоисотопа, которая выделяется непосредственно из организма. Поскольку содержание радиоисотопа в рационе находится на уровне нескольких мккюри, то вполне естественно, что при определении той части радиоисотопа, которая выделяется непосредственно из костной ткани, необходимо весьма тщательно отфильтровывать любое попадание в течение активности радиоисотопа, которая прошла через желудочно-кишечный тракт с продуктами питания.

В табл. 2 дается численное значение дозового коэффициента \( K_D \) для времени контакта до 10 лет и времени прошедшего после прекращения контакта до 10 лет. Таблица построена таким образом, что если содержание радиоисотопа на момент обследования \( (q(t_2)) \) выражать в единицах \( (10^{-10} \) кюри), то \( K_D \) дает интегральную дозу в бэрах при содержании в организме \( 1 \times 10^{-10} \) кюри радиоисотопа. Значения \( K_{1D} \), приведенные в центре клетки дают интегральную дозу для случая равномерного поступления радиоисотопа за все время контакта \( t_1 \), значения в левом нижнем углу дают дозу для поступления в начале контакта \( (t = 0) \), значения в правом нижнем углу дают дозу для случая поступления всей активности в последний день контакта.
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Таблица 2

ДОЗОВЫЙ КОЭФФИЦИЕНТ $K_d$, РАВНЫЙ ДОЗЕ НА $1 \cdot 10^{-10}$ КЮРИ

<table>
<thead>
<tr>
<th>$t_2 - t_1$</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1,4$\cdot 10^{-1}$</td>
<td>2,9$\cdot 10^{-1}$</td>
<td>4,23$\cdot 10^{-1}$</td>
<td>5,36$\cdot 10^{-1}$</td>
<td>6,44$\cdot 10^{-1}$</td>
</tr>
<tr>
<td></td>
<td>2,4</td>
<td>1,14</td>
<td>3,68</td>
<td>2,42</td>
<td>4,88</td>
</tr>
<tr>
<td>4</td>
<td>2,43$\cdot 10^{-1}$</td>
<td>3,68$\cdot 10^{-1}$</td>
<td>4,76$\cdot 10^{-1}$</td>
<td>5,91$\cdot 10^{-1}$</td>
<td>7,09$\cdot 10^{-1}$</td>
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<tr>
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<td>1,14</td>
<td>4,88</td>
<td>2,42</td>
<td>6,12</td>
</tr>
<tr>
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<td>4,31$\cdot 10^{-1}$</td>
<td>5,43$\cdot 10^{-1}$</td>
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<tr>
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<td>2,42</td>
<td>7,37</td>
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<tr>
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<td>4,88$\cdot 10^{-1}$</td>
<td>5,85$\cdot 10^{-1}$</td>
<td>7,12$\cdot 10^{-1}$</td>
<td>8,23$\cdot 10^{-1}$</td>
</tr>
<tr>
<td></td>
<td>6,12</td>
<td>1,14</td>
<td>7,35</td>
<td>2,42</td>
<td>8,55</td>
</tr>
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<td>6,35$\cdot 10^{-1}$</td>
<td>7,61$\cdot 10^{-1}$</td>
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<tr>
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<td>1,14</td>
<td>8,54</td>
<td>2,42</td>
<td>9,8</td>
</tr>
</tbody>
</table>

Выражение для интегральной дозы может быть записано в следующем виде: $D = K_d \cdot q(t_2)$, где $q(t_2)$ в единицах $10^{-10}$ кюри, а коэффициент $K_d$, дан в табл. 2.*

Величина эффективного параметра выведения $\lambda_{\text{эфф}}$ на время $t_2$ при различных сроках ($t_1$) равномерного поступления радио-226 в организм.

Для сравнения приведены $\lambda_{\text{эфф}}$ для случая концентрированного попадания в начале срока контакта ($t = 0$) и в конце срока ($t = t_1$).

ПРИЛОЖЕНИЕ

Ниже даны все подробности выкладок и математических рассуждений, использованных для получения приведенных в тексте формул и графиков для $q(t)$; $\lambda_{\text{эфф}}$, $K_d$, $D$.

Использованная модель предполагает, что удержание элементарного поступления в организм активности $q_1dt$ в момент $t$ определяется показательным законом:

$$dq(t_2) = q_1dt \cdot f(t_2 - t)^{-n},$$

dq(t_2) дает в таком виде количество активности, остающегося ко времени $t_2$ от поступления $q_1dt$ в момент $t$.

При равномерном потреблении со скоростью $q_1$ в единицу времени от $0$ до $t = t_1$ количество активности в критическом органе (кости) к моменту будет:

* После вычисления по величине $q(t_2)$ дозы по формуле $D = K_d \cdot q(t_2)$ следует произвести округление до второй значащей цифры.
Скорость выведения \( q(t_2) \) в момент \( t_2 \) определяется как скорость убыли в критическом органе \(-dq/dt\) в момент \( t_2\):

\[
q(t_2) = \int_{t_1}^{t_2} q(t_1) dt = q(t_1) \left[ (t_2 - t_1)^n - t_2^n \right].
\]

Если ввести в рассмотрение \( \lambda_{\text{эфф}} \) определив его по аналогии с \( \lambda_{\text{эфф}} \) для экспоненциальной модели выведения:

\[
\lambda_{\text{эфф}} = \frac{-dq}{dt},
\]

то оно уже будет функцией момента \( t_2 \) и вообще от динамики поступления в организм активности.

Как известно, для однократного введения в момент \( t = 0 \); \( \lambda_{\text{эфф}} \) степенной модели для момента \( t \) дается выражением:

\[
\lambda_{\text{эфф}}(t) = \frac{n}{t}.
\]

Для случая равномерного поступления от \( t = 0 \) до \( t = t_1 \) величину \( \lambda_{\text{эфф}}(t_2) \) вычисляем, используя выражение для \( q(t_2) \):

\[
\lambda_{\text{эфф}}(t_2) = \frac{\left( \frac{dq}{dt} \right)_{t_2}}{q(t_2)} = - \frac{q(t_1)A \left[ (t_2 - t_1)^n - t_2^n \right]}{n-1 \left[ (t_2 - t_1)^{n-1} - t_2^{n-1} \right]};
\]

\[
\lambda_{\text{эфф}}(t_2) = \frac{(1 - n) t_2^n - (t_2 - t_1)^n}{t_2^n (t_2 - t_1)^{n-1} [t_2^{n-1} - (t_2 - t_1)^{n-1}]}. \]

Видно, что \( \lambda_{\text{эфф}} \) меняется со временем и зависит от времени контакта \( t_1 \) и времени до наблюдения \( t_2 \). Физический смысл введенного \( \lambda_{\text{эфф}} \) тот, что оно дает относительную скорость выведения в данный момент. При степенной модели эта скорость не постоянна. Сохраняется однако правило перехода от скорости выведения (равной активности выделения для радия) к содержанию в организме \( q(t_2) \):

\[
q(t_2) = \frac{q(t_1) \lambda_{\text{эфф}}(t_2)}{\lambda_{\text{эфф}}(t_2)}.
\]

В табл.1 даны, кроме \( \lambda_{\text{эфф}} \) для случая равномерного поступления, величины \( \lambda_{\text{эфф}} \) для концентрированного поступления в начале контакта и в конце контакта. Эти величины считались по формуле:

\[
\lambda_{\text{эфф}}(t) = \frac{n}{t}.
\]

В таблице дана величина \( \lambda_{\text{эфф}} \) в 1/сут.
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При непрерывном поступлении со скоростью $q_1$ (кюри/сут. или кюри/рацион) в момент $t$ за время $dt$ поступит $q_1dt$ в организм человека, $f_1q_1dt$ в кровь и через единицу времени $f_1Aq_1dt$ поступит в костную ткань. После этого активность радия будет спадать по показательному закону и к моменту $t_2$ станет равной:

$$q_1f_1A(t_2 - t_1)^{-n}dt.$$

Текущее содержание радия в костной ткани во время накопления ($0 \leq t$) можно получить в этом случае так:

$$q(t_2) = \int_0^{t_2} q_1f_1A(t_2 - t_1)^{-n} dt = \frac{1}{1 - n} q_1f_1A(t_2^{-n} - 1);$$

для $1 \leq t_2 \leq t_1 + 1$.

Содержание после конца периода контакта ($t_3 \geq t_1 + 1$) выражается так:

$$q(t_2) = \int_0^{t_1} q_1f_1A(t_2 - t)^{-n} dt = \frac{q_1f_1A}{1 - n} [t_2^{-n} - (t_2 - t_1)^{-n}].$$

для $t_2 \geq t_1 + 1$.

Исходя из этих выражений для текущего содержания радио получим величину интегральной дозы ($D$):

$$D = D(0 \div t_1) + D(t_1 \div t_2) = \int_{0}^{t_1+1} P_1q(t_2/t_2 < t_1 + 1)dt_2 + \int_{t_1}^{t_2} P_1q(t_2/t_2 > t_1 + 1)dt_2.$$

Здесь $P_1$ - мощность дозы на 1 мк кюри радия в скелете ($P_1 = 8,05 \cdot 10^3$ бэр/сут. мк кюри радия); $q(t_2/t_2 < t_1 + 1)$ - текущее содержание радия в скелете перед началом контакта; $q(t_2/t_2 > t_1 + 1)$ - текущее содержание радия в скелете после окончания контакта. Вычисление дает:

$$D = \frac{P_1q_1f_1A}{1 - n} \left\{ \int_{0}^{t_1+1} (t_2^{-n} - 1)dt_2 + \int_{t_1+1}^{t_2} [t_2^{-n} - (t_2 - t_1)^{-n}] dt_2 \right\} =$$

$$= \frac{P_1q_1f_1A}{1 - n} \left\{ \frac{1}{2 - n} [t_2^{-n} - (t_2 - t_1)^{-n}] - t_1 \right\}.$$

Выразим теперь $q_1f_1A$ через активность суточного выделения $q_4$:

$$q_4 = -\frac{dq(t_2)}{dt_2} = q_1f_1A [(t_2 - t_1)^{-n} - (t_2)^{-n}];$$
Таким образом связь величины интегральной дозы с активностью выделений выражается следующей зависимостью:

\[
D = \frac{P_1q_1\left(\frac{t_2}{t_2 - (t_2 - t_1)^n}\right)^n}{[1 - n]} \left\{ \frac{1}{2 - n} \left[ \frac{t_2^{2-n} - (t_2 - t_1)^{2-n}}{2 - n} \right] - 1 \right\}.
\]

Обозначая через \(K_D\) множителей при \(q_1\) в этой формуле (дозу на единицу активности в выделениях) получим:

\[
D = K \cdot q_1,
\]

где \(K_D = \frac{P_1q_1\left(\frac{t_2}{t_2 - (t_2 - t_1)^n}\right)^n}{[1 - n]} \left\{ \frac{1}{2 - n} \left[ \frac{t_2^{2-n} - (t_2 - t_1)^{2-n}}{2 - n} \right] - 1 \right\}.
\]

Удобной единицей активности суточных выделений является 1 мккюри. Численные значения \(K_D\) при \(n = 0,52\) (радий) представлены на рис.3.

Пределные величины для дозы получаются в предложении концентрированного поступления радия в организм в начале контакта и в конце контакта.

Приведем без подробного объяснения выкладки для этого случая, считая, что общее поступление радио равно \(Q\).

\[
q = QAF_t t^{-n}; \quad t \geq 1;
\]

\[
q_4(t) = - \frac{dq_4}{dt} = QAF_t nt^{-n-1};
\]

\[
QAF_1 = \frac{q_4(t_2)}{n} t_2^{n+1};
\]

\[
q(t) = \frac{q_4(t_2)}{n} t_2^{n+1} \cdot t^{-n};
\]

\[
D = \int_{1}^{t_2} q(t) \cdot P_1 \cdot dt;
\]

\[
D = \int_{1}^{t_2} 8,05 \cdot 10^{-1} \cdot q_4 \cdot 10^{-5} \cdot \frac{1}{n} \cdot t_2^{n+1} \cdot t^{-n} \cdot dt;
\]
Интегральные дозовые нагрузки

Анализируя формулу
\[ D = K_{ID} \cdot q_{4} \]

и

\[ K_{ID} = \frac{8,05 \cdot 10^{-7}}{n(1 - n)} t_{2}^{n+1} [t_{2}^{2n} - 1] \approx 8,05 \cdot 10^{-7} \frac{t_{2}^{2}}{n(1 - n)} \]

(Последнее приближение справедливо с точностью ~3% для \( t_{2} \geq 3 \) года).

По этой формуле построен график 4 (рис. 4), который позволяет определить крайние возможные значения дозы. Для этого берется \( K_{D} \) для \( t = t_{2} - t_{1} \) и \( t = t_{2} \) и считается \( D = K_{ID} \cdot q_{4} \).

Литература


THE EXCRETION OF THORIUM X 
AND ITS DAUGHTER PRODUCTS 
AFTER INTRAVENOUS INJECTION IN MAN

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Abstract — Résumé — Аннотация — Resumen

THE EXCRETION OF THORIUM X AND ITS DAUGHTER PRODUCTS AFTER INTRAVENOUS INJECTION IN MAN. Thorium X (radium-224, 3.64 d half-life) has been widely used therapeutically in Germany since 1910. The main use today is for the therapy of Spondylarthrosis ankylopoetica (Morbus Bechterew-Struempell-Marie). 250-350 ¡¡c are injected intravenously in weekly doses of about 32 ¡ic.

The distribution of the gamma-emitting Th X-daughters in the human body was studied by means of a whole-body counter. Faeces and urine were measured without chemical treatment under a big NaI crystal in a mercury shield. The exhaled thoron was measured with a vibrating-reed electrometer arrangement.

The measurements show a rapid decrease of the body burden during the first eight days, where about 40% of the administered Th X is excreted. After this period a rather slow excretion modus was observed. These results are compared with those of radium-226 poisoning cases.

The decrease of the body burden, the amount of excreted Th X and Th B, and the exhalation of thoron can be described, in good agreement with the experimental values, in the first period by power functions, in the second period by exponential functions.

An explanation of the power function model as a superposition of exponential functions is discussed.

ÉLIMINATION PAR L’ORGANISME HUMAIN DU THORIUM X ET DE SES PRODUITS DE FILIATION APRÈS INJECTION PAR VOIE INTRAVENTEUSE. Le thorium X (radium 224, période de 3, 64 d) a été très utilisé à des fins thérapeutiques en Allemagne à partir de 1910. A l’heure actuelle, on l’emploie surtout pour le traitement de la spondylite ankylopoëtique (maladie de Bechterew-Strümpell-Marie). On injecte de 250 à 350 µc de thorium X par voie intraveineuse en doses hebdomadaires d’environ 32 µc.

La distribution dans le corps humain des produits de filiation du Th-X, qui émettent des rayons gamma, a été étudiée à l’aide d’un anthropogammamètre. On les a dosés dans les matières fécales et l’urine non traitées chimiquement, au moyen d’un grand cristal de NaI à l’intérieur d’une protection remplie de mercure. Pour mesurer le thoron exhalé, on a employé un électromètre à lame vibrante.

Ces dosages révèlent une diminution rapide de la charge corporelle durant les huit premiers jours, au cours desquels 40% environ du Th-X administré sont éliminés. Après ce délai, l’élimination a suivi un rythme plus lent. L’auteur compare ces résultats aux données fournies par des cas d’empoisonnement au radium 226.

La diminution de la charge corporelle, les quantités de Th-X et de Th-B éliminées et le taux d’exhalation du thoron peuvent être exprimés, en parfaite concordance avec les données expérimentales, par des fonctions de puissance durant la première période et par des fonctions exponentielles pendant la deuxième période.

L’auteur examine une possibilité d’expliquer le modèle fondé sur des fonctions de puissance par une superposition de fonctions exponentielles.

ВЫДЕЛЕНИЕ ТОРИЯ X И ПРОДУКТОВ ЕГО РАСПАДА У ЧЕЛОВЕКА ПОСЛЕ ВНУТРИВЕННОГО ВВЕДЕНИЯ. Торий X (радий-224, период полураствора 3,64 дня) широко использовался для терапевтических целей в Германии с 1910 года. В настоящее время он используется главным образом для лечения анкилозирующего спондилоартроза (болезнь Бехтерева-Штремпеля-Мари). 250–350 мккюр изотопа вводятся внутривенно, по 32 мккюри в неделю.

С помощью счетчика для измерения радиоактивности всего организма изучалось распределение гамма-излучающих дочерних продуктов тория X у человека. Измерение активности образцов экскрементов у мочи производилось без химической обработки под крупным кристаллом NaI за ртутным экраном. Содержание торона в выдыхаемом воздухе измерялось с помощью электрометра с язычковым преобразователем.
При измерениях обнаружено быстрое уменьшение содержания в организме торона в течение первых 8 дней, когда выделялось около 40% введенного тория X. После этого периода наблюдалось довольно медленное выделение. Полученные результаты сравнивались с данными излучения случаев отравления радием-226.

Снижение содержания изотопа в организме, количество выделяющегося тория X и тория B, и количество выдыхаемого торона могут быть охарактеризованы в хорошем соответствии с экспериментальными величинами, в первом периоде — с помощью функций мощности экспоненциальных функций.

Обсуждается объяснение модели функции мощности, как наложения функций экспоненциальных функций.

LA EXCRECIÓN DE TORIO X Y SUS PRODUCTOS DESCENDIENTES DESPUÉS DE LA INYECCIÓN INTRAVENOSA EN EL HOMBRE. El torio X (radio-224, periodo de 3,64 días) se viene utilizando ampliamente en Alemania con fines terapéuticos desde 1910. Hoy día se emplea principalmente en el tratamiento de la espondilitis anquilopoyética (Morbus Bechterew-Struempel-Marie), para lo cual se inyecta por vía intravenosa de 250 a 350 μc en dosis semanales de 32 μc aproximadamente.

La distribución en el cuerpo humano de los emisores gamma descendientes del Th-X se estudió empleando un antropogammametro. Las heces y la orina se examinaron sin tratamiento químico bajo un monocristal de NaI con protección de mercurio. El torón exhalado se midió utilizando un dispositivo a base de un electrómetro de lengüeta vibratoria.

Las medidas indicaron un rápido descenso de la carga corporal durante los primeros 8 d en los cuales se excreta un 40% del Th-X administrado. Después de este periodo la excreción tiende a hacerse más lenta. Éste resultado se compara con los casos de envenenamiento por el radio-226.

La disminución de la carga corporal, la cantidad de Th-X y Th-B excretada y la exhalación del torón pueden representarse, en buena correspondencia con los valores experimentales, por funciones potenciales en el primer periodo mencionado y por funciones exponenciales en el segundo.

El autor propone una explicación del modelo de función potencial como una superposición de funciones exponenciales.

1. INTRODUCTION

Thorium X (Ra224, 3,64 d half-life), the daughter product of radiothorium (Th228) in the naturally-radioactive thorium family, was discovered in 1902 by Soddy and Rutherford, and it was soon used as a possible remedy for many different diseases. About 30 publications are found in the medical literature before World War I. No animal experiments are known from this first period of application, and no contra-indication was found. Then, some deaths occurred, which can, today, easily be explained as the result of radiation damage to the blood-forming organs caused by very high doses of alpharadiation. The internal application of ThX was thenceforth (with one exception) practically abandoned; and today only certain skin diseases are treated by ointments or lacquers containing ThX.

In 1913 Bickel was the first scientist who reported a case of "ankylosing spondylarthritis" treated by intravenous injections of ThX. The "spondylarthritis ankylopoetica" is an inflammatory disease of the vertebral column, about 0.1% of the whole population is affected. Onset is at the age of about 20 yr and is followed by a progressive stiffening of the whole spine. The disease was exactly described at the end of the last century by Bechterew in Russia, by Struempell in Germany and by Pierre Marie in France.

The method of injecting ThX as a therapy of ankylosing spondylitis was introduced in 1925 by Leri in France, in England in 1944 by Hernaman-Johnson and in Germany 1946 by Troch.
By the courtesy of a hospital in Frankfurt we were able to make different physical measurements, mainly by application of scintillation-spectroscopy, at various time intervals after the therapeutic injection of ThX.

II. MEASURING INSTRUMENTS AND METHODS

The body burden is checked in our whole-body counter. The patient lies in the steel room on a plane bed. The 8-in by 4-in NaI-crystal is moved along the body axis. The pulses of the crystal are fed to a multichannel analyser. Unfortunately the ThX itself cannot be detected in vivo, as its gamma line of 241 keV has only a low intensity and is completely masked by the 239 keV peak of ThB. Thus the measurements with the whole-body counter can only give information on the distribution of ThB as measured by its 239 keV line, and ThC as measured by the 2.62 MeV peak of ThC'.

Additionally we have now the possibility of using a scintiscanner with a collimated 2-in by 2-in NaI crystal. The scanner stands in a room with normal radiation background. As the administered activity is much lower than in the cases where scintiscanning is normally used, it is difficult to get significant scintigrammes. Work is in progress to improve the resolution by using a bigger crystal and better shielding.

For the measurement of thoron exhalation the patient breathes into a mask. The exhaled air is dried and streams through a special ionization chamber. After measurement of the air flow velocity it is removed by a pump. The ionization current caused by the decay of thoron is measured by a vibrating-reed-electrometer and recorded by a strip-chart recorder. The faeces are sealed, as soon as possible, after excretion, into flat plastic bags of about 10 cm x 10 cm and are measured without chemical separation under a 3-in by 5-in NaI crystal in a steel and mercury shield. The activity of the samples is defined by counting the pulses of the peaks of 2.62 MeV (ThC') and 239 keV (ThB). The gamma-emitting daughter products of ThX are in most cases below transient equilibrium with ThX at the moment of excretion. By measuring in short time intervals the increase to the equilibrium value and then the decrease with the half-life of ThX, the activity of ThX at the moment of excretion can be determined by extrapolation.

The measurement in urine is similar. Each fraction of urine is collected in a plastic bottle with 10 cm³ of hydrochloric acid to avoid adsorption of ThB on the walls. Ten cubic centimeters of urine are placed in a plastic test tube and sealed and measured in a well-type NaI crystal inside another steel and mercury shield. With the faeces, mainly ThX is excreted, the observed daughter products being chiefly formed in the intestine. In the urine, however, only ThX is 3% of the total excretion in the first week [1-3] with a high excess of ThB and ThC. In the last few weeks it was possible to get daily blood samples from three patients during the first week after injection. Ten cubic centimeters of blood were centrifuged and the serum and the sediment were measured separately in the same manner as the urine samples. As a preliminary result I can say that the red blood cells contain very high amounts of ThB, while the ThX content is much lower and is contained in the blood serum.
By measuring the excretions without chemical separation and without concentrating by evaporation, we can count the sample within a few minutes after excretion, and no losses occur. The disadvantage is that, with increasing time after injection, the specific activity of the samples decreases, and long measuring times are needed.

III. RESULTS OF MEASUREMENTS

While in the past high doses of ThX were often administered, the usual dose today is 250–350 μc, given in weekly doses of 32.5 μc. ThX is separated chemically from the parent RdTh. An unavoidable admixture of about $10^{-5}$ c RdTh per c ThX was measured, in agreement with other authors [4]. One cubic centimetre of ThX solution is sealed in a vial and shipped to the hospital, where it is used as a rule about 24 h after separation. Thus the daughter products ThB and ThC are not yet in equilibrium with ThX. Usually about 3% of the ThX and 5–6% of the equilibrium values of ThB and 15–20% of the ThC remain in the vial and the syringe.

A short time after injection, measurements in the whole-body counter show a distribution of ThB similar to the observed distribution of nuclides which are uniformly deposited in the whole body ($K^{40}; Cs^{137}$) (see Fig. 1). Subsequent measurements, made 1 to 8 d after injection, show another form of distribution with a maximum in the liver region. After 8 d a new pattern is observed. As will be seen later, excretion and decay have then diminished the ThX and ThB deposits, the remainder of ThX being located at the places of bone metabolism, in the case of ankyllosing spondylitis preferentially in the diseased vertebral spine [5]. Because of the short half-life (54.5 sec) of the first daughter product, the noble gas thoron, most of the thoron de-
EXCRETION THORIUM X AND DAUGHTERS AFTER INJECTION

If we plot the counts measured in the liver region as a function of time on a semi-log and log-log scale (Figs 2 and 3), we see that the decrease of the liver region deposit of ThB can be described in the first week by a power function. In the second week the decrease is mainly determined by the radioactive decay of ThX. Similar behaviour was observed with measurements of the thoron exhalation. In the first week the decrease follows a power function, in the second and third week it is only slightly different from the physical decay of ThX, represented by a straight line in the semi-log scale (Figs 4 and 5).
Because of the rather long sojourn time of the faeces in the intestine, the maximum value of faecal excretion is reached 1-2 d after injection (Fig. 6). Up to 20% of the originally administered ThX activity was observed in a single sample. The amount of ThX excreted decreases quickly, following in the first week a power function with an exponent of about -6 to -7. After the first week about 35% of the injected amount is excreted in the faeces. Then the faecal excretion becomes irregular, the activity of the samples varying by factors of 10-15, as observed by other authors [6, 7]. The decrease of the mean values corresponds roughly to the decay of ThX (see Fig. 6). In the case shown in the curve of Fig. 6 the first sample, excreted 20 h, and
the second, excreted 45 h after the injection, contain lower amounts of ThX than would be expected from the curve. We may conclude from this fact that the faecal transport of ThX begins more than 45 h before excretion, but that even in the last 20 h an intake through the intestine must be assumed.
Excretion by urine, mainly of ThB and ThC, begins shortly after injection. ThX is only found in small amounts, the ratio between faeces and urine in the first week being 35:1. Plotting daily urinary excretion versus time results in another power function (Fig. 7). In the second week the activity of the urine could no longer be measured by the method used here [1-3].

Using the measured values for application and excretion, the ThX body burden can be estimated. Normalizing the administered amount by calculating the physical decay in the intervals between the excretions and subtracting the amounts excreted via faeces and urine results in the polygon curves shown in Figs 8 and 9. After the first week the excretion causes only a negligible decrease of the body burden, which is now mainly governed by the physical decay of ThX. As was found by many investigators [8-14] we may assume that ThX is deposited almost exclusively in the skeleton. The following estimations are based on this assumption.

To understand better the distribution of the administered ThX in the body, the following model is proposed: From the skeletal deposit — after its stabilization — a "compartment" at time zero is calculated by extrapolating the physical decay. A second compartment is formed in extrapolating the single faeces samples to time zero and summing up of the calculated values. The third compartment, much lower than the first two, concerns excretion in urine. The sum of these three compartments approximately equals the administered amount.

To answer the question whether a power function results from the combination of several exponential functions presupposes the evaluation of a sufficiently high number of cases. It has been proved to be very difficult to get the complete excreta of the patients, who as a rule are not bed-ridden and may leave the hospital for hours or even for days. Therefore animal experiments are needed to get statistically significant values.
IV. COMPARISONS WITH RADIUM POISONING CASES

In our institute we had, some years ago, several cases of poisoning with single doses of Ra\textsuperscript{226}. The questions of interest arising were:

1. excretion and retention of the bone-seeker Ra by the human body;
2. distribution of Ra in the body;
3. maximum permissible body burden;
4. mechanism of the toxic effect; and
5. therapeutic measures to accelerate the excretion.

Question (3) may be regarded as solved, mainly by the work of Rajewsky and Evans. The distribution in the human body after long time intervals has also been extensively studied. But in the case of the early reactions of the human body to single doses of Ra there is lack of information. As we have seen, the behaviour of ThX in the first week after administration is very similar to that of Ra\textsuperscript{226}, as far as observations could be made. We therefore believe that the therapeutic use of ThX may serve as a test to study in vivo the early stage of radium poisoning and the behaviour of the short-living daughter products radon-220, lead-212 and bismuth-212.

If animal experiments are taken into consideration, the reaction of different animal species, on the administration of bone-seekers, may be studied by the injection of ThX and comparing the results with those obtained in man.

REFERENCES

DISCUSSION

C. J. MALETSKOS: We have recently carried out similar studies as part of a programme to determine the relative absorption of radium and thorium by the gastro-intestinal tract of human beings, and our results, though the analysis is not yet complete, appear to confirm those you have obtained. I have, however, two comments. We find that most of the lead-212 remains in the blood after injection and, until this decays, the \( \gamma \)-output of the body will be more representative of the activity distributed in blood than of radium going to or distributed in bone. Moreover, the lack of equilibrium between lead-212 and radium-224 due to the injection procedure may cause additional complications in the \( \gamma \)-output of the body — although, with care, the effect of this can be minimized. For about the first five days, then, the better retention data are probably obtained from the excretion data you have used.

F. SCHALES: As regards your first comment, I hope it will be possible to estimate the ThX body content by analysing the absolute values and the changes in thoron exhalation.
MEASUREMENTS OF RADIUM IN RADIUM LUMINIZERS

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Abstract — Résumé — Аннотация — Resumen

MEASUREMENTS OF RADIUM IN RADIUM LUMINIZERS. A group of about 500 people, mostly women, who have worked in the radium luminizing industry over a period of about 50 yr have been measured to assess radium in the body.

Measurements have been made of both the exhaled radon and that which is retained in the body. The exhaled radon has been determined on breath samples taken using specially designed breathing apparatus by means of which radon-free air can be inhaled from a cylinder and subsequently exhaled into a collecting bag. The amount of gamma-emitting radon decay products in the body was measured in a low background laboratory using a sodium iodide crystal scintillation counter. This equipment was calibrated by means of a standard radium source placed at several points in a water-filled plastic model of the human body on the assumption that any radium in the body is distributed uniformly throughout the skeleton. The error of measurement of the total radium content of the body was estimated to be about 0.005 μg Ra.

Twenty people were found to have more than 0.1 μg Ra in their bodies, the largest measured amount being 0.6 μg. A further sixty people had amounts in excess of 0.05 μg but less than 0.1 μg. These results are correlated with the date of commencing luminizing and show that no person who commenced working after 1942 has an amount in excess of 0.05 μg in his body. This date can be related to the introduction by H. M. Government of a statutory order controlling the use of radium in the luminizing industry.

The exhaled radon fraction has been correlated with the total radium content for about thirty people having amounts varying from 0.01 μg to 0.6 μg. Over this range the fraction of radon found in the breath was about two thirds.

CHARGE CORPORELLE DE RADĪUM DANS L'INDUSTRIE DES PRODUITS LUMINESCENTS AU RADĪUM.

Un groupe d'environ 500 personnes, dont la plupart étaient des femmes et qui avaient travaillé une cinquantaine d'années dans l'industrie des produits luminescents, ont subi des examens dosimétriques en vue de déterminer la présence du radium dans leur organisme.

Les dosages ont porté à la fois sur le radon exhalé et sur le radon retenu dans le corps. Pour doser le radon exhalé, on a utilisé des échantillons d'air exhalé prélevés au moyen d'un appareil respiratoire spécial; grâce à cet appareil, de l'air exempt de radon contenu dans un cylindre peut être inhalé et exhalé dans un sac collecteur. On a mesuré la charge corporelle de produits de filiation du radon, qui émettent des rayons gamma, dans un laboratoire où le bruit de fond était faible, au moyen d'un compteur à cristal d'iode de sodium. On avait étalonné l'appareil au moyen d'une source de radium, placée en différents points d'un modèle du corps en matière plastique rempli d'eau, en supposant que tout le radium contenu dans le corps se trouve uniformément réparti dans l'ensemble du squelette. L'erreur que comportait la mesure de la charge corporelle totale de radium a été évaluée à environ 0,005 μg.

Les auteurs ont constaté que chez 20 personnes, l'organisme contenait plus de 0,1 μg de radium, la quantité maximum mesurée étant de 0,6 μg. Chez 60 autres personnes, la charge corporelle dépassait 0,05 μg mais restait inférieure à 0,1 μg. En comparant ces résultats et la date à laquelle les intéressés avaient commencé de travailler dans l'industrie des produits luminescents, les auteurs ont constaté en outre qu'aucune personne engagée après 1942 n'avait une charge corporelle supérieure à 0,05 μg. C'est cette année-là que le Gouvernement britannique a pris un arrêté portant contrôle de l'emploi du radium dans l'industrie des produits luminescents.

Les auteurs ont aussi comparé la fraction de radon exhalé et la charge corporelle de radium pour une trentaine de personnes chez qui la quantité était comprise entre 0,01 et 0,6 μg. Pour cette gamme de valeurs, la fraction de radon trouvée dans l'air exhalé était d'environ deux tiers.

ИЗМЕРЕНИЕ СОДЕРЖАНИЯ РАДИЯ У РАБОТАЮЩИХ С РАДИЕВЫМИ ЛЮМИНЕСЦЕНТНЫМИ СОСТАВАМИ. Обследовалась группа служащих 500 человек, преимущественно...
DETERMINACIÓN DEL RADIO EN TRABAJADORES DE LA INDUSTRIA DE LAS PINTURAS LUMINOSAS.

La memoria describe mediciones efectuadas con un grupo de unas 500 personas, en su mayoría mujeres, que habían trabajado en la industria de las pinturas luminosas a base de radio durante unos 50 años, con el fin de determinar la cantidad de radio presente en su organismo.

Se han efectuado mediciones del radón exhalado y del radón retenido en el cuerpo. El radón exhalado se determinó en muestras tomadas con un respirador especial que permite inhalar aire libre de radón, procedente de un cilindro, y recoger en una bolsa el aire exhalado. La cantidad de emisores gamma formados por desintegración del radón en el cuerpo se midió en un laboratorio de baja actividad de fondo por medio de un contador de centelleo provisto de un cristal de yoduro sódico. El aparato se calibró con ayuda de una fuente patrón de radio situada en diversos puntos de un maniquí de material plástico lleno de agua, partiendo del supuesto de que todo el radio está distribuido uniformemente en el esqueleto. Se calculó que el error de medición del contenido total en el organismo era del orden de 0,005 μg de Ra.

En veinte personas se hallaron cantidades superiores a 0,1 μg de Ra, siendo la mayor cantidad encontrada 0,6 μg. Otras sesenta personas presentaron cantidades superiores a 0,05 μg pero inferiores a 0,1 μg. Analizando los datos en función de la fecha en que cada individuo comenzó a trabajar en la industria, se encuentra que ninguno de los que empezaron después de 1942 arroja valores superiores a 0,05 μg. Esta fecha coincide con la aprobación por el Gobierno británico de una nueva ley tendiente a controlar el empleo del radio en la industria de las pinturas luminosas.

Los autores establecieron una relación entre la fracción de radón exhalado y el contenido total de radio de unas 30 personas que daban valores comprendidos entre 0,01 μg y 0,6 μg. Comprobaron que en ese intervalo, la fracción de radón exhalado representa un valor del orden de dos tercios del total.

1. INTRODUCTION

When fixing maximum permissible levels of body radioactivity for human occupational exposure, information is required concerning the effects on people who have been exposed to the hazard of taking the various radio-nuclides into the body under normal working conditions for considerable periods of time. Such data is very limited and only in the case of workers in the radium luminizing industry is there any considerable history of exposure.
Since the earliest appreciation of the harmful effects of accidentally acquired radium luminous compound by MARTLAND et al. [1], other investigators have reported clinical effects [2-3] and estimates of the related body contents [4-6]. Such data form the basis for the present maximum permissible body burden of radium, 0.1 μc, which is recommended by the International Commission on Radiological Protection (ICRP) [7]. This is about one-tenth of the lowest amount observed to be present in seriously injured radium luminizers in New Jersey, United States [8]. However, this information inevitably came from a limited number of workers who were presented for medical examination because of symptoms which could be associated with the practice of luminizing. In this respect, therefore, it possibly provides a biased view of the risks involved by luminizers in general.

In the hope of obtaining further useful information, an investigation of the past experiences of British luminizers was commenced in 1957. The process of luminizing has been carried out in Great Britain since the beginning of the First World War, and involved the largest number of luminizers during the Second World War. Following the early American experience, the occupation of luminizing was brought under the medical supervision of the Ministry of Labour in about 1941, and mainly through the Ministry's records, information was obtained on about 2000 people. A study population was selected by Dr. J. T. Boyd of the Medical Research Council's Radiation Registry, which included all ex-luminizers whose records suggested at least three years luminizing together with a few currently employed workers who had more than ten years working experience [9]. The group was later extended to include workers with less than three years experience, but who had luminized during the early part of the 1939-1945 war, for reasons which will be apparent later. A large number of the study population have been traced, and most of them have agreed to be referred to this Unit for measurements of body radioactivity. Contact is being maintained with all the people who have been measured. Measurements are reported on a group of 470 people, mostly women, who worked in the radium luminizing industry over the period from 1915 onwards. Other investigators have also shown an interest in similar studies [10-12].

2. MEASUREMENT OF RADIUM IN THE BODY

The measurement of radium involves a determination of the amount of radon retained in the body and that exhaled in the breath. In all cases, the fraction of radon retained in the body has been measured by means of a whole-body counter which detects the gamma-ray emitting daughter products, RaB and RaC. In a proportion of cases, the fraction of radon escaping from the body in the exhaled breath was also measured.

2.1. Measurements of body radioactivity

2.1.1. Whole-body counter

The whole-body counter, which was established in 1957, is shown diagramatically in Fig. 1, and a photograph of the actual arrangement of the
Diagram of arrangement of detectors and shielding for the whole-body counter detectors in relation to the position occupied by the body is shown in Fig. 2. Primary shielding is provided by placing the counter in a room excavated in the local chalk, because the chalk was found to have a very low gamma-ray
RADIUM LUMINIZERS

This is primarily due to the low concentration of potassium, about 20 ppm. The inside of the room is lined with \( \frac{1}{4} \)-in aged lead plates. The detector comprises four NaI(Tl) crystals, each 11 cm diam. \( \times \) 5 cm thick, optically coupled through fused silica windows to 5-in photomultipliers. The output pulses are mixed, amplified and fed to a 100-channel pulse-height analyser which records the spectrum of pulses corresponding to gamma-ray energies ranging from 100 keV to 2.4 MeV. Pulses corresponding to higher energies are recorded on a separate scaler. In addition, the amplified pulses are fed to a single-channel analyser which accepts those pulses corresponding to gamma-ray energies ranging from 1.6 to 2.4 MeV. The person to be measured lies supine, with the head supported by a pillow, on a stretcher which can be wheeled into position beneath the crystals. The distance between adjacent crystals is 45 cm, and the surface of the stretcher is 33 cm below the crystal faces.

2.1.2. Calibration

A radium source supplied and standardized by the Radiochemical Centre, Amersham, England, was used to calibrate the apparatus. It is enclosed in a small Monel metal cylinder, 9 mm long and 1.6 mm diam., with a wall thickness of 0.5 mm. The radium content is stated to be 1.24 \( \mu \)c with a maximum error of \( \pm 6\% \). This source is placed at several positions in a water-filled polyethylene model of the human body, based on a design by Bush [14] and shown in the photograph, Fig. 2. It consists of ten cylinders of the dimensions shown in Table I. The radium source was placed in turn at

<table>
<thead>
<tr>
<th>Part of model</th>
<th>Cross-section</th>
<th>Length (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>19 cm ( \times ) 14 cm ellipse</td>
<td>20</td>
</tr>
<tr>
<td>Neck</td>
<td>13 cm circle</td>
<td>10</td>
</tr>
<tr>
<td>Thorax</td>
<td>30 cm ( \times ) 20 cm ellipse</td>
<td>40</td>
</tr>
<tr>
<td>Abdomen</td>
<td>36 cm ( \times ) 20 cm ellipse</td>
<td>20</td>
</tr>
<tr>
<td>Thigh (2)</td>
<td>15 cm circle</td>
<td>40</td>
</tr>
<tr>
<td>Leg (2)</td>
<td>12 cm circle</td>
<td>40</td>
</tr>
<tr>
<td>Arm (2)</td>
<td>10 cm circle</td>
<td>60</td>
</tr>
</tbody>
</table>

Total mass 70 kg (150 lb); Total height 170 cm (5 ft 7 in)

the centres of the sections corresponding to the anatomical regions, head, thorax, abdomen, thighs, legs and arms. It is assumed that any radium in the body is more or less uniformly distributed throughout the skeleton and, therefore, the contribution from the source at each position, to the total response of the counter, can be weighted according to the mass of the skeleton
TABLE II

PROPORTION OF CALIBRATION TIME ACCORDING TO ESTIMATED SKELETAL BONE CONTENTS OF PARTS OF MODEL OF HUMAN BODY

<table>
<thead>
<tr>
<th>Part of model</th>
<th>Estimated skeletal bone content</th>
<th>Total skeletal wt. (as a proportion of 15 min)</th>
<th>Counting time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>Skull + Lower jaw</td>
<td>18.4</td>
<td>168</td>
</tr>
<tr>
<td>Thorax*</td>
<td>2 Clavicles, 2 Scapulae,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sternum + Ribs, § Spinal column</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomen</td>
<td>Pelvis + § spinal column</td>
<td>12.9</td>
<td>116</td>
</tr>
<tr>
<td>Thigh (each)</td>
<td>Femur</td>
<td></td>
<td>105</td>
</tr>
<tr>
<td>Leg (each)</td>
<td>Tibia, fibula + foot</td>
<td>12.1</td>
<td>109</td>
</tr>
<tr>
<td>Arm (each)</td>
<td>Humerus, Radius, ulna + hand</td>
<td>7.5</td>
<td>68</td>
</tr>
</tbody>
</table>

* The neck was incorporated in the thorax.

in each of the six anatomical regions. Table II shows how the total observation time of 15 min is subdivided. Values for the skeletal weight have been given by SPIERS and BURCH [15]. In fact, the counting rate does not vary appreciably at the six positions, being within about ± 5% of the mean value. This means that the response of the counter is sensibly independent of changes in the distribution of radium over a median horizontal plane of the body. Figure 3 shows a spectrum of the pulses obtained by this method of calibration and that of a woman luminizer. It will be seen that the general features of the spectrum from radium in the woman are reproduced in the calibration spectrum.

2.1.3. Method

The amounts of RaB and RaC in the body were estimated from observations on two parts of the radium spectrum, namely, on pulses corresponding to gamma-rays of energies greater than 100 keV and those corresponding to gamma-rays in the energy band 1.6 - 2.4 MeV. The former method has the greatest intrinsic sensitivity for the detection of gamma-rays emitted by the body. However, it suffers from the disadvantage that the spectrum includes pulses arising from the gamma-rays emitted by the naturally occurring K⁴⁰ and the fission product Cs¹³⁷, both of which are present in humans. An allowance has to be made, therefore, for both these radionuclides when estimating radium. The second energy band includes pulses arising from the 1.76 MeV gamma-rays of RaC which account for one of the prominent peaks in the radium spectrum. Observations in this band have the
advantage that gamma-rays from Cs\textsuperscript{137} are not included and inaccuracies due to interference by K\textsuperscript{40} are small. The apparatus was calibrated for potassium and Cs\textsuperscript{137} by filling models of the body, shown in Fig. 2, with solutions of known concentrations of potassium chloride and caesium-137 chloride respectively. Luminizers were usually measured for 1 h, followed or preceded by a measurement of background, also for 1 h, using a model of the body filled with distilled water. The reproducibility of the calibration was checked daily by measurement of check sources of Cs\textsuperscript{137}, K\textsuperscript{40} and radium which had been cross-checked at the time of calibration. Under these conditions the standard error of a measurement, due to statistical errors of counting alone, was about ±2.5 nc RaB and RaC.

An estimate was also made of the amount of mesothorium-I (MsTh-I) from observations on an energy band around 2.6 MeV, which includes a prominent gamma-ray energy in the Thorium C\textsuperscript{7} spectrum. The standard error of a measurement due to statistical errors of counting alone was about 2.5 nc MsTh-I. MsTh-I, which has been used in luminizing, is an isotope, Ra\textsuperscript{228}, of radium. However, there is no record of any widespread use of this material in luminous compound in Great Britain. No measurable amount of MsTh-I was found in any of the luminizers in this series, but since the half-life is 6.7 yr this gives no guarantee that the radionuclide was not present in the body initially.

2.2. Measurement of exhaled radon

2.2.1. Radon assay

When radon decays by the emission of an alpha particle the daughter product, RaA, is positively charged due to the emission of delta-rays. Therefore, atoms of RaA will be attracted to a negatively charged electrode. If such an electrode is coated with a scintillator, the subsequent alpha particles emitted by RaA and RaC\textsuperscript{1} will produce light flashes which can be counted by conventional means. This method, which has been described by BRYANT and MICHAELIS [16], forms the basis for the design of the apparatus used and shown in Fig. 4.

The electrode is a perspex hemisphere mounted beneath a perspex window in a 3-1 chamber of stainless steel. The negative potential is applied to the hemisphere by a support rod which passes through a high-voltage insulator in the chamber wall. The lower curved surface of the hemisphere is coated with zinc sulphide luminescent powder and hygroscopic agent, magnesium perchlorate, to render it conducting. Scintillations on the surface of the hemisphere are detected by a photomultiplier tube mounted above the perspex window. Pulses from this tube are counted in scaling equipment. To permit the chamber to be filled with the sample and subsequently emptied, two pipes closed by vacuum taps are fitted into the chamber walls.

2.2.2. Calibration

The equipment is calibrated with radon from a solution of radium of known activity: 1 pc of radon in the chamber gives a counting rate of about 120 cph whereas the background counting rate, obtained when the chamber is filled
with radon-free air from a cylinder, and using a freshly made zinc sulphide screen, is about 5 to 10 cph. The standard error of measurement ranges from better than ± 0.5% at 10 pc to ± 5% at 1 pc. An exchange of radon samples of activity about $10^{-12}$ c produced agreement to better than 5% with another laboratory. The apparatus and method will be described in detail elsewhere.

2.2.3. Breath sampling

Before a breath sample is taken, the subject rests for 10 min or more to allow the breathing rate to stabilize. The subject then breathes radon-free air through a specially designed breathing apparatus shown in Fig. 5. The exhaled air passes to a two-position tap which, for the first three minutes of a measurement, is open to the atmosphere. This allows atmospheric radon to be flushed from the lungs of the subject. After this, the exhaled breath is collected in a Douglas bag for five minutes. An aliquot of this sample is transferred to a previously evacuated radon chamber and the radon measured. From this, the amount of radon exhaled in the sampling period is determined, and the associated radium in the body calculated from the fact that 126 pc of radon emanates from 1 μc of radium in one minute.

Errors may arise due to incomplete flushing of atmospheric radon from the lungs prior to measurement. Work at present in progress appears to show that radon is not eliminated from the lungs as rapidly as had been thought. Other errors due to leakage of atmospheric air into the mask or to re-breathing of exhaled air are small in the present apparatus.
3. DISCUSSION OF RESULTS

Since radon in breath was measured for only a few luminizers, quite late on in the series, it was necessary in most cases to assume a value for the fraction of radon exhaled in order to estimate the radium in the body from the whole-body counter measurements. From published data [3, 5; 6, 15, 17], the fraction was taken to be two thirds, and therefore the quoted values of radium have been obtained by multiplying the measured contents of RaB and RaC by three. It will be seen later that our own measurements of radon in breath suggest that the factor three may be slightly high, and therefore that the values of radium calculated here are correspondingly overestimated.

The distribution of radium among the 470 people measured up to the end of 1963 is shown in the histogram (Fig. 6). From this diagram it will be seen that 45 people (9.4%) had more than 0.05 μc; twenty (4.2%) of these being in excess of 0.1 μc; the largest amount measured was 0.6 μc radium. Two hundred and sixty-four people (56.2%), contained no significant amount of radium, i.e. less than 0.01 μc.

As the occupation of luminizing has become more closely controlled since the early days, the relationship between radium in the body and year of commencement of luminizing was investigated and this is shown in Fig. 7.
It will be seen that of the 227 people (48.3%) who commenced luminizing after 1941, no person has acquired an amount in excess of 0.05 μc. In relation to this, it is noted that in Britain, at the beginning of the 1939-1945 war, it had been realized that the luminizing industry would be considerably expanded during war-time, and in view of the serious sequelae known to have occurred among American workers, the occupation of luminizing was brought under the medical supervision of the Ministry of Labour. The results of this supervision and advice were finally embodied in a statutory order dated 1 April, 1942 [18]. It is clear from Fig. 7 that this, and the medical supervision which preceded it, had the desired effect.

Table III shows the age of commencement of luminizing, the total period spent luminizing and the date of measurement for those workers who acquired more than 0.1 μc radium. It will be seen that most people in this group started luminizing early in their working life; the average age of commencing luminizing was just over 16 yr. In his paper Boyd found that, for the first 300 luminizers, the proportion of young workers increased steadily with the amount of radium in the body [9]. There is no obvious relationship between radium content and duration of luminizing, but since so many factors can affect the intake of radium, the lack of correlation is perhaps not surprising. The impression gained is that personal habits may be of the greatest importance.

Results are reported here on measurements of radon in the breath of 29 people. All but two of these were women and all had acquired the radium in their bodies several years previously. Figure 8 shows the relationship between the amounts of radium in the body as determined by whole-body counting and by breath analysis (circled points). The true radium content is the sum of these two amounts. A line was drawn through the circled
Distribution of estimated radium in the body among luminizers

The points in Fig. 8, the best fit being obtained by the method of least squares. The slope of the line is $0.712 \pm 0.019$ from which it may be deduced that, on average, $42 \pm 2\%$ of the radon produced from the radium in these people is retained in the body. This value is 1.4 times greater than that at present assumed by ICRP [7] in the calculation of the effective energy of radium in bone. According to the present basis of these recommendations, any increase in the value of the retained radon fraction automatically increases the value of the maximum permissible body burdens which are recommended for all bone-seeking radionuclides. However, it is too early yet to comment on the significance of the difference we have obtained. Our experiments are continuing, particularly with regard to accuracy. Mention has been made above about the error caused by breathing radon in the atmosphere, but the effect of this is to reduce the value we have obtained for the retained fraction and the true value may be higher than the value, $42\%$ reported. The other important source of error may be in the absolute calibration of the whole-
Fig. 7
Distribution of estimated radium in the body with year of commencing luminizing.

Fig. 8
Relationship between radium in the body determined by whole-body counting and breath analysis.
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TABLE III

WORK EXPERIENCE OF LUMINIZERS WITH RADIUM CONTENTS IN EXCESS OF 0.1 μC

<table>
<thead>
<tr>
<th>Radium content in body (μC)</th>
<th>Period of work</th>
<th>Date of measurement</th>
<th>No. of years luminizing</th>
<th>Age of commencing luminizing (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.57</td>
<td>1940-44</td>
<td>25/4/62</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>0.56</td>
<td>1939-45</td>
<td>10/7/62</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>0.54</td>
<td>1916-40</td>
<td>15/4/59</td>
<td>24</td>
<td>14</td>
</tr>
<tr>
<td>0.51</td>
<td>1941-43</td>
<td>26/4/62</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>0.41</td>
<td>1933-46</td>
<td>30/5/62</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>0.38</td>
<td>1940-42</td>
<td>25/4/62</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>0.28</td>
<td>1940-43</td>
<td>14/7/60</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>0.26</td>
<td>1940-45</td>
<td>16/10/58</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>0.23</td>
<td>1915-49</td>
<td>16/11/62</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>0.23</td>
<td>1938-41</td>
<td>21/12/60</td>
<td>2½</td>
<td>15</td>
</tr>
<tr>
<td>0.21</td>
<td>1939-45</td>
<td>14/6/62</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>0.21</td>
<td>1940-44</td>
<td>31/5/62</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>0.20</td>
<td>1933-40</td>
<td>8/6/60</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>0.20</td>
<td>1940-41</td>
<td>26/1/61</td>
<td>1½</td>
<td>19</td>
</tr>
<tr>
<td>0.16</td>
<td>1940-41</td>
<td>13/7/60</td>
<td>1½</td>
<td>15</td>
</tr>
<tr>
<td>0.15</td>
<td>1939-41</td>
<td>1/6/60</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>0.14</td>
<td>1939-40</td>
<td>26/4/62</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>0.12</td>
<td>1939-40</td>
<td>31/5/62</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>0.11</td>
<td>1940-42</td>
<td>19/7/60</td>
<td>1½</td>
<td>16</td>
</tr>
<tr>
<td>0.10</td>
<td>1940-43</td>
<td>13/6/62</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

body counter and we would like to make intercomparisons between the counter used for these measurements and other systems.

Three points are shown on Fig. 8, for a case where the first measurement was made within a few weeks of the intake of radium luminous compound. The retained radon fraction is clearly very much lower, a fact referred to previously by MAYS et al. [17], namely, that this fraction increases with the age of the radium deposit in bone. For persons who have recently acquired radium, therefore, the most sensitive method of detecting radium in the body is by measurements of radon in breath, although no estimation will be complete without measurements of both the retained and exhaled fractions.

REFERENCES

TWO CASES OF CHRONIC OCCUPATIONAL EXPOSURE TO RADIOACTIVE MATERIALS

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Abstract — Résumé — Аннотация — Resumen

TWO CASES OF CHRONIC OCCUPATIONAL EXPOSURE TO RADIOACTIVE MATERIALS. This paper describes the results and interpretation of measurements of radioactivity in the bodies and in the excreta of two subjects with a long (up to 16 yr) history of exposure to radium-226, strontium-90 and thorium-228. Measurements were made in 1957, 1959, 1960 and 1963.

The radium content of subject A showed no perceptible decrease between 1957 (0.13 μc) and 1963 (0.14 μc), and it was more than 30% higher in 1959. The excretion rate observed in 1957 was consistent, on the power function retention model, with a chronic intake of about 2 nc/d for the previous 10 yr, while the much lower excretion rate in 1963 indicated that there had not been a recent intake. The radium content of subject B decreased from 1.19 μc in 1959 to 1.07 μc in 1963, at a rate corresponding to a biological half-life of about 25 yr, yet the excretion rate in 1963 suggested a much faster fall in body content. This suggested that there had been a small intake of radium not long before.

The strontium-90 content of subject A decreased from 5.0 μc in 1957 to 3.0 μc in 1963, corresponding to a biological half-life of about 9 yr. Consideration of a power function retention model for strontium in man showed that the findings were consistent with a chronic intake for four years up to 1957 and then no further intake, although the excretion rate observed in 1963 was at least five times greater than that calculated there may have been a small intake shortly before the measurements in 1963. The retention of strontium-90 by subject B indicated a biological half-life of about 6 yr, agreeing with that deduced from the excretion rate (4.5-8.0 yr).

After an initial four-fold increase, the thorium-228 content of subject A decreased exponentially between 1959 and 1963 with an effective half-life of at least 1.4 yr. Subject B's content increased from 1959 to 1960, but the decrease from 1960 to 1963 was not significantly different from that due to radioactive decay with a half-life of 1.90 yr.

The paper concludes with a discussion of the value of the exponent in the power function retention equation for radium in man.
fois plus important que le taux calculé. La rétention du strontium 90 par le sujet B indiquait une période biologique d'environ six ans, ce qui est conforme à la valeur déduite du taux d'excrétion (4, 5-8, 0 a).

Après un accroissement initial quadruple, la charge de thorium 228 chez le sujet A a décru selon une courbe exponentielle entre 1959 et 1963 avec une période effective d'au moins 1,4 a. La charge chez le sujet B a augmenté de 1959 à 1960, mais la diminution de 1960 à 1963 n'était pas sensiblement différente de celle qui était due à la décroissance radioactive avec une période de 1,90 a.

L'auteur termine en étudiant la valeur de l'exposant dans la fonction de puissance utilisée comme modèle de rétention du radium chez l'homme.

ДВА СЛУЧАЯ ХРОНИЧЕСКОГО ПРОФЕССИОНАЛЬНОГО ОБЛУЧЕНИЯ РАДИОАКТИВНЫМИ МАТЕРИАЛАМИ. В докладе приводятся результаты и интерпретация измерений радиоактивности организма и выделений у двух человек с длительной (до 16 лет) историей облучения радием-226, стронцием-90 и торием-228. Измерения производились в течение 1957, 1959, 1960 и 1963 годов.

У пациента A не обнаружено заметного снижения содержания радио в период между 1957 (0,13 мккюри) и 1963 (0,14 мккюри), в 1959 оно было на 30% выше. Скорость выделения в 1957 году была значительной согласно модели задержки, вычисленной с помощью уравнения силовой функции, при хроническом поглощении порядка 2 мккюри в день в течение предыдущих десяти лет. Значительно более низкая скорость выделения наблюдалась в 1963 году, что указывает на отсутствие нового поступления изотопа. Содержание радио у пациента B снизилось с 1,19 мккюри в 1959 году до 1,07 мккюри в 1963 году со скоростью, соответствующей периоду полувыведения около 25 лет, хотя скорость выделения в 1963 году указывала на значительно более быстрое уменьшение содержания изотопа в организме. Это указывает на то, что незадолго до этого имело место поглощение малых количеств радио.

Содержание стронция-90 у пациента A снизилось с 5,0 мккюри в 1957 году до 3,0 мккюри в 1963 году, что соответствует периоду полувыведения в 9 лет. Рассмотрение модели задержки стронция у человека с помощью уравнения силовой функции показало, что эти данные соответствуют хроническому поглощению в течение 4 лет до 1957 года, и что затем не происходило значительного поглощения, хотя скорость выделения в 1963 году была по меньшей мере в 5 раз больше рассчитанной, могло иметь место поглощение малых количеств изотопа до начала измерений в 1963 году. Задержка стронция-90 у пациента B соответствует периоду полувыведения около 6 лет, что согласуется с величиной, полученной на основании скорости выделения (4,5-8 лет).

После начального четырехкратного повышения содержания тория-228 у пациента A снизилось экспоненционально в период между 1959 и 1963 годами с эффективным периодом полувыведения не менее 1,4 года. Содержание его у пациента B повысилось в период с 1959 до 1963 года, но снижение в период с 1960 по 1963 не отличалось значительно от уровня, определяемого радиоактивным распадом с периодом полураспада 1,9 лет. Обсуждается значение экспоненты в уравнении силовой функции для задержки радио у человека.

DOS CASOS DE EXPOSICIÓN CRÓNICA PROFESIONAL A SUSTANCIAS RADIOACTIVAS. En la memoria se exponen los resultados y la interpretación de las mediciones de la radiactividad del organismo y de las excreciones de dos sujetos con un largo historial hasta 16 años de exposición al radio-226, al estronio-90 y al torio-228. Las mediciones se efectuaron en 1957, 1959, 1960 y 1963.

El contenido de radio del sujeto A no acusó ninguna disminución apreciable entre 1957 (0,13 μC) y 1963 (0,14 μC), en 1959 presentó en cambio un aumento superior al 30%. La velocidad de excreción observada en 1957 era compatible, con arreglo al modelo de retención exponencial, con una absorción de carácter crónico de unos 2 μC/d durante los 10 a precedentes, mientras que la velocidad de excreción mucho más baja observada en 1963 indicaba la ausencia de absorción reciente. Por su parte el contenido de radio del sujeto B disminuyó de 1,19 μC en 1959 a 1,07 μC en 1963, a un ritmo que corresponde a un período biológico de 25 a; no obstante la velocidad de excreción observada en 1963 parece indicar una disminución mucho más rápida de la carga corporal. Este hecho sugiere que se había producido una pequeña absorción de radio poco tiempo antes.

El contenido de estronio-90 del sujeto A pasó de 5,0 μC en 1957 a 3,0 μC en 1963, lo que corresponde a un período biológico de unos 9 a. La aplicación de un modelo de retención exponencial para calcular el contenido de estronio en el organismo humano mostró que los resultados eran compatibles con una absorción crónica que duró 4 años (hasta 1957), y que después de esta última fecha no había habido absorción considerable.
1. INTRODUCTION

1.1. The maximum permissible body burdens for occupational exposure to bone-seeking radionuclides are derived from the value of 0.1 μc for radium-226, and this value is based on considerations of the late effects of this nuclide in the bodies of various persons [1]. There is however, a paucity of data on the behaviour in the human body of radioactive bone-seekers and it is of the greatest importance that such cases of contamination as do arise should be investigated thoroughly so that maximum permissible levels can be as soundly based as possible. This paper described the results and interpretation of measurements of radioactivity in the bodies and excreta of two subjects with a long history of exposure to radioactive bone-seeking materials.

1.2. The subjects have been engaged in the manufacture of luminous paint containing radium since 1946; the amounts involved in the first few years were quite small, but they steadily increased to a maximum of the order of 10 c/a in 1956-57, and decreased substantially after that time. Between 1954 and 1959, strontium-90 was also used and the quantities were generally two to three times those of the radium. Very little of this radionuclide has been handled since 1960. During 1957 to 1959 radiothorium (thorium-228) was used, but no more than 0.5 c/a. Subject A was 33 yr old in 1957 when our investigations began; his body radioactivity was measured then, and again in 1959, 1960 and 1963. In addition a 24-h urine sample and a single faecal sample were analysed for radium-226 and strontium-90 in 1957, while in 1963 a sample of urine (200 ml) was analysed for these radionuclides and for creatinine. Subject B, a female, was 32 when her body radioactivity was first measured in 1959; further measurements were made in 1960 and 1963, and on the last occasion a sample of urine (400 ml) was analysed for radium-226, strontium-90 and creatinine. The rate of exhalation of radon-222 was also measured for both subjects, except that the breathing rate of subject A was not determined in 1957.

2. EXPERIMENTAL METHODS

2.1. The body radioactivity was measured with a whole-body gamma-ray spectrometer at AERE, Harwell. This equipment used four crystals of
thallium-activated sodium iodide, 10.8 cm diam. by 5.1 cm thick in a substantial lead shield 10.2 cm thick. The apparatus and methods of calibration have been described in detail elsewhere [2, 3] and will not be discussed here. However it is worth noting that the assessment of the strontium-90 contents of the two subjects depended rather critically on the accurate prediction of the counting-rates from the gamma-ray emitters present (i.e. K\textsuperscript{40}, Cs\textsuperscript{137}, Th\textsuperscript{228} et seq. and Ra\textsuperscript{226} et seq.). In view of this there may be substantial systematic errors on the estimated Sr\textsuperscript{90} contents but as these were always calculated in the same way the errors should always be in the same direction. In 1959 and 1960 the distribution of the radioactivity in subject B was investigated with a slit collimated crystal and "profile" curves were obtained [4].

2.2. The rate of exhalation of radon in the breath was measured by a standard technique which has been described elsewhere [5].

2.3. The radium-226 and strontium-90 contents of urine and faeces were determined by standard radiochemical methods [6] and the creatinine contents of the urine samples were analysed by a modified method of FOLIN [7] and JONES [8] and OAKLEY [9].

3. RADIUM

3.1. The results of the measurements of the body contents of radium are set out in Table I; the values under the heading "Retained radon fraction" were obtained from the measurements of body radioactivity, while those under the heading "Exhaled radon fraction" were calculated from the rate of exhalation of radon. The values for the ratio of the exhaled radon fraction to the total radium are within the range found by others for subjects with long-standing radium burdens [10-12] although our values tend to be lower than the average of about 0.65. The body contents are plotted semi-logarithmically as a function of time in Fig. 1; for subject A there is no perceptible decrease in the six years since the first measurement and the scatter of the points is greater than can be accounted for by experimental errors. This suggests that there was further intake, especially during 1958 and 1959. In the case of subject B there was a slow decline and the slope of the straight line drawn through the points corresponds to an effective half-life of about 25 yr. We shall discuss this below.

3.2. The results of the analysis for radium in urine and faeces are shown in Table II. We shall consider first the data for subject A, especially those obtained in 1957, when the body content was 127 nc. An excretion rate of 160 pc/d with this body content corresponds to an apparent biological half-life of 550 d. Alternatively, if we assume that the fractional retention of radium in this man can be described by the power function equation [10]

\[ R_t = 0.54 t^{-0.52}, \quad (t \geq 1 \text{ d}) \]

we can easily calculate that the retention and excretion rate observed, cor-
<table>
<thead>
<tr>
<th>Date</th>
<th>Subject A</th>
<th>Subject B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Retained radon fraction (nc)</td>
<td>Exhaled radon fraction (nc)</td>
</tr>
<tr>
<td>1.11.57</td>
<td>62</td>
<td>65*</td>
</tr>
<tr>
<td>9.11.59</td>
<td>70</td>
<td>106</td>
</tr>
<tr>
<td>31.10.60</td>
<td>59</td>
<td>74</td>
</tr>
<tr>
<td>9.10.67</td>
<td>47</td>
<td>96</td>
</tr>
</tbody>
</table>

*Breathing rate assumed to be 7.5 l/min.

**TABLE 1**
RADIUM CONTENTS OF THE TWO SUBJECTS

CHRONIC EXPOSURE TO RADIOACTIVE MATERIALS
Radium contents of the two subjects plotted semi-logarithmically as a function of time. The slope of the straight line drawn through the points for subject B corresponds to a biological half-life of approximately 25 yr.

**TABLE II**

RADIUM IN THE EXCRETA OF SUBJECTS A AND B

<table>
<thead>
<tr>
<th>Date</th>
<th>Subject A</th>
<th>Subject B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Urine</td>
<td>Faeces</td>
</tr>
<tr>
<td>6.11.57</td>
<td>8 pc/24 h</td>
<td>152 pc</td>
</tr>
<tr>
<td>9.11.63</td>
<td>1.5 ± 1.0 pc/l</td>
<td></td>
</tr>
</tbody>
</table>

responded to the entry into the blood of about 5.4 μc of radium some 410 d earlier. From the subsequent observations that the radium content of subject A increased and in 1963 was the same as, or slightly higher than in 1957, it must be concluded that the exposure was definitely not a single one and in fact may have approximated to chronic exposure during the whole time that large amounts of radium were being handled (10 yr). As the amounts increased the techniques used were improved and a reasonable assumption would be that the average daily intake remained constant. Integration of the above retention equation gives the following for the retention at time t following exposure for t_m days (t > t_m):
\[ R_t = 1.125 \times (t - 1)^{0.48} - (t - t_m)^{0.48} \]

where \( m \) is the amount entering the blood per day. We then find that the retention of 127 nc and the excretion rate of 160 pc/d in November, 1957 would result from a value for \( m \) of about 2 nc/d for 10 yr. The build-up of the body content with these assumptions would then have been as shown in Fig. 2, where the calculated decrease for no further exposure is also shown. The measured content two years later was more than twice that calculated, indicating a substantial further intake during 1958 and/or 1959, but the decrease between 1959 and 1960 was much as might be expected if there had been no exposure. There must also have been exposure between 1960 and 1963, when the content was about the same as calculated for an intake (to the blood) of 2 nc/d for the whole 16 yr. If exposure stops now, then the decrease should be as shown and the body content might fall below the maximum permissible level in about three years' time. Some indication that exposure may have ceased by October, 1963 may be seen from the urinary excretion rate at that time. The 24-h output of radium in the urine must have been between about 2 ± 1.3 pc (for 1.3 l total urine volume) and 3 ± 2 pc (for 2 l total urine volume, as suggested by the creatinine excretion) and these values are three to four times less than the urinary excretion rate in 1957. This indicates that there had not been a recent intake.

3.3. The situation with regard to subject B was quite different; the radium content was nearly ten times higher than that of subject A and it showed a distinct fall between 1959 and 1963, yet she was exposed to essentially the same working conditions. It is tempting to conclude that her burden resulted
largely from a small number (perhaps only one) of large exposures, and that only about one tenth of her content was acquired chronically. Unfortunately the excretion data are inadequate to test this suggestion. The 24-h output of radium in the urine in October, 1963 must have been in the range 35 pc (for 1.4 l total urine volume) to 62.5 pc (for 2.5 l total urine volume, as suggested by the creatinine excretion). If the urinary excretion was only 5% of the total radium excretion, the daily output of 700-1250 pc would correspond to an apparent biological half-life in the range 600-1070 d, yet the decrease in the body content between 1959 and 1963 suggested a biological half-life of about 25 yr. We must conclude that there had been an intake of radium not long before the measurement in October, 1963, and the true rate of decrease of the long-standing burden must have been between these two extremes.

3.4. The distribution of the radioactivity in subject B was examined in 1959 and 1960 with a slit-collimated crystal, and the "profile curves" obtained are shown in Fig. 3. Also plotted is a scan of the distribution of the radium in a long-standing (25 yr) case [13], and this scan shows very similar qualitative features to our profile curves, indicating that the skeleton of subject B contained most of the total activity. It is noteworthy that the only significant differences in the counting-rates observed in 1959 and 1960 were in the chest region (30-40 cm from the top of the head); this suggests that in 1959 there may have been some "insoluble" material in the lung, which had been largely eliminated one year later. Since nearly 30% of the total counting-rate from the whole body was attributed to bremsstrahlung from strontium-90 we are not able to say whether the possible lung content was of this radionuclide or radium-226, or both.

4. STRONTIUM-90

4.1. The best estimates of the contents of strontium-90 in the two subjects are shown in Table III; although the relative errors amount to about ± 5%, there may be systematic errors on these values as they depend on accurate predictions of the whole-body counting-rates at low energies due to the gamma-ray emitters. It is possible that the contents of subject A have been under-estimated by as much as 50%, and those of subject B by rather less. The results are plotted semi-logarithmically as a function of time in Fig. 4. For subject A, the "best" line (shown dashed) through all the points corresponds to an effective half-life of 6.9 yr (biological half-life 9.2 yr or 3350 d). The slope of the straight line fitting the points for subject B corresponds to a shorter effective half-life of 4.9 yr (biological half-life 5.95 yr or 2170 d).

4.2. The results of the analyses for strontium-90 in the excreta of the two subjects, set out in Table IV, may be used in principle in much the same way as were the data for radium, but the uncertainties introduced by the unknown errors on the values for the body contents may be considerable. The total daily excretion rate of 5.05 nc by subject A in 1957 when his body content was about 5 μc, corresponded to an apparent biological half-life of about 690 d, yet the decrease between 1957 and 1959 was at a much lower
"Profile curves" of the radioactivity in subject B, compared with a scan obtained with a cylindrical collimator in a case of a long-standing (25 yr) radium burden [13].

TABLE III

STRONTIUM-90 CONTENTS OF THE TWO SUBJECTS

<table>
<thead>
<tr>
<th>Date</th>
<th>Sr(^{90}) in subject A (μc)</th>
<th>Sr(^{90}) in subject B (μc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.11.57</td>
<td>5.0</td>
<td>-17.9</td>
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<tr>
<td>9.11.57</td>
<td>3.7</td>
<td>16.0</td>
</tr>
<tr>
<td>31.10.60</td>
<td>3.7</td>
<td>10.2</td>
</tr>
<tr>
<td>9.10.63</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>

we calculate that the retention and excretion rate observed corresponded to the entry into the blood of at least 30 μc about 210 d earlier. The subsequent retention is easily calculable and is shown by the straight line in the lower half of the double logarithmic plot of Fig. 5; the results of the measurements made in 1959, 1960 and 1963, when corrected for radioactive
Strontium-90 contents of the two subjects plotted semi-logarithmically as a function of time. The straight line drawn through the points for subject B corresponds to an effective half-life of 4.9 yr; in the case of subject A, the dashed line represents an effective half-life of 6.9 yr.

**TABLE IV**

**STRONTIUM-90 IN THE EXCRETA OF SUBJECTS A AND B**

<table>
<thead>
<tr>
<th>Date</th>
<th>Subject A</th>
<th></th>
<th>Subject B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Urine</td>
<td>Faeces</td>
<td>Urine</td>
</tr>
<tr>
<td>6.11.57</td>
<td>3.17 nc/24 h</td>
<td>1.88 nc</td>
<td>-</td>
</tr>
<tr>
<td>9.10.63</td>
<td>0.79 nc/l</td>
<td>-</td>
<td>1.34 nc/l</td>
</tr>
</tbody>
</table>

decay since 1 November 1957, all lie substantially above this line, showing that the elimination was slower than predicted on the assumption of a single intake early in 1957. The alternative assumption is of chronic exposure during the four years of handling of strontium-90 prior to the first measurement in 1957, and then no further exposure. The calculated content is then as shown in the upper half of Fig. 5 and the estimated contents (corrected for decay) fit very well to the calculated curve. Although this suggests strongly that the content in 1957 was a consequence of chronic exposure, it is perhaps a little surprising that there is no real evidence for further intake especially during 1958 and 1959 when quite large amounts of strontium-90 were handled.
4.3. Some confirmation of the correctness or otherwise of the latter assumptions might come from a comparison of the calculated and observed excretion rates in 1963. The calculated rate of 260 pc/d is to be compared with an observed rate in the range 1340-2040 pc/d (depending on the 24-h urine volume, and calculated with the assumption of faecal excretion equal to 30% of the urinary excretion [15]). The very big discrepancy is difficult to explain; part of it may be attributable to the systemic error in the strontium-90 content, but otherwise the fact that the observed excretion rate was higher than calculated, suggests that there had been a further intake prior to the measurements in October, 1963; a small quantity of strontium-90 was in fact handled during 1963. From the plot in the upper half of Fig. 5 it seems that any intake in 1963 must have been small compared with the existing burden.

4.4. In the case of subject B, the 24-h urinary output of strontium-90 must have been between 1.87 nc and 3.35 nc (again depending on the 24-h urine volume). If we again assume an endogenous faecal excretion equal to 30% of the urinary excretion [15], we deduce that the total daily excretion of strontium-90 in October, 1963 must have been in the range 2.43-4.35 nc, when the body content was 10.2 μc. This corresponds to a biological half-life in the range 1625-2900 d (about 4.5-8.0 yr); the observed decrease in the content of subject B (Fig. 4) corresponded to a biological half-life of about.
6 yr which is within the range just deduced. The indications are that there were no further significant intakes of strontium-90 after 9 November 1959; as large amounts of strontium-90 were not handled after this time, this conclusion is not altogether surprising.

4.5. The rates of elimination of the strontium-90 by the two subjects, corresponding to biological half-lives (Fig. 4) of as much as 9.2 yr (3350 d) for subject A and about 6 yr (2170 d) for subject B, are longer than previously reported for adult man. Using the short-lived strontium-85; several workers have reported biological half-lives of about 840 d (range 679-977 d) [16] or 915 d (range 675-1200 d) [17, 18], but in no case was it possible to continue the study for more than 600 d. However, WENGER and SOUCAS[19] reported an approximate value of 0.00028 d⁻¹ for the slope of the urinary excretion rate curve for one subject who had had chronic exposure to strontium-90 for several years, but whose exposure ended at least 940 d before the start of the study. This corresponded to a biological half-life of about 2500 d, but a value of about 337 d was observed in another case where exposure ceased just before urine sampling started [19]. Thus the elimination rate depends on the time since exposure ended, and it is by no means certain that the long values observed by us are necessarily the longest. At the same time there is good evidence that the power function equation deduced from a 1-yr study [14] of the retention of strontium-85 may be valid over much longer periods of time (~10 yr).

5. THORIUM-228

5.1. The values set out in Table V and plotted in Fig. 6, represent lower limits for the thorium-228 contents of subjects A and B, because they were deduced from the whole-body counting-rates at energies above 1.7 MeV and the gamma-rays responsible came from the nuclide Tl²⁰⁸ (ThC¹¹), which is

<table>
<thead>
<tr>
<th>Date</th>
<th>Th²²⁸ in subject A (nc)</th>
<th>Th²²⁸ in subject B (nc)</th>
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</thead>
<tbody>
<tr>
<td>1.11.57</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>9.11.59</td>
<td>24</td>
<td>37</td>
</tr>
<tr>
<td>31.10.60</td>
<td>15</td>
<td>62</td>
</tr>
<tr>
<td>9.10.63</td>
<td>4.5 ± 1.6</td>
<td>20.4</td>
</tr>
</tbody>
</table>
the final member of the thorium decay chain. Thus any preferential elimina-
tion from the body of Ra\(^{224}\) (ThX, 3.64 d), Em\(^{220}\) (Tn, 54.5 s) or Pb\(^{212}\)
(ThB, 10.6 h) would reduce the gamma-ray emission from the deposit in vivo.

5.2. Since November 1959, the thorium-228 content of subject A has de-
creased approximately exponentially, with an effective half-life of 1.42 yr
(biological half-life 5.62 yr or about 2000 d). The decrease in the content
of subject B between 1960 and 1963 is apparently only slightly greater than
would be expected by radioactive decay. Taking the slope of the line joining
the two points at its face value, we have an effective half-life of about 1.84 yr
(biological half-life 52.8 yr), but it must be emphasized that this is only
based on two measurements. Because of the lack of human data on the bio-
logical half-life of thorium in man, it is obviously highly desirable that fur-
ther measurements be made of the content of subject B in order to get an
accurate value for the biological half-life.
6. DISCUSSION AND CONCLUSIONS

6.1. One of the principal objectives in a long-term study such as that described above, is the determination of the retention equations for the various radio-elements. Is the radium retention equation, which was deduced essentially from two sets of measurements 19 yr apart [10], applicable in the cases of chronic exposure represented by subjects A and B? Is the strontium retention equation, which was deduced from measurements lasting about one year [14], applicable over longer periods? Is the multi-exponential model a better fit than the power function at long times after exposure ends?

In particular, since the values of the exponent (b) in the power function equations describing the retention of calcium, strontium, barium and radium in the dog are all essentially equal to 0.2 [20,21], and the same value has been found for strontium retention in man [14,16], it is pertinent to enquire whether the value of 0.52 [10] for radium is as universally applicable as is commonly assumed. These are the questions we would hope to try to answer, but it is unfortunately impossible to give an unambiguous answer to them.

6.2. Because of the fluctuations in the radium content of subject A we are not able to make use of those data, and the excretion rate of subject B in October, 1963 suggested that there had been a recent intake. However, if we ignore this latter observation we can use the values for the radium content of subject B to calculate an effective exposure date for a single intake of radium with the alternative assumptions of b = 0.5 and b = 0.2. For the former, we find that there must have been a single intake of about 180 μc in July, 1943 to give a retention of 1.19 μc in November, 1959. This is obviously absurd since the subjects did not start working with radium at all until 1946, and only in large quantities in the early 1950's. A much slower release is predicted by the value of b = 0.2, and the observed values for the body content would be consistent with a single intake of about 11 μc in May 1954, which would be entirely reasonable. Nevertheless, we are unable to decide in favour of the smaller value for b because of the unknown increase in the burden deduced from the high excretion rate in 1963. The larger this increase, the more likely it becomes that the retention is best expressed by a power function with b = 0.5. In this connection it is worth mentioning that attempts to confirm the value of 0.5 by re-measurement of those patients on whose radium contents the value was originally based, suggested that it was not too low [22], i.e., the content decreased in nine years a little more than predicted. Also, a value b = 0.78 was observed in one case following accidental inhalation of radium sulphate, after the radium had translocated from lung to skeleton, and the equation was a good fit to the data from 100-2312 d after intake [23].

6.3. We have already commented that the power function equation for the retention of strontium may well be valid for as long as 10 yr (see Fig. 5). A multi-exponential model might give just as good a fit, as we see from the plots in Fig. 4, but we cannot assume that these represent the component with the longest biological half-life.

6.4. There are no reports in the literature of the retention in man of thorium
other than the studies on thorotrast, where the colloidal nature of the in­
jected material, and the massive doses administered resulted in deposition
almost exclusively in the cells of the reticulo-endothelial system [24, 25].
Data for thorium of high specific activity injected into rats (thorium-234) [26]
agreed with those for dogs (thorium-228) [27], in that in both cases some
two-thirds of the material injected was retained with such a long biological
half-life as to be indeterminate. This is essentially the case for our subject
B (Fig. 6) and it might also apply to subject A if we consider only the results
of the measurements in 1960 and 1963. It is plain that the biological half-life
of thorium-228 in these two subjects is not less than 2000 d and it may be
very much longer. We can only conclude by stressing the need for further
study of the retention of the thorium-228, in both subjects if possible.

6.5. The type of study reported here suffered from the disadvantage of the
possibility of re-contamination of the subjects between the measurements,
and as we have seen, this certainly took place. Even where it was not ob­
vious, re-contamination may have confused the interpretation of the long­
term retention, but as we have tried to show, the excretion rate was a use­
ful guide. We hope to be able to continue measurements of the kind des­
cribed as the importance of such long-term follow-up studies needs no
justification.

REFERENCES

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THE EFFECTS OF INTERNAL CONTAMINATION WITH RADIONUCLIDES CONTAINED IN LUMINOUS PAINT

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Abstract — Résumé — Аннотация — Resumen

THE EFFECTS OF INTERNAL CONTAMINATION WITH RADIONUCLIDES CONTAINED IN LUMINOUS PAINT. The Department of Radiological Health in the Institute of Occupational Health in Belgrade performs the medical control of workers exposed to internal contamination with radioactive materials in luminous paint.

Thirty-six workers were exposed to internal radiation of radionuclides during a number of years. The health condition of these workers was checked continuously and systematically during the last year. In the health control were included clinical and haematological examinations and radiography of the bones. Special attention was paid to the determination of radionuclides in urine (quantitative determination of polonium, radium and thorium) and in the body (whole-body counting).

The clinical results, haematological changes (anaemia, leucopenia, leucocytosis, lymphopenia and thrombocytopenia) whole-body counting measurements and the values of polonium (from 0 - 30 pc/l) and radium (from 0 - 24 pc/l) in the urine are presented and discussed.

The results of the health control of workers previously exposed to internal contamination at some places of work are also given. Hygienic conditions in the luminous paint industry where the controlled people were engaged are presented.

EFFETS DE LA CONTAMINATION INTERNE PAR LES RADIONUCLÉIDES CONTENUS DANS LES PEINTURES LUMINEUSES. Le département d'hygiène radiologique de l'Institut de médecine du travail de Belgrade assure le contrôle médical des ouvriers exposés à une contamination interne par les substances radioactives contenues dans les peintures lumineuses.

Trente-six ouvriers ont été exposés à une contamination interne par des radionucléides au cours d'une période de plusieurs années. Leur santé a fait l'objet d'un contrôle permanent et systématique au cours de l'année dernière. Ce contrôle comportait notamment des examens cliniques, des analyses hématologiques et la radiographie des os. On a apporté une attention particulière au dosage des radionucléides contenus dans l'urine (détermination quantitative du polonium, du radium et du thorium) et dans le corps entier (anthropogammamétrie).

Les auteurs présentent et discutent les résultats; observations cliniques, altération du sang (anémie, leucopénie, leucocytose, lymphopénie et trombocytopenie), dosages au moyen d'un anthropogammamètre et concentrations du polonium (de 0 à 30 pc/l) et du radium (de 0 à 24 pc/l) dans l'urine. Ils donnent également les résultats du contrôle sanitaire d'autres ouvriers qui avaient été exposés à une contamination interne sur certains lieux de travail.

 Ils décrivent les conditions d'hygiène dans lesquelles travaillent les ouvriers utilisant des peintures lumineuses.

ЭФФЕКТ ВНУТРЕННЕГО ОБЛУЧЕНИЯ РАДИОИЗОТОПАМИ, СОДЕРЖАЩИМИСЯ В КРАСКАХ. Отдел радиологической безопасности Института охраны труда Белграда провел медицинское обследование рабочих, подвергающихся внутреннему заражению радиоактивными веществами, содержащимися в светящихся красках.

Тридцать шесть рабочих подвергались внутреннему облучению радиоизотопами в течение нескольких лет. Состояние здоровья рабочих непрерывно и систематически контролировалось в течение прошлого года. В контроль входили клиническое и гематологическое обследование и радиография скелета. Особое внимание обращалось на содержание радиоизотопов в моче (количествоное определение полония, радия и тория) и в организме (измерение радиоактивности всего организма).

Представлены и обсуждаются клинические результаты, гематологические изменения (анемия, лейкопения, лейкоцитоз, лимфопения, тромбоцитопения), данные измерения радиоактивности всего организма и содержание полония (от 0 до 30 мкмкккури/л в моче).
EFFECTOS DE LA CONTAMINACIÓN INTERNA DEBIDA A PINTURAS LUMINOSAS QUE CONTIENEN RADIONÚCLIDOS. El Departamento de Protección Radiológica del Instituto de Medicina del Trabajo de Belgrado se encarga de la vigilancia médica de los trabajadores expuestos a contaminación interna por sustancias radiactivas contenidas en las pinturas luminosas.

Por espacio de varios años, 36 trabajadores han estado expuestos a las radiaciones internas emitidas por radionúcleidos. Su estado de salud se vigiló continua y sistemáticamente durante el pasado año. ese control comprendió análisis clínicos, hematológicos y radiografías de los huesos. Se ha prestado particular atención a la evaluación de los radionúcleidos en la orina (determinación cuantitativa de polonio, radio y torio) y en todo el organismo (antropogammadmetría).

Se exponen y examinan los resultados clínicos, las alteraciones hematológicas (anemia, leucopenia, leucocitosis, linfopenia y trombocitopenia), los resultados del examen antropogammadimétrico y las concentraciones de polonio (de 0 a 30 pc/1) y de radio (de 0 a 24,0 pc/1) en la orina.

También se exponen los resultados de la vigilancia médica de trabajadores anteriormente expuestos a contaminación interna.

Se describen las condiciones higiénicas de los trabajos con pintura luminosa a que se dedicaban las personas controladas.

INTRODUCTION

In recent decades clocks and watches with fluorescent dials have come into increasing use. A fluorescent substance, usually zinc-sulphide, is mixed with an alpha or beta emitter. Radioactivity excites the fluorescence. Radium, mesothorium and strontium-90 have been used. Since these substances are relatively radiotoxic, promethium-147 or tritium have been applied in recent years as substitutes.

The danger from such radioactive emitters was not recognized until 1928 - the first cases were reported in New Jersey. Dr. Martland reported [1] 14 deaths resulting from the use of radium sulphate in dial-painting. The body burden of radium found in the women who died was 10 - 180 μg. In survivors, the range observed was 2 - 10 μg. He observed destruction and cancer of the bone and blood disturbances such as aplastic anaemia.

Subsequent observations and experiences confirmed these findings. BEHRENS [2] reported a swelling and thickening on the periosteum, together with hyalinization and vascular changes (Watson and Scarborough). It has also been observed that the mandibula is more liable to necrosis than the maxilla (Stewart, Lawrence).

HASTERLIK [3] established that moderate anisocytosis and poikilocytosis of the red blood cells seemed to be constant findings in individuals with body burdens in excess of 2 μg of radium.

GLENN and co-workers [4] discuss the case of a woman who worked 14 months with radium and mesothorium and who became blind and died from cancer of the spheroid sinus 39 years later.

MÜLLER [5] reported in 1961 on the follow-up of 103 workers in the luminizing industry. The body burden of Sr in these cases was estimated to be of the order of tens of microcuries and the body burden of Ra was
THE EFFECTS OF INTERNAL CONTAMINATION

about 0.01 µg or less. Haematological studies revealed signs of irritation of the erythroblast series in the bone marrow.

HURSH [6] found in 1950 that the body burden in people not occupationally exposed is $1.2 \times 10^{-10}$ g of Ra$^{226}$.

WENGER and MILLER [7] estimated body burdens of radium in 70 Swiss workers who had done luminizing work at home and in industry, by using whole-body spectrometry and by measuring the amount of radon in the expired air. The radium body burdens varied from 0.01 to 1 µc. It was observed that the workers in industrial production were more contaminated than the others.

OBSERVATIONS AND RESULTS

In Yugoslavia to date there has been no reporting of work experience and general state of health of individuals working with luminizing paints.

In the course of a few years, the Department of Radiation Health in the Institute of Occupational Medicine, Belgrade, examined workers potentially exposed to internal radioactive contamination. Since 1959, it has followed 36 of these workers occupied with luminous materials in the watch industry. In the past year, working conditions, and clinical and radiotoxic investigations have been observed systematically.

Control of working conditions

The dial-painting mixture used in these plants incorporates Ra$^{226}$, in equilibrium with its daughters. The mixture is stored in a specially constructed bunker. The specific activity of the mixture is 2.15 µg radium per gram. The total amount of the substance used in November 1963 was 47.3 µc of Ra$^{226}$.

The exposure rate outside the door (with 1 mm of Pb) of the bunker (measurements are taken with monitor "Tracerlab" S 4-14) was 1 mr/h with the door closed and 1.5 mr/h with the door open.

In the room where luminous paints are applied, the daily supply of the mixture (usually 200 g) is stored in a closed box (with 1 cm of Pb). The exposure rate over the box is most frequently 25 mr/h.

The exposure rate in various working places varies from 1 mr/h to 50 mr/h. The most frequent exposure rates where work is in progress (outside the glove boxes) is 2-3 mr/h. The most severe contamination observed on working surfaces and on parts of tools did not exceed twice the maximum permissible concentration. The most severe contamination observed on working overalls and shoes was 12 MPC for alpha and 3 MPC for beta emitters. On the hands, up to 450 MPC for alpha and 100 MPC for beta emitters were measured. The maximal value of the concentration in the working atmosphere was less than 10% of the MPC.

Medical examination

In the course of five years, the medical condition of 36 women engaged or previously employed in dial-painting was checked systematically. Special attention has been paid to anamnesis, changes in the blood and in the bones.
The most frequent subjective troubles were faintness and headache. Only three workers had gastric symptoms. We have found one case (2.8%) of thrombocytopenia (under 160,000), in the worker with the highest amount of radium and polonium in urine (K.O.).

In Table I, haematological results are presented. Seventeen persons (47.2%) showed some changes. Of these eight (22.2%) showed anaemia (under 3,500,000), five (14.0%) showed lymphocytoses (over 40%), two (5.5%) showed lymphopenia (under 20%). One woman had eczema professionale, but not in connection with this work (sensibilization to nickel, sodium bichromate and solvents in galvanization). Four persons exhibited chronic conjunctivitis. Radiographies of the mandibula have been taken in 28 cases with no positive pathological findings.

Radiotoxicological findings

To establish the radioactive body burdens of these workers, bio-assay has been employed, i.e. determination of Ra\(^{226}\), Po\(^{210}\) and thorium in the urine.

Radium-226 in the urine has been determined by the emanometric method, Po\(^{210}\) by the method of electrodeposition on silver plates [8], and thorium by the extraction and spectrophotometric method. The quantities of Ra\(^{226}\) found in urine are presented in Tables II and III, these of Po\(^{210}\) in Tables IV and V. Thorium has not been found in any urine samples.

Table III shows that in 1963 57% of the urine samples contained more than 1 pc of Ra\(^{226}\) and in 1964 only 15% contained that amount of Ra\(^{226}\). This improvement followed precautionary measures taken in the past year.

Table V shows that about 20% of the workers had more than 1 pc of Po\(^{210}\)/l of urine, both in 1963 and in 1964. Only four persons (Table IV) had more than 5 pc of Po\(^{210}\)/l of urine.

To estimate the body burden of Ra\(^{226}\), in one case (O.K.), who had 25.40 pc/l, the total number of counts over 1.6 MeV was measured in an unshielded room, using a 4-in x 4-in NaI(Tl) crystal. The number of counts was compared with that from a phantom containing 2 \(\mu\)c of Ra\(^{226}\) in 30 l of water. Under the same conditions, three persons with the normal amount of Ra\(^{226}\) produced the same number of counts. Contamination with Ra\(^{226}\) could be established but the body burden could not be accurately determined.

DISCUSSION

Radium-226 disintegrates to Rn\(^{222}\). About 60% of Rn\(^{222}\) from the decay of Ra\(^{226}\) in the bone is exhaled with expired air. The rest disintegrates in the body through short-lived products to Pb\(^{210}\) and Po\(^{210}\) and stable lead. Po\(^{210}\) is excreted and is measurable in the urine. The amount of Ra\(^{226}\) in a 24-h urine sample with the maximum body burden of 1 \(\times\) 10\(^{-7}\) g should be about 2 \(\times\) 10\(^{-11}\) g [9]. The quantities of polonium are negligible [10]. Hursh [9] cited that it is not possible to determine the body burden of Ra\(^{226}\) only by measuring the content of the urine, because the main part of the Ra\(^{226}\) may not be from the body burden, but from recent contamination. Our results (Table III) appear to confirm Hursh's observation, i.e. they were
RESULTS OF HAEMATOLOGICAL EXAMINATIONS

<table>
<thead>
<tr>
<th>Years of employment</th>
<th>Anaemia (under 3500 000)</th>
<th>Leucopenia (under 4000)</th>
<th>Leucocytosis (over 9000)</th>
<th>Lymphocytosis (over 40%)</th>
<th>Lymphopenia (under 20%)</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 5</td>
<td>7 (19.4%)</td>
<td>1 (2.8%)</td>
<td>1 (2.8%)</td>
<td>4 (11.1%)</td>
<td>2 (5.5%)</td>
<td>13 (36.1%)</td>
<td>28</td>
</tr>
<tr>
<td>6 - 10</td>
<td>1 (2.8%)</td>
<td>-</td>
<td>-</td>
<td>1 (2.8%)</td>
<td>-</td>
<td>5 (13.9%)</td>
<td>7</td>
</tr>
<tr>
<td>11 - 15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 (2.8%)</td>
<td>1</td>
</tr>
<tr>
<td>16 - 20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>21 - 30</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>8 (22.2%)</td>
<td>1 (2.8%)</td>
<td>1 (2.8%)</td>
<td>5 (14.0%)</td>
<td>2 (5.5%)</td>
<td>18 (52.7%)</td>
<td>36</td>
</tr>
</tbody>
</table>
higher in 1963 than in 1964 because of recent internal contamination. The quantities of Po$^{210}$ in the urine were much more constant in both years (1963

<table>
<thead>
<tr>
<th>No.</th>
<th>Subject</th>
<th>Age</th>
<th>Years of employment</th>
<th>Radium in urine (pc/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1963</td>
</tr>
<tr>
<td>1</td>
<td>B.O.</td>
<td>30</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>G.J.</td>
<td>29</td>
<td>3</td>
<td>1.95</td>
</tr>
<tr>
<td>3</td>
<td>Gm.J.</td>
<td>32</td>
<td>5</td>
<td>1.90</td>
</tr>
<tr>
<td>4</td>
<td>D.G.</td>
<td>30</td>
<td>10</td>
<td>1.79</td>
</tr>
<tr>
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<td>Z.Z.</td>
<td>30</td>
<td>10</td>
<td>2.1</td>
</tr>
<tr>
<td>6</td>
<td>J.D.</td>
<td>28</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>J.Z.</td>
<td>30</td>
<td>10</td>
<td>1.25</td>
</tr>
<tr>
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<td>K.M.</td>
<td>29</td>
<td>2</td>
<td>1.6</td>
</tr>
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<td>K.O.</td>
<td>34</td>
<td>12</td>
<td>24</td>
</tr>
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<td>K.M.</td>
<td>38</td>
<td>4</td>
<td>2.2</td>
</tr>
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<td>L.D.</td>
<td>34</td>
<td>7</td>
<td>2.3</td>
</tr>
<tr>
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<td>Lj.M.</td>
<td>48</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>M.M.</td>
<td>28</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>M.R.</td>
<td>34</td>
<td>5</td>
<td></td>
</tr>
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<td>M.M.</td>
<td>30</td>
<td>4</td>
<td>1.79</td>
</tr>
<tr>
<td>16</td>
<td>N.O.</td>
<td>39</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>P.Z.</td>
<td>29</td>
<td>4</td>
<td>1.02</td>
</tr>
<tr>
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<td>O.K.</td>
<td>40</td>
<td>6</td>
<td>1.49</td>
</tr>
<tr>
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<td>T.D.</td>
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<td>4</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>T.D.</td>
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<td>10</td>
<td>3</td>
</tr>
<tr>
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<td>V.C.</td>
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<td>3</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>T.B.</td>
<td>31</td>
<td>6</td>
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</tr>
<tr>
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<td>V.B.</td>
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<td>1</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Š.D.</td>
<td>29</td>
<td>9</td>
<td>3.24</td>
</tr>
<tr>
<td>25</td>
<td>P.Lj.</td>
<td>37</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>26</td>
<td>B.M.</td>
<td>-</td>
<td>-</td>
<td>1.6</td>
</tr>
</tbody>
</table>
TABLE III

SUMMARY OF FINDINGS FOR RADIUM-226 IN THE URINE OF RADIUM WORKERS

<table>
<thead>
<tr>
<th>Radium-226 (pc/l)</th>
<th>1963</th>
<th>1964</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>0.5 - 1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>1. - 5</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>26</td>
</tr>
</tbody>
</table>

and 1964) and this may indicate that it is possible to estimate the body burden of Ra\textsuperscript{226} through Po\textsuperscript{210} in the urine.

CONCLUSION

Thirty-six women employed in the watch industry have been exposed to radium in dial-painting mixtures. Clinical examination has shown only some changes in the blood (anaemia, lymphocytosis). Radiotoxicological examination has shown some cases in which levels of both Ra\textsuperscript{226} and Po\textsuperscript{210} were over 5 pc per litre of urine. The amounts of Po\textsuperscript{210} in the urine were more constant in the course of successive measurements and may possibly be of help in estimating the body burden of Ra\textsuperscript{226}. 
<table>
<thead>
<tr>
<th>No.</th>
<th>Subject</th>
<th>Age</th>
<th>Years of employment</th>
<th>Polonium in the urine (pc/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1963</td>
</tr>
<tr>
<td>1</td>
<td>B.O.</td>
<td>30</td>
<td>5</td>
<td>1.45</td>
</tr>
<tr>
<td>2</td>
<td>G.J.</td>
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<td>1.18</td>
</tr>
<tr>
<td>3</td>
<td>Gm.J.</td>
<td>32</td>
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<td>0.38</td>
</tr>
<tr>
<td>4</td>
<td>D.G.</td>
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</tr>
<tr>
<td>5</td>
<td>Z.Z.</td>
<td>30</td>
<td>10</td>
<td>2.89</td>
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</tr>
<tr>
<td>7</td>
<td>J.Z.</td>
<td>30</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>K.M.</td>
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<td>2</td>
<td>0.23</td>
</tr>
<tr>
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<td>K.O.</td>
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</tr>
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<td>0.1</td>
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<td>0.58</td>
</tr>
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<td>0.15</td>
</tr>
<tr>
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<td>T.B.</td>
<td>31</td>
<td>8</td>
<td>0.1</td>
</tr>
<tr>
<td>23</td>
<td>V.B.</td>
<td>34</td>
<td>1</td>
<td>8.75</td>
</tr>
<tr>
<td>24</td>
<td>Š.D.</td>
<td>29</td>
<td>9</td>
<td>0.1</td>
</tr>
<tr>
<td>25</td>
<td>P.Lj.</td>
<td>37</td>
<td>3</td>
<td>0.43</td>
</tr>
<tr>
<td>26</td>
<td>B.M.</td>
<td>-</td>
<td>-</td>
<td>0.24</td>
</tr>
</tbody>
</table>
THE EFFECTS OF INTERNAL CONTAMINATION

TABLE V

SUMMARY OF FINDINGS FOR POLONIUM-210
IN THE URINE OF RADIUM WORKERS

<table>
<thead>
<tr>
<th>Polonium-210 (pc/l)</th>
<th>No. of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1963</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>17</td>
</tr>
<tr>
<td>0.5 - 1</td>
<td>4</td>
</tr>
<tr>
<td>1 - 5</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
</tr>
</tbody>
</table>

REFERENCES


DISCUSSION

C. J. MALETSKOS: Could you tell me at what radium-226 body burdens you observed the haematological changes you described?

M. KILIBARDA: Thrombocytopenia was found in the case with the highest amounts of radium-226 (25.40 pc/l of urine) and polonium-210 (30.1 pc/l). The other haematological changes were not in correlation with the quantities of radium-226 and polonium-210 excreted in the urine.

C. R. HILL: You suggest that polonium-210 excretion in the urine may be a useful index of radium-226 body burden. Our own measurements (unpublished) indicate that such polonium-210 excretion may be strongly dependent on the age of the radium deposit (being relatively less for old deposits). Have you any results which might confirm or refute this possibility?

M. KILIBARDA: No, but we would like to do further work on that.
EXPOSURE FOLLOWING INGESTION OF WATER CONTAINING RADON-222

I.Ö. ANDERSSON AND I. NILSSON
AB ATOMENERGI, STUDSVIK, NYKÖPING, SWEDEN

Abstract — Résumé — Аннотация — Resumen

EXPOSURE FOLLOWING INGESTION OF WATER CONTAINING RADON-222. There exist wells in Sweden that supply water for consumption which has radon-222 concentrations above 100 nc/L. We have investigated the problem of estimating the radiation dose to man following ingestion of radon-rich water.

Two subjects were each given about one litre of radon-rich water and the external γ-radiation was studied by repeated measurements in a whole-body counter. Chair geometry and an 8 in x 4 in NaI (Tl) scintillation spectrometer were applied. The decay of the gamma activity was followed until the signal was indiscernible from background radiation. By analysing the decay curve and particularly the decay of the 0.6 MeV peak of RaC, it was possible to determine a biological half-life (T_b) of radon in the body. With knowledge of T_b we could calculate the energy absorbed in the body at an intake of radon and radon daughters and thus determine the radiation dose to total body. A value of the radon concentration (MPC)_W that corresponds to a dose rate of 0.1 rem/week to total body was obtained. Preliminary results are for T_b = 35 min and for (MPC)_W = 6 × 10^{-4} μC/m^3.

CONTAMINATION A LA SUITE D'UNE INGESTION D'EAU CONTENANT DU RADON 222. Il existe en Suède des puits alimentant un réseau de distribution d’eau potable qui contiennent une eau dans laquelle on trouve des concentrations de radon 222 supérieures à 100 nc/L. Les auteurs ont cherché à évaluer la dose à laquelle l’homme est soumis à la suite de l’ingestion d’une eau riche en radon.

On a fait absorber à deux sujets un litre d’une eau riche en radon et on a étudié les rayons gamma externes par des mesures répétées au moyen dun anthropogammamètre. Dans une géométrie de la position assise, on a utilisé un spectromètre à cristal de NaI (Tl) de 20 × 10 cm. On a observé la décroissance de l’activité gamma jusqu’au point où l’on ne pouvait plus distinguer le signal du mouvement propre. En analysant la courbe de décroissance, et notamment la décroissance de la crête de 0,6 MeV du RaC, on a pu déterminer la période biologique (T_b) du radon dans le corps. Connaisant T_b, les auteurs ont pu calculer l’énergie absorbée dans le corps lors d’une ingestion de radon et de produits de dégradation du radon et déterminer ainsi la dose à l’organisme entier. Ils ont obtenu, pour la concentration maximum admissible du radon dans l’eau (CMA)_E, une valeur qui correspond à un débit de dose de 0,1 rem/sem à l’organisme entier. Les résultats préliminaires sont : T_b = 35 min et (CMA)_E = 6 × 10^{-4} μC/m^3.

ОБЛУЧЕНИЕ В РЕЗУЛЬТАТЕ УПОТРЕБЛЕНИЯ ВОДЫ, СОДЕРЖАЩЕЙ РАДОН-222. В Швеции имеются источники снабжения населения водой с содержанием радона свыше 100 ммкюри/л. Исследовался вопрос об измерении дозы радиации, получаемой человеком в результате употребления воды, богатой радоном.

Каждый из двух пациентов выпил около одного литра богатой радоном воды, и при помощи повторных измерений счетчиком для измерения радиоактивности всего организма было проведено исследование внешнего гамма-излучения. Использовались сцинтилляционный спектrometer с кристаллом 20 × 10 см NaI (Tl) и геометрия кресла. Спад гамма-активности происходил до тех пор, пока сигнал стал неотличим от фонового радиации. Путем анализа кривой спада, и в частности спада максимума 0,6 Мэв RaC, оказалось возможным определить период полувыведения (T_b) радона из организма. Зная T_b, можно подсчитать энергию, абсорбированную в организме при посредстве радона и продуктов его распада, и таким образом определить дозу радиации всего организма. Была получена величина концентрации радона (MRC)_W, соответствующая мощности дозы в 0,1 бэр/неделю для всего организма. Предварительные результаты для T_b = 35 мин и для (MRC)_W = 6 × 10^{-4} ммкюри/см^3.

EXPOSICIÓN CONSIGUIENTE A LA INGESTIÓN DE AGUA QUE CONTIENE RADÓN-222. Existen en Suecia pozos de agua potable cuya concentración de radón-222 es superior a 100 nc/L. Los autores han estudiado
I.Œ. ANDERSSON and I. NILSSON

el problema de evaluar la dosis de radiación en el cuerpo humano a consecuencia de la ingestión de agua con alto contenido de radón.

Se administró a dos sujetos un litro, aproximadamente, de agua con alto contenido de radón y se estudió la radiación gamma externa mediante exámenes repetidos con un antropogammámetro. Se utilizó una geometría de silla y un espectrómetro de centelleo con cristal de NaI(T1), de 8 pulg × 4 pulg. Se observó la disminución de la actividad gamma hasta el momento en que no fue posible discernir la respectiva señal de la radiación de fondo.

Por análisis de la curva de desintegración y, en particular, de la atenuación del máximo de 0,6 MeV correspondiente al RaC, se pudo determinar el periodo biológico del radón en el cuerpo (Tg). Una vez conocido Tg, los autores pudieron calcular la energía absorbida en el cuerpo a raíz de la absorción de una cantidad dada de radón y de sus descendientes y determinar, de ese modo, la dosis de radiación al cuerpo entero. Obtuvieron para la concentración del radón (CMA)a un valor que corresponde a una intensidad de dosis de 0,1 rem/semana aplicada al cuerpo entero. Según los resultados preliminares, Tg = 35 min y (CMA)a = 6 \times 10^{-4} μSv/cm².

1. INTRODUCTION

It is well known that in nature water exists which is highly radioactive due to the presence of radon-222 and its daughter products. It happens that radon-rich water is used as drinking-water for people and animals. There are several examples of this in our country. We have considered the problem of estimating the radiation dose which follows the intake of radon-rich water. The ICRP radiation protection guide gives no information for this case.

To obtain data for dose calculations, measurements have been carried out with a whole-body radioactivity counter on human subjects after intake of natural radon-rich water. The decay of the gamma radiation from the human body has been followed. Radon itself is not a gamma-emitter but its daughter products RaB and RaC are. By gamma-spectrum measurements it was possible to study selectively the RaC content in the body. The form of the RaC decay curve has been used to determine the radon retention as a function of time after intake. This will give the fraction of the ingested radon atoms that disintegrates in the body and the radiation dose to total body can be calculated. The radon concentration in water (MPC)w that delivers a certain maximum permissible dose rate to total body can also be determined.

2. EXPERIMENTS

Radon disintegrates in the following decay series:

\[
\begin{align*}
\text{Rn}^{222} & \xrightarrow{3.82 \text{ d}} \text{RaA} \xrightarrow{3.05 \text{ min}} \text{RaB} \xrightarrow{26.8 \text{ min}} \text{RaC} \xrightarrow{19.7 \text{ min}} \text{RaD} \\
\text{Po}^{218} & \xrightarrow{160 \mu s} \text{RaD} \\
\text{Pb}^{214} & \xrightarrow{21.8 \text{ min}} \text{Bi}^{214} \xrightarrow{50.1 \text{ min}} \text{Po}^{214} \xrightarrow{3.82 \text{ d}} \text{RaA}
\end{align*}
\]

The radioactive transitions and the half-life are indicated for each substance. The RaD decay chain can be ignored in this connection. Radon-222, RaA
INGESTION OF WATER CONTAINING RADON-222

and RaC decay by α-emission and RaB and RaC by β, γ-emission. If the radon content in a sample does not change appreciably during a period of about two hours, e.g. if the sample is sealed, an equilibrium state will be reached where each of the decay products has the same disintegration rate as Rn\textsuperscript{222}. The gamma radiation has been utilized for radioisotope measurements in this investigation. Table I shows the energy and relative intensity of the dominating gamma photons from RaB and RaC [1].

<table>
<thead>
<tr>
<th>E\textsubscript{γ} (MeV)</th>
<th>Number of quanta per disintegration</th>
</tr>
</thead>
<tbody>
<tr>
<td>RaB</td>
<td></td>
</tr>
<tr>
<td>0.24</td>
<td>0.105</td>
</tr>
<tr>
<td>0.29</td>
<td>0.241</td>
</tr>
<tr>
<td>0.35</td>
<td>0.377</td>
</tr>
<tr>
<td>RaC</td>
<td></td>
</tr>
<tr>
<td>0.61</td>
<td>0.471</td>
</tr>
<tr>
<td>0.77</td>
<td>0.053</td>
</tr>
<tr>
<td>0.94</td>
<td>0.033</td>
</tr>
<tr>
<td>1.12</td>
<td>0.166</td>
</tr>
<tr>
<td>1.24</td>
<td>0.060</td>
</tr>
<tr>
<td>1.38</td>
<td>0.048</td>
</tr>
<tr>
<td>1.40</td>
<td>0.040</td>
</tr>
<tr>
<td>1.76</td>
<td>0.163</td>
</tr>
<tr>
<td>2.20</td>
<td>0.083</td>
</tr>
</tbody>
</table>

The radon-rich water that has been used in the experiments was taken from a bored well located in Masugnsbyn in northern Sweden. The well has been the water supply for a family for over fifteen years. Samples were taken directly from a water-tap into 1-l containers made either of tin or of polyethylene. The containers were carefully sealed after filling to prevent loss of radon. It usually took four days to transport the samples to the laboratory.

The first batch of samples was used for control purposes. The decay of the gamma activity was measured. The tin containers were used to be sure there was no leakage. A sample was placed close to the 4 in × 4 in NaI(Tl) crystal in a scintillation spectrometer. The counting rate in the energy band 40–2540 keV was measured as a function of time over a period of 11 d. Two samples were investigated. The observed half-time of the decay, 3.85 ± 0.05 d, was in good agreement with the half-life of Rn\textsuperscript{222}, 3.8 d. The samples were measured again after fifteen days to make sure that there were no long-lived activities present.
The radon content in the water was determined by measurements on the 0.61-MeV gamma radiation from RaC in a scintillation spectrometer. The counter arrangement had earlier been calibrated. The photopeak efficiency as a function of photon energy was known for a 1-1 sample in a standard position. The counting rate in the 0.61-MeV photopeak then determines the absolute emission rate of 0.61-MeV photons in the sample. A correction has to be applied for the contribution in the 0.61-MeV photopeak band of photons of energies above 0.61 MeV. Since the yield of 0.61-MeV quanta per RaC decay is known (Table I) the disintegration rate of RaC could be calculated. The disintegration rate of radon is the same as that of RaC since radioactive equilibrium exists. The sample container in the calibrated arrangement was a 1-1 polyethylene bottle of the same type as was used to collect the radon water samples for the ingestion experiment. The radon content of a sample could then be determined without opening the container.

The whole-body radioactivity counter used for the measurements was the Hugo II-facility at the AB Atomenergi Research Laboratories at Studsvik. It consists of an iron room with inner dimensions 2.5 m × 3 m × 1.90 m (height) and 16-cm thick walls. The detector is an 8 in × 4 in NaI(Tl) crystal scintillation counter. Chair geometry is applied and the surface of the crystal is located 38 cm from the back and the seat of the chair. The detector is connected to a pulse-height analyser, Nuclear Data ND 130 A. 127 channels are used to cover the gamma energy interval 0 - 2540 keV.

The ingestion experiment was carried out on two human male subjects. Before intake they showered, put on clean dress and had their normal pulse-height spectra determined in a 20-min measurement in the body counter. Subject A then consumed a 1-1 sample of radon-rich water. The Rn$^{222}$ content was 69 nc. He was immediately taken to the body counter for two consecutive 10-min measurements. Subject B then ingested his 1-1 sample, which also contained 69 nc of Rn$^{222}$, and had two 10-min measurements in the body counter. Subjects A and B were then alternately measured in the body counter till five hours after the intake. The counting time was 10 min except in the last measurement of each subject, where 20 min was used to increase statistical accuracy. The urine was collected and measured. No gamma activity from radon decay products was detected in the urine.

Figure 1 shows examples of the pulse-height spectra that were obtained. The spectrum of a subject before intake shows the usual contributions from Cs$^{137}$ (30 nc) and K$^{40}$ (13 nc). The contribution from radon and its decay products one hour after intake is also displayed. The gamma lines that were given in Table I appear here quite clearly. The activity from radon and daughters present in the body could be measured up to five hours after intake.

The data in Table I indicate that the gamma photons which have energies above 0.35 MeV all come from RaC disintegrations. The counting rate in the energy band 560 - 2540 keV can then be considered to give information about the RaC content in the body. The net contribution in this energy band due to the intake has been calculated for all the measured spectra. The result for the spectrum taken directly after intake has been given the value 100. The retention in per cent has then been determined as a function of time for each subject. Figure 2 shows the results. There is good agreement between the results for the two subjects. The curve indicates approxi-
Energy (MeV)

Fig. 1
Scintillation counter pulse-height spectra of subject A

Fig. 2
Decay of the counting rate in the energy band 660 - 5560 keV

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mately how the RaC content in the body varies after an intake of radon in equilibrium with its daughter products. The form of the RaC retention curve is dependent on the rate of decay of the ingested RaA, RaB and RaC atoms and also on the radon concentration in the body as a function of time after intake. A main part of the radon atoms will leave the body before they decay. Since it is necessary to know the fraction of ingested radon atoms that disintegrates in the body to be able to carry out dose calculations, we have tried to obtain this information from the curve in Fig. 2.

3. CALCULATIONS AND RESULTS

It is assumed that the radon content in the body decays exponentially after intake. An emission constant $\lambda_0$ indicates the rate of the elimination. It is also assumed that radon and its decay products are in radioactive equilibrium in the sample that is ingested.

The differential equation system that describes the disintegration rates (N) of the different components in the radon decay chain can be written:

$$\frac{dN_{Rn}}{dt} = -\lambda_0 N_{Rn}$$
$$\frac{dN_{RaA}}{dt} = -\lambda_{RaA} (N_{RaA} - N_{Rn})$$
$$\frac{dN_{RaB}}{dt} = -\lambda_{RaB} (N_{RaB} - N_{RaA})$$
$$\frac{dN_{RaC}}{dt} = -\lambda_{RaC} (N_{RaC} - N_{RaB})$$

The initial activities at the time $t = 0$ are $N_{Rn} = N_{RaA} = N_{RaB} = N_{RaC} = A_0$. $\lambda_{RaA}$, $\lambda_{RaB}$ and $\lambda_{RaC}$ are the radioactive decay constants of RaA, RaB and RaC respectively.

The solution is most readily obtained by using Laplace-transformations. Since the measurements were made on RaC it is the formula for $N_{RaC}$ that is of interest:

$$N_{RaC} = A_0 \left[ \frac{\lambda_{RaA} \lambda_{RaB} \lambda_{RaC}}{(\lambda_{RaA} - \lambda_0)(\lambda_{RaB} - \lambda_0)(\lambda_{RaC} - \lambda_0)} e^{-\lambda_0 t} \right.$$

$$+ \left. \frac{\lambda_0 \lambda_{RaB} \lambda_{RaC}}{(\lambda_0 - \lambda_{RaA})(\lambda_{RaB} - \lambda_{RaA})(\lambda_{RaC} - \lambda_{RaB})} e^{-\lambda_{RaB} t} \right.$$

$$+ \left. \frac{\lambda_0 \lambda_{RaA} \lambda_{RaC}}{(\lambda_0 - \lambda_{RaB})(\lambda_{RaA} - \lambda_{RaB})(\lambda_{RaC} - \lambda_{RaB})} e^{-\lambda_{RaA} t} \right.$$

$$+ \left. \frac{\lambda_0 \lambda_{RaA} \lambda_{RaB}}{(\lambda_0 - \lambda_{RaC})(\lambda_{RaA} - \lambda_{RaC})(\lambda_{RaB} - \lambda_{RaC})} e^{-\lambda_{RaC} t} \right]$$
The parameter $\lambda_0$ appears in the formula for $N_{RaC}$. By comparing theoretical and experimental RaC retention curves it should be possible to determine $\lambda_0$. In Fig. 3 $N_{RaC}$ is shown as calculated from the formula above for different values of $\lambda_0$.

To obtain a RaC retention curve from the experimental results shown in Fig. 2 it is necessary to apply a correction for the change in counting efficiency due to the redistribution of radioactivity that occurs during the first few hours after intake. The size of this correction was taken from K42 ingestion experiments. This is an approximation and a certain error has to be accepted. The RaC retention curve after correction for the geometry effect is given by the dashed curve in Fig. 3. Comparison of theoretical and experimental curves gives $\lambda_0 = 1.40 \pm 0.15 \text{ h}^{-1}$. The assumption that radon is eliminated exponentially from the body seems to be justified because there is a rather good agreement between measured and calculated curves. The effective half-life of radon in the body that corresponds to the observed value of $\lambda_0$ is $30 \pm 3 \text{ min}$. The fraction of ingested radon atoms that disintegrates in the body is also determined by $\lambda_0$ and it is $100 \frac{\lambda_{Rn}}{\lambda_0} = 0.54 \pm 0.06\%$. $\lambda_{Rn}$ is the radioactive decay constant of $\text{Rn}^{222}$.

The radiation dose to total body from an intake of radon in equilibrium with its decay products RaA, RaB, RaC and RaC' can now be calculated.
If the ingested sample contains $A_0$ dps of each of the components in the decay chain the total effective absorbed energy when all radioisotopes have decayed is:

$$\frac{A_0}{\lambda_0} \sum \frac{E \times QF}{\lambda_{RaA}} + \frac{A_0}{\lambda_{RaA}} \sum \frac{E \times QF}{\lambda_{RaB}} + \frac{A_0}{\lambda_{RaC}} \sum \frac{E \times QF}{\lambda_{RaC}}$$

The four terms represent the contributions from the ingested atoms of Rn, RaA, RaB and RaC respectively. The dose from the ingested RaC atoms can be ignored. $E \times QF$ is the effective absorbed energy when one radioisotope x has passed through the decay chain down to RaD. E is the absorbed energy per disintegration and QF is the quality factor.

With the numbers inserted the effective absorbed energy is:

$$A_0 \left[ \frac{192}{\lambda_0} + \frac{137}{\lambda_{RaA}} + \frac{78}{\lambda_{RaB}} + \frac{77}{\lambda_{RaC}} \right] = 8.4 \times 10^5 A_0 \text{ MeV}$$

The dose equivalent averaged over total body is:

$$A_0 \times 8.4 \times 10^5 \times \frac{1.6 \times 10^{-3}}{7 \times 10^4} = 1.9 \times 10^{-7} \times A_0 \text{ rem.}$$

The ICRP radiation protection guide [2] suggests as a limit on the average internal dose to total body to a large population 0.001 rem/week. The maximum permissible concentration in water of radon in equilibrium with its daughters, $(MPC)_w \mu\text{c/cm}^3$, can be calculated for this case. The daily intake of water is assumed to be 2200 cm$^3$.

$$(MPC)_w \times 2200 \times 3.7 \times 10^4 \times 1.9 \times 10^{-7} = 0.001 \times 1/7,$$

$$(MPC)_w = 9 \times 10^{-6} \mu\text{c/cm}^3.$$ 

For an individual in the population at large a limit on the dose to total body of 0.01 rem/week is suggested. $(MPC)_w$ for this case would be $9 \times 10^{-6} \mu\text{c/cm}^3$.

The radon-rich water that was used in the experiments is actually used by a family as drinking-water. The Rn$^{222}$ concentration in the water at the time the samples were collected was 130 nc/L. The $(MPC)_w$ values given above show that this will correspond to a dose rate of 720 mrem/yr. However, it is probably more realistic to assume an intake of water which is half of the amount, 2200 cm$^3$, that was used in the $(MPC)_w$ calculations and also to assume some release of radon from the water before intake due to boiling and agitation. The dose to total body would then be in the region 150-360 mrem/yr.

This investigation has not given any information about the distribution of the radioisotopes in the body after intake. The consequence is that it has only been possible to determine the average dose to the total body and to obtain $(MPC)_w$ values under the assumption that the total body is the critical organ.
REFERENCES


DISCUSSION

W. JACOBI: The radiation exposure of this special group of persons depends on the real Rn content of the ingested food and drinking water. Have you measured the fraction of Rn which emanates from the water and is lost before the water is used?

I. Ö. ANDERSSON: The release of radon from the water used for the household has not been measured.

J. RUNDLE: Since you use a single crystal and "tilting chair" geometry, could changes in distribution in the early period following ingestion have confused the picture? Secondly - though I realize this is difficult to do have you attempted to analyse the data to get some information on the simultaneous retention of RnB?

I. Ö. ANDERSSON: A correction for the change in the distribution was deduced from potassium-42 ingestion measurements made in the same counting geometry. The counting rate in the RnC band was increased by an amount ranging from 0-20%, depending on the time after intake.

The RnB retention curve has not been studied.

C. R. HILL: You indicate a biological half-life of about 30 min for ingested radon in the human body. Is it possible that this figure applies only to one body compartment and that other compartments may exist having much longer half-lives? As a check on this possibility and on the general conclusions of your paper, have you considered measuring lead-210 or polonium-210 in the urine of members of the family referred to in the paper, who have very high levels of radon in their drinking water?

I. Ö. ANDERSSON: Members of the family were measured in the body counter two days after they had left their home. The results indicate no compartment having a half-life longer than about one day which could give an important contribution to the dose to the body. Lead-210 and polonium-210 analysis is definitely of interest for this case, but this has not yet been done.

G. W. DOLPHIN: Have you compared your data with those of Hursh (Rochester University)? Hursh has found that the retention of radon could be represented by three exponential terms, the details of which I cannot recall.

I. Ö. ANDERSSON: No. We have not done this.

W. V. MAYNEORD: I am a little unhappy at the assumption that radon is excreted exponentially. It was shown by Stefan Meyer about 1929 that, after ingestion of water containing radon, the exhaled air has at first a low activity. The activity rises to a maximum some half-hour to an hour after ingestion and the falls slowly for an hour or two. Our own experiments show a similar time pattern for the activity of exhaled air. The excretion pattern, however, varies with the age, weight, pulse-rate, smoking habits and other
characteristics of the subject, and Meyer even suggested the use of this pattern in the diagnosis of a number of pathological conditions of the lung.

In our own experiments the fraction of radon exhaled in this way was found to vary from some 50% to 90% for different subjects.

B. RAJEWSKY: We have done a lot of work on the excretion of radon after ingestion of water. I agree with Professor Mayneord that it is a very complex process, but it is possible to standardize this process and get an exponential curve. To do this, however, we need to know the exact clinical condition of the patients.
STRONTIUM
(Session 12)
THE ASSESSMENT OF RADIOACTIVE BODY BURDENS OF THE ALKALINE EARTHS

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HEADINGTON, OXFORD, ENGLAND

Abstract — Résumé — Аннотация — Resumen

THE ASSESSMENT OF RADIOACTIVE BODY BURDENS OF THE ALKALINE EARTHS. The difficulties in obtaining data on the metabolism of bone-seeking radioactive isotopes in man are widely appreciated, especially on the distribution of the isotope between different bones and the microscopic distribution within the same bone. If a full understanding of the metabolism in man is to be obtained, there is at present no alternative but to resort to the use of experimental animals. The calcium and strontium metabolism of the rabbit, which is the smallest animal to have similar skeletal structure to that of human bone, has been studied. The research was planned to include as many parameters as possible. These included specific activity measurements of plasma, urine and faeces, total retention in the skeleton as well as individual bones and in some cases soft tissues. In addition the microscopic distribution of the isotope was studied by quantitative autoradiographic techniques at different time intervals.

The results have been considered in the light of various models proposed for the retention of bone-seeking isotopes in mammals and the limitations of each of these models have been assessed. Measurements have been made over sufficiently long time intervals compared with the life-span of the rabbit to enable predictions to be made about the long-term behaviour in man. The results indicate that none of the existing models is completely satisfactory but that a modification of the power function is the most useful. The importance of exchange, as well as resorption, for the removal of radioactive isotopes from the skeleton is well illustrated by the quantitative autoradiographic measurements.
A study has been made of the calcium and strontium metabolism of the rabbit, which is the smallest animal to have a similar bone structure to that of man. The research was planned to include as many parameters as possible. These included specific activity measurements of plasma, urine and faeces, total retention in the whole skeleton, individual bones, and soft tissues. In addition the microscopic distribution of the isotope was studied by quantitative autoradiographic techniques at different time intervals.

The excreta data and the variation in isotope concentration in individual bones have already been reported for the same animals as those considered in the present text (LLOYD [1]). The autoradiographic results have also been discussed (LLOYD [2]). The present communication is therefore confined to a consideration of the experimental values obtained for skeletal and whole-body retention in relation to different models which have been proposed for the retention of the alkaline earths in mammals.

Measurements have been made both at short times after injection as well as over sufficiently long times, compared with the life span of the rabbit, to enable predictions to be made about the long-term behaviour in man.
2. METHODS

Young adult rabbits (7 months old) were given single intravenous injections of high specific activity Ca$^{45}$ or Sr$^{90}$ + Y$^{90}$. The animals were sacrificed serially at time intervals from 10 min to 100 d after injection. Litter mates were used for comparison of Ca$^{45}$ and Sr$^{90}$ kinetics. The doses administered (200 $\mu$Ci/kg body weight for Ca$^{45}$ and 100 $\mu$Ci/kg body weight for Sr$^{90}$) were chosen to be sufficiently high to provide conveniently short exposure times (of a few days) for the autoradiographic studies but low enough for no gross radiation damage to be expected over the period of study. (MacPHerson, Owen and VAUGHAN [3]). Further details of the method have been given elsewhere (Lloyd [1]). The total skeletal retention of all animals was determined by direct measurement. After ashing, all the bones were assayed for Ca$^{45}$ and stable Ca in the animals injected with Ca$^{45}$. For the animals injected with Sr$^{90}$, stable Ca and stable Sr measurements were made in addition to the radioactive assays. At the time of sacrifice, blood samples were also collected and analysed. In addition Ca$^{45}$ and stable Ca measurements were made on the whole of the soft tissues of two animals injected with Ca$^{45}$ and sacrificed at one day.

3. EXPERIMENTAL RESULTS

3.1. Plasma

At times greater than three days after injection, the specific activities of Ca$^{45}$ and Sr$^{90}$ in plasma (expressed as the percentage of the injected dose per gram of calcium and per milligram of strontium respectively) were found to be the same as the specific activities in the urine within the experimental error of the measurements. At earlier times, when the activity in the plasma was changing rapidly with time, the specific activity of urine was higher than the specific activity of plasma since the daily collection of urine represented the integral of the plasma specific activity over the whole period whereas the plasma was taken at the end of the time interval. Figure 1 shows the activity of Ca$^{45}$ and Sr$^{90}$ in plasma obtained by direct measurement. The results are expressed as the percentage of the injected dose per gram of calcium plotted against time after injection. Assuming a mixing time of ten minutes, the volume of the mixing pool, calculated from the specific activity in the plasma, would appear to be about 120 mg of calcium for both Sr$^{90}$ and Ca$^{45}$. This represents about 0.5% of the total body calcium.

3.2. Distribution of Ca$^{45}$ between plasma, bone, soft tissue and excreta

Table I shows the distribution of activity between plasma, bone, soft tissue and excreta given as the mean values for two animals injected with Ca$^{45}$ and sacrificed at one day.

The specific activity of the plasma corresponds to the value obtained at the end of the first day. The average value over the first day was obtained by numerical integration and was found to be 250% per gram of calcium. Values of the specific activity for bone and soft tissue indicate that about
Graph showing the concentration of Sr$^{90}$ and Ca$^{45}$, expressed as a percentage of the injected dose per gram of calcium, in litter mates sacrificed at time intervals between 10 min and 100 d.

TABLE I

Ca$^{45}$ IN ADULT RABBIT ONE DAY AFTER INTRAVENOUS INJECTION

<table>
<thead>
<tr>
<th>Tissue</th>
<th>% injected dose</th>
<th>Ca (g)</th>
<th>% injected dose per g Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>1.4</td>
<td>0.0125</td>
<td>110</td>
</tr>
<tr>
<td>Gut and contents</td>
<td>10.6</td>
<td>0.20</td>
<td>52</td>
</tr>
<tr>
<td>Other soft tissues</td>
<td>8.3</td>
<td>0.60</td>
<td>14</td>
</tr>
<tr>
<td>Bone</td>
<td>49</td>
<td>20</td>
<td>2.5</td>
</tr>
<tr>
<td>Urine</td>
<td>7</td>
<td>0.10</td>
<td>70</td>
</tr>
<tr>
<td>Faeces</td>
<td>11</td>
<td>0.35</td>
<td>32</td>
</tr>
</tbody>
</table>

1% of bone and about 5–6% of the soft tissue calcium (excluding gut) has exchanged with plasma by one day. If the volume of the extracellular fluid and the plasma represent 16% and 4.5% respectively of the body weight, as in human adults (PITTS [4]), the activity in the extracellular fluids at one day would be expected to be

$$\frac{16}{4.5} \times 1.4 \times 0.6 = 3\%,$$

where 0.6 represents the fraction of ionized calcium in the plasma. This
value is somewhat lower than the percentage of the dose found in the soft
tissue, which suggests that some cellular calcium is also exchangeable. It
is probable that some of the cellular radiocalcium is associated with cartilage,
since previous measurements with Sr^{90} (LLOYD [5]) showed that the concen-
tration of Sr^{90} in cartilage was about ten times the concentration found in the
liver (a tissue with a high blood content).

3.3. Plasma-bone interrelationships

Figure 1 shows the relationship between the specific activity of the
plasma and the specific activity of the skeleton as a whole. Although the
total activity in the plasma is about the same as the activity found in the
whole skeleton at 10 min, (~15% of the injected dose), the specific activity
in plasma is about 1000 times the specific activity in bone at this time. The
plasma values do not equal the bone specific activities until about 10 d after
injection. At longer times the plasma values fall below the values for the
bone, but no equilibrium between the plasma specific activity and the bone
specific activity is apparent up to 100 d. It is however possible that at later
times equilibrium may be established. Measurements are currently being
made to extend the range of these measurements to one year.

A comparison of the curves for Sr^{90} and Ca^{45} indicates that at short
times no significant difference exists between the concentration of Ca^{45} and
Sr^{90} in the plasma but with increasing time the Sr^{90} concentration falls
more rapidly than the Ca^{45} concentration. (This was reflected in the urine
excretion values, already reported (LLOYD [1])). With increasing time the
loss of activity from the plasma for both isotopes becomes approximately
parallel.

Similarly in bone the uptake of both isotopes at short times is the same
but with increasing time the two curves diverge. The maximum uptake of
Sr^{90} occurs at about 2 h compared with the later time of about 12 h for the
maximum for Ca^{45}. At later times the rate of loss of both isotopes from
the bone is approximately the same and the concentration of Ca^{45} is 1.5 - 2
times the concentration of Sr^{90} expressed as the percentage of the injected
dose per gram of calcium.

4. DISCUSSION OF MODELS

Having discussed the distribution of Ca^{45} and Sr^{90} in the rabbit as a
function of time it is now necessary to examine how this information fits the
mathematical models which have been proposed for the description of whole-
body retention.

Values for whole-body retention have been derived from the present
results by assuming that at 9 d, 30 d and 100 d the total activity of Sr^{90} and
Ca^{45} is to be found in the skeleton. The retention obtained by subtracting
the activity in the excreta from the activity injected has been normalized to
fit these skeletal retention values. In this way the results are free from
inaccuracies due to cumulative losses which must inevitably occur in the
summation of excreta data over long periods.
4.1. Single exponential model

The determination of the maximum permissible dose by ICRP [6] has been based on both the single exponential model and the power function model. Other workers (BISHOP, HARRISON, RAYMOND, SUTTON and RUNDO [7]; LINIECKI [8]) have shown that in man the single exponential model is not an adequate description of the retention of strontium.

![Graph of whole-body retention of Ca\(^{45}\) and Sr\(^{90}\) as a function of time, plotted semi-logarithmically](image)

Figure 2 shows the average values for the whole-body retention of Ca\(^{45}\) and Sr\(^{90}\), obtained in the present study, expressed as the percentage of the injected dose as a function of time on a semi-log plot. Since the plot cannot be represented by a single straight line, it is obvious that a single exponential function cannot be used to describe retention.
4.2. Multi-exponential model

The curve (Fig. 2) for Ca$^{45}$ can, however, be adequately described as the sum of three exponentials up to 100 d according to the equation

$$R = 71 \exp\left(-\frac{0.693t}{1.5}\right) + 7.7 \exp\left(-\frac{0.693t}{10.8}\right) + 21.3 \exp\left(-\frac{0.693t}{135}\right),$$

where $R$ is the body retention expressed as the percentage of the injected dose and $t$ is in days. The corresponding expression for Sr$^{90}$ requires the use of four exponentials and is described by the equation

$$R = 69.6 \exp\left(-\frac{0.693t}{0.4}\right) + 6.4 \exp\left(-\frac{0.693t}{2.0}\right) + 12.0 \exp\left(-\frac{0.693t}{6.8}\right) + 12.0 \exp\left(-\frac{0.693t}{135}\right).$$

These formulae show a higher rate of removal of Sr$^{90}$ compared to that for Ca$^{45}$ at short times, but at longer times the rates of removal appear to be similar.

Bishop et al. showed that following a single injection of Sr$^{90}$ into man, the retention could be described either by a three term exponential model or by a power function, each of these models being an equally good fit. In the case of the rabbit, where the lifespan is about one tenth that of man, the last term of the equation has a half-life of 135 d. However, unless the isotope disappears completely from the skeleton, it is not certain that the longest half-life is truly representative of the fraction which is retained for the longest time. This difficulty in extrapolating to times beyond the range of the experimental results is the chief limitation of the multi-exponential model.

4.3. Power function model

The power function can also be used to represent the whole-body retention. The same data as those used in Fig. 2 have been replotted in Fig. 3 using logarithmic axes. The straight line portion of the plot for Ca$^{45}$ can be described by the power function $R = 0.54 t^{0.31}$. The corresponding expression for Sr$^{90}$ is given by $R = 0.32 t^{0.31}$. As seen in Fig. 3 there is a marked divergence from the straight line plot at short times in the case of Sr$^{90}$, while for Ca$^{45}$ this divergence is slight. Similar divergences from the power function have been observed in man at short times after intravenous injections of Sr$^{90}$ (BISHOP et al. [7]; COHN, LIPPINCOTT, GUSMANO and ROBERTSON [9]). This difference in the shape of the Ca$^{45}$ and Sr$^{90}$ retention curves is reflected in the greater rate of clearance of Sr$^{90}$ relative to Ca$^{45}$ from the plasma at short times.

The results, expressed in terms of either the power function or the multi-exponential model, indicate that the rate of loss of both isotopes is similar after the initial more rapid release of Sr$^{90}$.
The time exponent of the power function appears to vary slightly for different species but, apart from a value of 0.52 obtained by NORRIS, SPECKMAN and GUSTAFSON [10] for Ra$^{226}$ in man, (recently confirmed by MARINELLI, MILLER and LUCAS [11]) the values reported lie within the range 0.12 to 0.32 for all the alkaline earths in all species ranging from mouse to man (MAYS, CHRISTENSEN, LLOYD, ATHERTON, PARMLEY and PITCHFORD [12]). Although it is generally recognized that the power function represents the long-term data, it has been criticized as an interpretative model because its metabolic significance remains unexplained. On this basis it was considered to be undesirable for use in extrapolation beyond the range of experimental verification (ICRP [6]).

MARSHALL [13] has recently attempted to assign a deeper biological significance to the power function by considering the net movement of calcium-like ions to and from the plasma as the sum of a large number of body processes which can be represented diagrammatically by "closed loops", each loop being linked with the "plasma pool".

He has suggested that the expression for body retention is better satisfied by a power function followed by an exponential function, the latter being reached at a time, $t_\infty$, when the isotope in the body has reached equilibrium. He has also shown how the time of equilibrium, and hence the time when the exponential function would be expected to replace the power function, can be obtained from a knowledge of the specific activity of plasma and bone.

Applying his formula to the present results for the Ca$^{45}$, $t = 40$ d. This is, in fact, the time when the last exponential shown in Fig. 2 becomes operative. However, as already stated, it is not possible to be certain whether this is the final exponential describing retention up to time $t = \infty$.

If, as suggested by Marshall, equilibrium exists between plasma and bone at this time, then the rate of loss of activity from both plasma and bone should be the same. Figure 4 shows the curve obtained for the specific activity of plasma for Ca$^{45}$ plotted semi-logarithmically. The final exponential has a half-life of 95 d compared with the value of 135 d for bone. Hence
these measurements would suggest that up to the period of 100 d the plasma activity continues to fall more rapidly than that for bone.

However, that a divergence from the power function at longer time intervals does exist is clearly indicated by Figs. 5 and 6 where the specific activity of Ca$^{45}$/g Ca and Sr$^{90}$/mg Sr are plotted for daily urine samples collected from different animals up to 100 d after injection. The urine specific activities can be taken to be identical to the plasma specific activities after the first few days, as discussed previously. Values for the specific activity of faeces and bone (Figs. 5 and 6), also indicate a divergence from straight line plots, the specific activity in bone falling off more rapidly and the specific activity of faeces falling off less rapidly than the power function at long times after injection. The exact time at which a divergence from the best straight line plot occurs is difficult to determine, but these measurements would suggest that the divergence begins to appear at about the time when the bone specific activity curve crosses the plasma curve. This would be consistent with the process of exchange between plasma and bone, whereby the release of the isotope would be expected to increase when the plasma specific activity begins to fall below the specific activity of bone. With increasing time, the specific activity in bone would be expected to fall more rapidly, and the specific activity of plasma less rapidly, in an attempt to restore equilibrium against the higher concentration gradient, which would be expected in the absence of such an exchange process. Evidence for such a long-term exchange process has been clearly demonstrated in the autoradiographic measurements made during the present study (LLOYD [2]).
Specific activity of Ca$^{45}$ in bone, urine and faeces as a function of time, plotted logarithmically

4.4. Exchange model

KULP and SCHULERT [14] have proposed a simple model for the retention of Sr$^{90}$ in man due to "fall-out", based on a constant rate of exchange of bone mineral. This model can therefore be described as a single exponential and hence cannot be applicable over the entire period as already discussed. No account is taken of the faster rate of exchange of the radioisotope at short times compared with that at later times after administration, as demonstrated in the present results.

4.5. Compartment model

Yet other workers have attempted to express their findings in terms of compartments and rates (HEANEY and WHEDON [15]; RICH, ENSINCK and FELLOWS [16]; AUBERT and MILHAUD [17]; GLASS and NORDIN [18]; AUBERT, BRONNER and RICHELLE [19] and DOLPHIN and EVE [20]). Perhaps the most widely used of the compartment models is the one proposed by BAUER, CARLSSON and LINDQUIST [21] who based their model on
Specific activity of Sr\(^{85}\) in bone, urine and faeces as a function of time, plotted logarithmically.

Observations made over the first five days after intraperitoneal injections of Ca\(^{45}\) into rats. More recently BAUER and RAY [22] have applied the same calculations to the metabolism of Sr\(^{85}\) in five normal adults studied for five days. BAUER, CARLSSON and LINDQUIST [23] attempt to explain the processes involved in terms of two fractions: (1) the exchangeable fraction which is proportional to the serum specific and (2) the fraction accreted which is proportional to the integral of the serum specific activity curve. This is expressed mathematically as

\[ B^*_t = k_1 S^*_t + k_2 \int_0^t S^*(t) \, dt, \]

where \( B^*_t \) is the amount of isotope in tissue B at time \( t \); \( S^*_t \) is the specific
activity of the serum at time $t$; $\int_0^t S^*(t) dt$ is the integral of the serum specific activity from time $t_0$ to time $t$; $k_1$ and $k_2$ are constants.

The authors then suggest that $k_1$ and $k_2$ can be interpreted as biological functions, where $k_1$ represents the size of the "exchangeable pool" $E$, and $k_2$ is the accretion rate $A$.

By taking values for the retention, serum specific activity and the integrated specific activity at two different time intervals, two simultaneous equations are obtained which can be solved for $E$, the size of the "exchangeable pool", and $A$, the accretion rate.

This model was applied to the measurements obtained in the present study for the rabbits injected with $\text{Ca}^{45}$ and values for $A$ and $E$ were calculated for different time intervals.

These values are listed in Table II together with the experimental values used in the calculation.

TABLE II

CALCULATION OF $E$ AND $A$ FROM BAUER, CARLSSON AND LINDQUIST'S FORMULA FOR DIFFERENT TIMES AFTER INJECTION

<table>
<thead>
<tr>
<th>Time (d)</th>
<th>Body retention (R)</th>
<th>Plasma S. A.</th>
<th>$\int_0^t S^*(t) dt$</th>
<th>$A$ gCa/d</th>
<th>$E$ gCa</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>46</td>
<td>2.83</td>
<td>125.3</td>
<td>0.26</td>
<td>4.6</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>1.13</td>
<td>133.6</td>
<td>0.07</td>
<td>36.8</td>
</tr>
<tr>
<td>30</td>
<td>28</td>
<td>0.49</td>
<td>147.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>28</td>
<td>0.43</td>
<td>149.5</td>
<td>0.033</td>
<td></td>
</tr>
<tr>
<td>95</td>
<td>19.3</td>
<td>0.20</td>
<td>165.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>18.6</td>
<td>0.19</td>
<td>166.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In each case a 5-d interval was chosen for solving the simultaneous equations. The three sets of values for $A$ and $E$ refer to the early period, middle, and end periods, respectively. The accretion rate $A$, obtained for a mean time of $7\frac{1}{2}$ d after injection is a factor of eight greater than the value obtained at a mean time of $97\frac{1}{2}$ d, while the size of the exchangeable pool $E$ appears to increase by a factor of 15 over the same time.

Bauer et al. originally suggested, that their formulae should be valid only for relatively short time intervals before resorption became an important factor for the removal of the radioactive calcium from the bone. In addition the formulae were not considered to be valid for very short time intervals before equilibrium of the isotope in the "exchangeable pool" could be established. For these reasons the periods of about 5 - 10 d are commonly used for the calculations. The value for the accretion rate calculated for these times give 0.26 g of calcium per day.

From balance studies carried out for all the animals the average net retention of calcium was found to be 7.2% of the diet which is equivalent to
0.06 g of calcium per day. In addition, measurements on the increase of body weight over the 100-d period lead to a value of 0.04 g of calcium for the daily accretion, hence it must be concluded that the value obtained by Bauer's formula at times of 5-10 d shows an accretion rate which is about 5 times too high. However, it is interesting to note that the values obtained for the later time intervals are in reasonable agreement. These values predict an average turnover time of about 400 d, for the rabbit skeleton. GLASS and NORDIN [18] have also shown that in humans the accretion rate calculated as above varies from 4 to 14 mg/kg body weight per day depending on the time for which the calculations were made. The higher values correspond to short time intervals and the lower values to time intervals of 20-25 d.

BAUER et al. [23] deduced the average turnover time of the adult skeleton to be 5-6 yr. This time is much shorter than the 30-40 yr postulated by KULP and SCHULERT [14], and BRYANT and LOUITT [24] as assessed by Sr90 fall-out data. The short time predicted by Bauer et al. reflects the higher value of the accretion rate as calculated from measurements taken over periods of about 5-10 d. The main difficulty therefore in using Bauer's formulae to calculate accretion rates would appear to be the uncertainty as to the best time to choose for the calculation.

Similarly in the calculation of the size of the exchangeable pool, E, the values obtained in this work vary from 4.6 g (about 20% of the body calcium) at 5-10 d, to 69 g (about 3½ times the body calcium) at 95-100 d. Although 20% of the body calcium may be a reasonable figure for the exchangeable fraction at 5-10 d, the figure for the 95-100 d period is obviously too large. An upper limit can be put on the amount of exchangeable calcium by considering the dietary intake. In round figures, the intake was 1 g of calcium per day, i.e. 100 g for 100 d. About 50% of this is absorbed, and hence the maximum amount of calcium with which the body calcium could exchange is 50 g. Less than half of this is available for exchange, as indicated by a maximum uptake of 50% of the injected dose; hence 25 g for the 100-d period would appear to be an upper limit to the size of the exchangeable pool, compared with 69 g calculated from Bauer's model.

However, as already pointed out, Bauer's model was not originally intended for use at these long times when losses due to bone resorption become important; hence the lack of agreement is not surprising. It seems, however, that an increase in the size of the exchangeable fraction, as predicted by Bauer's model, does in fact occur as more skeletal mineral is made available for exchange. The failure of Bauer's model to provide a complete fit to the experimental data reported here is almost certainly due to an oversimplification in the original concept that bone could be represented by two isolated compartments whose volume remained constant with time and which were independent of each other, i.e. a short-term exchangeable fraction and an unexchangeable fraction of bone. In the light of the autoradiographic measurements reported here and elsewhere (ROWLAND [25]; ROWLAND and MARSHALL [26]) exchange has been shown to be an important factor in the loss of activity from areas of bone which have hitherto been considered non-exchangeable.
5. CONCLUSIONS

(1) The specific activity of plasma was found to fall off more rapidly than the specific activity of bone throughout the period of study up to 100 d. Hence no equilibrium was established between plasma and bone.

(2) In the light of the experimental evidence reported here, none of the five models considered for the whole-body retention of the alkaline earths has proved to be entirely satisfactory.

The two models which appear to provide the best fit to the data, over the whole time period, are the multi-exponential and the modified power function models. However, both these models were considered to be unsatisfactory for extrapolation to times beyond the range of experimental verification, because it is not certain whether the last term in each expression is valid to time, $t = \infty$.

(3) Changes in compartment sizes and exchange rates with time, which have been demonstrated in the present work illustrate the limitations of both compartment and exchange models.

ACKNOWLEDGEMENTS

I am indebted to Dr. Janet Vaughan who has been a constant source of encouragement throughout this work.

I am also grateful to Dr. S. Kshirsagar, Mrs. A. Webster, Mrs. W. Fidler and Miss F. Schofield, who have assisted at various stages of the research.

REFERENCES

DISCUSSION

W. GIESE: You mentioned that the specific activity of calcium in plasma showed no significant difference from that of calcium in urine when measured one day after intravenous injection of calcium-45 into the adult rabbit. In your Table 1, however, you give figures of 110 and 70 for the specific activity of calcium in plasma and in urine respectively. It would be interesting to know if we are here dealing with true differences, such as have been reported for both humans and animals, or if they are due to different sampling times.

E. LLOYD: The difference between the plasma specific activity and the urine specific activity at one day is due to the fact that the plasma was taken at the end of the one-day period whereas the urine value represents the integral of the plasma specific activity over the whole day. Most of the cases where specific activity has been shown to be different for urine and plasma refer to animals which were maintained on a depleted diet.
RETENTION OF RADIONUCLIDES BY INFANTS
I. STUDY TECHNIQUES AND ERROR EVALUATION

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Abstract — Résumé — Аннотация — Resumen

RETENTION OF RADIONUCLIDES BY INFANTS: I. STUDY TECHNIQUES AND ERROR EVALUATION.
Retention of radionuclides and stable chemicals in infants aged 1 to 11 months has been measured since 1960.
Infants volunteered by staff members for study in their respective home environments were selected, after consultation
with the family pediatrician and our staff physician. The infants were fed commercially prepared pre-
packaged foods ad lib, in terms of quantity and kind. These foods, the air breathed, and the water used directly
and in preparation of the formula constituted the normal intake of radionuclides and stable chemicals of interest.
Aliquots of the food, water, diapers, and paper tissues used are analysed. Excreta were collected in
disposable diapers, and separated into those containing urine or feces. Retention of the following radionuclides
and stable elements was or will be determined: strontium-90, strontium-89, cesium-137, radium-226,
calcium, strontium, phosphorus, and potassium.

The study differs from previous ones in several ways. The radionuclides and stable elements were at
normally encountered concentrations and in their normally encountered chemical forms. Air and water contami-
nated at environmental levels and commercially available food materials were the only sources of intake,
since no radionuclides or stable chemicals were added to the diet. The infants studied were normal, healthy
(not hospitalized) youngsters in their home environments.

The major problems in this study consisted of (1) controlling and maintaining records of all of the food
intake, (2) collecting all of the excreta, (3) obtaining an excreta sample large enough for accurate measure-
ment of the radionuclide and stable components contained; and (4) measuring radionuclide and stable component
concentrations in the intake and excreta accurately enough that significant retention values could be computed.
A case worker was utilized for control of intake and excreta information and an electronic computer for
data processing. Intake values of the analysed components were checked by comparing "phantom meals" with
computed amounts based on aliquots. A special paper diaper with a low stable strontium concentration was
developed and utilized. Calcium and phosphorus retention values were computed and are now available for
30 infants. Strontium-90 retention relative to calcium was found to be higher in infants than in adults.
été les seules sources d'absorption, aucun radionucléide ni élément stable n'ayant été ajouté au régime. Les enfants en bas âge observés étaient des sujets normalement sains (jamais hospitalisés), vivant dans leur milieu familial.

Les principaux problèmes à résoudre au cours de cette étude portaient sur les opérations suivantes: a) Vérifier et comptabiliser toutes les quantités de produits alimentaires ingérées; b) Recueillir tous les excréta; c) Prélever un échantillon d'excréta assez volumineux pour permettre un dosage précis des radionucléides et des éléments stables qu'il contenait; d) Mesurer les concentrations de radionucléides et d'éléments stables dans les substances absorbées et dans les excréta, de façon assez précise pour pouvoir calculer des valeurs significatives de la rétention.

Les auteurs ont eu recours à un enquêteur pour la vérification des renseignements sur les quantités absorbées et les excréta, et ont utilisé un ordinateur pour le traitement des données. Ils ont contrôlé les quantités absorbées des éléments étudiés en comparant des « repas fantômes » aux quantités calculées d'après les parties alitiques. Ils ont mis au point et utilisé des couches en papier spécial ayant une faible concentration en strontium stable. Ils ont calculé la rétention du phosphore et du calcium et ils disposent des valeurs correspondantes pour 30 enfants en bas âge. Ils ont constaté que le rapport entre la rétention du strontium 90 et celle du calcium était plus élevé chez les enfants en bas âge que chez les adultes.

ЗАДЕРЖКА РАДИОИЗОТОПОВ У ДЕТЕЙ: I. ИЗУЧЕНИЕ МЕТОДА И ОПРЕДЕЛЕНИЕ ОШИБКИ. Начиная с 1960 года проводится измерение степени задержки радиоизотопов и устойчивых химических соединений у детей в возрасте от 1 года до 11 лет. За детьми с согласия родителей велись наблюдения в соответствующей домашней среде, дети отбирались после консультации с детским врачом, лечившим ребенка, и врачом лаборатории. Дети пытались готовыми продуктами ad lib определенного качества и ассортимента. Пищевые продукты, вдыхаемый воздух и вода, используемые непосредственно и в процессе подготовки формулы, являлись источником нормального поступления в организм изучаемых радиоизотопов и устойчивых химических соединений.

Продукты анализировались на образцах пищевых продуктов, воды, используемых салфеток и бумаги. Выделения собирались в подлежащие удалению салфетки, отдельно моча и кал. Определялось или будет определяться задержка следующих радиоизотопов и устойчивых элементов: стронций-90, стронций-89, цезий-137, радий-226, кальций, стронций, фосфор и калий.

Эти исследования значительно отличаются от предыдущих. Радиоизотопы и устойчивые элементы находились в обычных концентрациях и в обычно встречающихся химических формах. Воздух и вода, загрязненные до уровня окружающей среды, и имеющиеся в продаже пищевые продукты были использованы как естественные источники подкормки, поскольку никакие радиоизотопы и устойчивые химические соединения не добавлялись. Исследуемые дети представляли собой обычных здоровых (негоспитализированных) детей в их обычной домашней среде.

Основные проблемы при проведении этих исследований заключались в 1) контролировании и регистрации всей потребляемой пищи, 2) сборе всех выделений, 3) получении достаточно больших образцов выделений для точного измерения содержания радиоизотопов и устойчивых компонентов, и 4) достаточно точном измерении концентраций поглощенных и выделяемых радиоизотопов и устойчивых компонентов, чтобы можно было получить достоверные величины задержки изотопов.

Для сбора информации о поглощении и выделении и для обработки данных был привлечен специальный сотрудник и использована электронная счетная машина. Величины поглощения анализируемых компонентов проверялись путем сравнения "контрольных образцов пищи" с расчетными данными, полученными при измерении образцов. Использовались специальные бумажные салфетки с низкой концентрацией устойчивого стронция. Были рассчитаны величины задержки кальция и фосфора для 30 детей. Установлено, что задержка стронция-90 по сравнению с кальцием у детей больше, чем у взрослых.

RETENCIÓN DE RADIONÚCLIDOS EN LOS NIÑOS DE PECHEO: I. TÉCNICAS DE ESTUDIO Y CÁLCULO DEL ERROR. Desde 1960 se viene midiendo la retención de ciertos radionúclidos y elementos estables en los niños de pecho de uno a once meses. Los niños, puestos a disposición voluntariamente por funcionarios para el estudio en el ambiente familiar, se seleccionaron previa consulta con el pediatra de la familia y el médico de la institución de los autores. Los niños consumen alimentos de tipo comercial corriente, ya preparados y empaquetados, sin restricción en lo que se refiere a cantidad y calidad. Estos productos alimenticios, el aire inhalado y el agua utilizada directamente y en preparación del biberón constituyen la absorción normal de radionúclidos y de elementos estables de interés,
Se analizan partes alícuotas de los productos alimenticios, del agua, de los pañales y del papel higiénico utilizados. Las excreta se recogen en pañales que se desechan después de utilizados, separándose los que contienen orina de los que contienen heces. Se ha determinado o se determinará la retención de los siguientes radionúclidos y elementos estables: estroncio-90, estroncio-89, cesio-137, radio-226, calcio, estroncio, fósforo y potasio.

El estudio difiere en varios aspectos de los anteriormente realizados. Los radionúclidos y elementos estables se presentan en concentraciones y formas químicas normales. Las sustancias absorbidas provienen exclusivamente del aire y del agua, cuyo grado de contaminación es el mismo que el del medio ambiente, y de los alimentos que se adquieren en el comercio, pues ningún otro radionúcluido ni elemento estable se añade a dicha dieta. Los niños examinados disfrutan de salud normal (no están hospitalizados) y permanecen en el ambiente familiar.

Los principales problemas de este estudio consistieron en: a) llevar cuenta y razón de todos los alimentos ingeridos, b) recoger todas las excreta, c) obtener una muestra de las excreta suficientemente grande para poder determinar cuantitativamente los radionúclidos y elementos estables contenidos, d) medir las concentraciones de radionúclidos y elementos estables en los alimentos y en las excreta con exactitud suficiente para poder determinar los valores significativos de retención.

Con objeto de fiscalizar la información relativa a alimentos ingeridos y a excreciones se utilizaron los servicios de una persona dedicada especialmente a esa tarea, recurriéndose a una calculadora electrónica para la elaboración de los datos. Los valores de ingestión de los componentes analizados se han comprobado comparando «comidas tipo de referencia» con las cantidades calculadas partiendo de las partes alícuotas analizadas. Se ha preparado y utilizado un pañal de papel especial con baja concentración de estroncio estable. Se han calculado los valores de retención para el calcio y el fósforo en el caso de 30 niños. Las observaciones efectuadas demuestran que la retención relativa de estroncio-90, referida al calcio, es más elevada en los niños que en los adultos.

INTRODUCTION

Deposition in bone and the long physical and biological half-lives of strontium-90 make it a potential major source of radiation exposure to humans. Because of higher retention of bone minerals in infants, radiation exposure may be higher than in adults; moreover, radiation effects may be greater because of increased radiation sensitivity in the immature cells of infants. The increased retention would be expected from the accretion and more rapid turnover of bone mineral in infants and the high specific activity of strontium-90 in their foods compared to that in bone. Because of the difficulty of obtaining infant tissues for analysis, few data on their strontium-90 concentrations are available. The reported data show higher concentrations relative to calcium than do bones of older children and adults [1, 2, 3]. A value near 0.2 for the observed ratio* of human adult bones is given [4, 5]. In animal experiments, the observed ratio is somewhat greater for younger animals than for older ones [6, 7, 8].

In June 1961 [9], we reported the absence of significant discrimination between strontium-90 and calcium in a group of five infants observed for a total of 25 28-d periods. Studies by other investigators support this observation [10, 11]. The present paper describes the methods used in the metabolic balance study carried out in the home, discusses the problems encountered, estimates precision, and identifies sources of error. A complete analysis and evaluation of data obtained with 32 infants over a period of 250 28-d periods is under way.

* $(\text{strontium/calcium})_{\text{bone}}/ (\text{strontium/calcium})_{\text{diet}}$
Infant metabolism studies are difficult to perform. Commonly, the infant is fed and his excreta are collected in a metabolic ward under direction of medical personnel; every effort is made to eliminate losses of food and excreta. Under the necessary physical restraints, the duration of a study is generally three days or less \[12, 13, 14\]. Consequently, small collecting errors assume great significance, the number of available normal subjects is limited, and the psychophysiological effects of the physical restraint may affect intake and retention.

In an effort to measure retention under more normal conditions, a balance study was performed with normal infants in their home environment for an average of eight consecutive periods per infant. Commercially available pre-analysed infant foods and milk formulae containing no chemical additives or tracers were used. The specific food items consumed by the infant were selected by the mother. The diet represents that which is currently fed infants of middle-class families in the United States, with the early addition of solid foods. Paper diapers were furnished for collection of excreta. The study was co-ordinated by a staff physician and a visiting case worker; however, immediate responsibility for observing the protocol of the study was with the mother of the infant. The study was discussed with the family physician. Medical histories were obtained from the family physician and the parents. Behaviour and growth records were kept. Every effort was made to minimize analytical errors and collection losses. Gross deviations from intake and excretion norms established within the study were observed in 5% of the balance periods.

The ingestion of strontium-90 from fallout under environmental conditions was measured, since no radioactive tracer was added. The most serious analytical problem was the precise measurement of strontium-90 in the foods (average intake of 150 pc per 28-d period) and in the excreta (approximately 100 pc per period). Strontium-89 was measured when present, and gamma spectra are available for computing concentrations of potassium-40, caesium-137, and other gamma-emitting fission products. The concentration of stable strontium was measured to determine specific activity. Calcium was determined to observe the magnitude of discrimination between strontium-90 and calcium, and phosphorus because of its metabolic relationship to calcium and potential effect on strontium-90 retention.

**PROCEDURE**

Parents who were staff members of the United States Public Health Service or students at the College of Medicine, University of Cincinnati, volunteered their infants prior to birth. After detailed interviews of the parents, an infant was started in the experiment at approximately four weeks of age for a two-week trial period. If the trial results were satisfactory, the infant was continued in the experiment until nine or ten months of age, at which time close control over intake became more difficult. Infants were removed from the experiment if they moved from the city, became seriously ill; or were obviously out of control with regard to intake and excretion.
Intake material

Commercially available milk formulae and infant foods were obtained in homogeneous lots and made available to the mother on a free selection basis. Large aliquots of each food item and milk were ashed and analysed. The milks included liquid formulae and evaporated milk for dilution with water and occasionally whole or skimmed milk. The other foods consisted of available varieties of single servings of cereals, vegetables, fruits, meats, and juices. Pre-analysed special foods, vitamins and medicines were also supplied as needed. Milk formulae, prepared to ± 10 ml in a graduate by the mother, were measured and diluted daily. The residual milk was measured daily; the difference represented consumed milk (Form 1, Appendix A). Consumption of additional water was also measured and a large composite sample was analysed. Sealed jars of food were weighed to within 0.1 g by the case worker and reweighed after use. The difference was recorded as the consumption of the particular food item (Form 2, Appendix A). The mother reported and attempted to correct for all losses, such as breakage and spillage. Food not retained by the infant as a result of spitting, drooling and vomiting was collected by the mother on paper wipes provided for this purpose and submitted for analysis.

To provide data for calculating the inhalation of strontium-90, suspended air particles were collected at the laboratory (located within a 10-mile radius of all homes of infants) by drawing air through a membrane filter at the rate of 1 m³/h. Filters were changed daily, composited for the 28-d period, and then analysed for strontium-90 and for strontium-89 when present [15].

Excreta collection

Paper diaper inserts were obtained in large quantities for use within the infant plastic pants to collect excreta. Soiled diapers were collected daily and their number was recorded. Paper wipes were supplied to clean the infants and to collect excreta from the plastic pants and other surfaces. The number used was recorded and then the wipes were added to the diaper collections for analysis. Initially, all soiled diapers and wipes were combined; after the first 13 infants had been studied, however, diapers containing only urine were collected and analysed separately from the soiled wipes and the diapers containing faeces and urine. Soiled diapers and wipes were composited for the 28-d period before analysis. Representative lots of unused diapers and wipes were analysed to provide "blank" values. Because the original diapers contained too much insoluble residue and stable strontium, a new low-ash diaper was developed and used with the last 12 infants [16].

* Gerber Products Company, 445 State St., Fremont, Michigan; Wilson Milk Company, Division of Dean Milk Company, Indianapolis, Indiana; Karo syrup from Best Foods, Division of Corn Products Company, New York, N.Y.; Similac from Ross Laboratories, Columbus, Ohio; Enfamil, So-Bee, Tri-Vi-Sol, and Poly-Vi-Sol from Mead-Johnson and Company, Evansville, Indiana. The use of these products does not constitute endorsement of the product by the Public Health Service.

** Playtex Drypers from International Latex Corp., Playtex Park, Dover, Delaware; Chux Diapers from Chix Baby Products, Division Chicopee Mills, Inc., 47 Worth St., New York, N.Y. The use of these products does not constitute endorsement of the product by the Public Health Service.
Record keeping and computation

Infant length and weight were measured weekly by the mother and recorded (Form 1, Appendix A). Consumption of medicines and unanalysed food, the state of health of the infant, known losses of food or excreta, and circumstances leading to the possibility of such losses (travel, use of babysitter) were also recorded on this form. The case worker checked the information on the forms with the mother, and recorded food consumption values (Forms 2 and 3, Appendix A).

Analytical methods

All samples of food, excreta, diapers, and air filters were ashed at 500°C. These residues were analysed by gamma spectroscopy using a 10 cm × 10 cm NaI(Tl) crystal housed in a steel shield (walls 10 cm thick). Spectra were recorded over a range of 3 MeV at 20 keV per channel; the resulting scans are available for quantifying all detectable gamma emitters.

Weighed aliquots of ash were dissolved in nitric acid and analysed for strontium-90, strontium-89, strontium, calcium, and phosphorus. Radiostrontium was isolated and counted to measure total strontium. The sample was set aside for two weeks to allow ingrowth of yttrium-90, which was separated [17] and counted in an anti-coincidence counter with a background of approximately 0.8 cpm. The amount of strontium-90 was calculated from the yttrium-90, and the difference between total strontium and strontium-90 gave the strontium-89 present. Sample count rates were of the order of 10 cpm.

Of the stable elements, calcium was measured by the determination of oxalate with KMnO₄ [18]. Phosphorus was determined by the formation of the yellow molybdovanadophosphate complex upon addition of ammonium molybdate and metavanadate to the ash in solution. A spectrophotometer was used to compare intensity of colour formation at 390 nm [19] with an established calibration curve. Strontium was separated by oxalate and nitrate precipitations and by absorption and elution on a cation-exchange resin. It was measured with the spectrophotometer at 461 nm [20].

Calcium and strontium in water were precipitated as the carbonate, purified, and measured as above. Phosphorus in water was determined directly by means of the molybdovanadophosphate complex.

Sample criteria

A 28-d collection period was used because in that time the sample size became large enough to allow analysis with a 5% standard deviation. For gamma spectral analysis, the entire sample (generally more than 100 g of ash) was used; radiostrontium analysis was performed on 10-g samples; calcium and phosphorus were measured in ash samples of approximately 1 g; and strontium analysis was performed on samples containing approximately 0.5 g of calcium.

All data were recorded for computer analysis. From the intake and excretion values, the retention of each substance per study period was determined.
Quality control

The reliability of the usage values reported by the mother and case worker and the completeness of excreta collection were compared with norms developed in the study. All analyses were performed in duplicate (blind duplicates toward the end of the study); the strontium-90 content of milk, the most important source of ingested strontium-90 for infants, was measured in duplicate samples by different methods in two separate laboratories. For comparing calcium and phosphorus analyses of the infant foods and milk formulae, the manufacturer's values were also available at times.

RESULTS AND DISCUSSION

Of critical importance to the results of this study are: (1) meticulous adherence of mother and case worker to protocol, (2) the amount of intake and excretion by uncontrolled paths, and (3) analytical precision.

The enthusiasm and meticulousness of the mothers and case workers are demonstrated to some degree by information in Table I. Data on six infants were omitted; two of the infants were breast fed and their excreta were collected for comparison with infants fed from other sources of milk, two were excluded because of unsatisfactory adherence to protocol, and two others were withdrawn by their mothers. A review of the remaining 250 retention values showed extreme values which were excluded in the preliminary analysis for the reasons cited in Table I. Data for a few single periods also were not analysed because the infants were ill or had travelled during the period.

One means of checking the reliability of data was consistency of food consumption and diaper usage. As shown in Table II, the consumption of milk by four infants selected at random did not change appreciably from period to period. Milk consumption increased slowly with growth until a gradual change to solid foods reversed this trend. An appreciable difference in a value for an infant during a single month was considered an indication of non-adherence to protocol. Similar indicators of internal control were retention values for strontium-90, calcium and phosphorus, and their ratios.

The major uncontrolled pathways were considered to be the inhalation of strontium-90 (an insignificant amount of stable strontium, calcium and phosphorus would be expected to be taken in by this route) and the excretion of all substances by sweating and drooling. A correction for inhaled airborne particles containing strontium-90 was made by measuring the concentration of strontium-90 in the air and using mean values of the volume of air inhaled by infants [15]. The computed intake through inhalation of strontium-90 was less than 2% of the total during the period of study between 1960 and 1964. For several months in the summers of 1962 and 1963, however, as much as 10% of the total intake was computed to be inhaled. Excretions of calcium and phosphorus by-sweating [21] are estimated to be 0.18 and 0.045 g per 28-d period, respectively. The loss of strontium-90 by sweating might be expected to be proportional to the loss of calcium. Losses of calcium and phosphorus in salivary excretion are reported to be 0.062 and 0.19 g per litre [22]. At an assumed salivary excretion of 100 ml
TABLE I
INFANTS AND PERIODS NOT INCLUDED IN DATA ANALYSIS

<table>
<thead>
<tr>
<th>Infant #</th>
<th>Period*</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>01-61</td>
<td>Gastro-intestinal illness</td>
</tr>
<tr>
<td>5</td>
<td>entire</td>
<td>Use of calcium-containing talcum powder</td>
</tr>
<tr>
<td>7</td>
<td>entire</td>
<td>Mother stopped study after only 2 months</td>
</tr>
<tr>
<td>8</td>
<td>02-61</td>
<td>Negative calcium balance with weight gain</td>
</tr>
<tr>
<td>9</td>
<td>09-61</td>
<td>Negative phosphorus balance with weight gain, and positive calcium balance</td>
</tr>
<tr>
<td>10</td>
<td>entire</td>
<td>Breast-fed infants in study only to compare their excreta with that of bottle-fed infants</td>
</tr>
<tr>
<td>13</td>
<td>10-61</td>
<td>Infant on extended vacation</td>
</tr>
<tr>
<td>14</td>
<td>06-62</td>
<td>Twins on extended vacation</td>
</tr>
<tr>
<td>15</td>
<td>06-62</td>
<td>Twins on extended vacation</td>
</tr>
<tr>
<td>17</td>
<td>12-61</td>
<td>Extremely high positive retention</td>
</tr>
<tr>
<td>19</td>
<td>08-62</td>
<td>Extremely low phosphorus retention with extremely high calcium retention</td>
</tr>
<tr>
<td>20</td>
<td>07-62</td>
<td>Negative phosphorus balance with weight gain, and positive calcium balance</td>
</tr>
<tr>
<td>21</td>
<td>10-62</td>
<td>Very low calcium retention with a high phosphorus retention</td>
</tr>
<tr>
<td>22</td>
<td>10-62</td>
<td>Same as 20, 10-62</td>
</tr>
<tr>
<td>24</td>
<td>10-62</td>
<td>Negative calcium and phosphorus balance with weight gain</td>
</tr>
<tr>
<td>27</td>
<td>entire</td>
<td>Careless measuring and collecting</td>
</tr>
<tr>
<td>28</td>
<td>06-63</td>
<td>Hospitalized for pneumonia</td>
</tr>
<tr>
<td>35</td>
<td>entire</td>
<td>Mother stopped study</td>
</tr>
</tbody>
</table>

* There are 13 28-d periods plus 1 d in a year. The study began on 19 July 1960, the 3rd day of period 9-60.

per day, the elemental losses per period would be 0.17 and 0.53 g, respectively. Losses through tears (1/2 cm³ per day on the average) [22], nail clippings, hair cutting, etc., would be expected to be negligible. These data indicate that sweating and drooling contribute about 4% each to the overestimation of calcium retention and about 1.5 and 16.6%, respectively, to the overestimation of phosphorus retention.

Overestimation of retention is unavoidable in a metabolic balance study because of losses during feeding and losses during excreta collection [23].
**TABLE II**

**UNIFORMITY OF MILK INTAKE BY PERIODS—RANDOMLY SELECTED DATA**

(ml per 28-d period)

<table>
<thead>
<tr>
<th>Infant</th>
<th>18</th>
<th>19</th>
<th>04</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Milk A</td>
<td>Milk B</td>
<td>Period</td>
<td>Milk</td>
</tr>
<tr>
<td></td>
<td>Milk</td>
<td>Milk</td>
<td>Period</td>
<td>Milk</td>
</tr>
<tr>
<td>13-61</td>
<td>7960</td>
<td>10750</td>
<td>08-60</td>
<td>8430</td>
</tr>
<tr>
<td>01-62</td>
<td>8370</td>
<td>10230</td>
<td>09-60</td>
<td>8430</td>
</tr>
<tr>
<td>02-62</td>
<td>8470</td>
<td>11110</td>
<td>10-60</td>
<td>9330</td>
</tr>
<tr>
<td>03-62</td>
<td>8940</td>
<td>10170</td>
<td>11-60</td>
<td>9740</td>
</tr>
<tr>
<td>04-62</td>
<td>9080</td>
<td>10730</td>
<td>12-60</td>
<td>9040</td>
</tr>
<tr>
<td>05-62</td>
<td>9380</td>
<td>10590</td>
<td>13-60</td>
<td>8610</td>
</tr>
<tr>
<td>06-62</td>
<td>9720</td>
<td>10200</td>
<td>01-61</td>
<td>8130</td>
</tr>
<tr>
<td>07-62</td>
<td>10020</td>
<td>10880</td>
<td>02-61</td>
<td>8240</td>
</tr>
</tbody>
</table>

For example, with 2% losses of both food and excreta during a study period, use of food containing 150 pc and collection of excreta containing 100 pc would mean that 147 pc was actually ingested and 102 pc excreted. The true retention would be 45 pc rather than 50, which is an overestimate of 11%. These systematic losses can be minimized in a carefully controlled study, and estimated with tracers. For this reason, barium sulphate is currently being used as a tracer to evaluate the efficiency of excreta collection. In the absence of these results, it is estimated that systematic losses in feeding and faecal collection are 5% or less, leading to an overestimate of 22% or less for retention of strontium-90 and calcium.

Unlike these substances, phosphorus is appreciably excreted in urine, and collection losses for the latter may be larger as a result of losses during bathing and diaper changes. The ratio of strontium-90 retention to calcium retention obtained in this study is less in error than either value by itself because the losses are similar for both substances; if their metabolic paths were identical, the losses would cancel and the ratio would have no systematic error.

As a result of their experience in measuring strontium-90 and the pertinent stable elements at environmental levels, the laboratory group was able to minimize analytical errors. Extreme care had to be exercised in preventing radioactive contamination from other samples; for example, one set of samples was found to have been contaminated by the relatively high fallout concentrations in the air during September 1961 [24]. Contamination
by solids scaling from furnace walls and the ashing containers was also a problem. A ceramic container was utilized after difficulties were experienced with heat-resistant glass and steel containers.

The precision of measurement is indicated in Table III by the results of analyses of milk by two laboratories, and in Table IV by the deviation from the means of duplicate analyses of excreta. From these values, the standard deviations for strontium-90, strontium, calcium and phosphorus analyses were taken to be 3, 7, 2, and 2%, respectively. Values from an analysis of 30 "phantom meals" (duplicates of the food other than milk consumed by a particular infant during a 28-d period) performed early in the study compared with the sum of the amounts ingested based on analysis of the individual food components supported the magnitude of these estimated

### Table III

**Analytical Results for Milk by Two Laboratories**

<table>
<thead>
<tr>
<th>Milk</th>
<th>No. of tests</th>
<th>Ca (g/l)</th>
<th>Sr$^{90}$ (pC/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laboratory 1</td>
<td>Laboratory 2</td>
<td>Laboratory 1</td>
</tr>
<tr>
<td>Formula 1</td>
<td>4</td>
<td>1.31</td>
<td>1.27</td>
</tr>
<tr>
<td>Formula 2</td>
<td>4</td>
<td>1.13</td>
<td>1.16</td>
</tr>
<tr>
<td>Evaporated milk</td>
<td>7</td>
<td>2.33</td>
<td>2.32</td>
</tr>
<tr>
<td>Soybean formula</td>
<td>3</td>
<td>1.62</td>
<td>1.58</td>
</tr>
</tbody>
</table>

### Table IV

**Average Deviation from the Mean of Duplicate Excreta Analyses**

<table>
<thead>
<tr>
<th>Element</th>
<th>Concentration range</th>
<th>No. of observations</th>
<th>Average deviation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>0.5±5% (urine)</td>
<td>15</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>5-21% (faeces)</td>
<td>13</td>
<td>1.5</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>4-10%</td>
<td>33</td>
<td>1.6</td>
</tr>
<tr>
<td>Strontium</td>
<td>0.002-0.04%</td>
<td>23</td>
<td>7.3</td>
</tr>
<tr>
<td>Strontium-90</td>
<td>0.1-6 pC</td>
<td>29</td>
<td>3.7</td>
</tr>
</tbody>
</table>

* Data provided by R. Velten, RHRA, Cincinnati, Ohio.
† 10-g sample size.
deviations. The best straight line for the two sets of values has a slope of 0.98 for strontium-90, calcium and phosphorus, and the extrapolated phantom meal values at zero intake by the summed meal were -5 pc, 0.0 g, and 0.2 g per period, respectively. Based on standard deviations given above and preliminary average values for intake and excretion, the analytical error in the retention values are shown in Table V to be 7 to 8% for strontium-90, calcium and phosphorus. The estimated error in the strontium retention value was 40%; this resulted from the higher standard deviation (7%) in the analysis combined with the strontium content of the diaper, which equalled that of the faecal material. Because of the magnitude of this error, a new paper diaper insert was developed; its stable strontium content is only one-tenth that of the original. Analyses that will lead to stable strontium balances are now being completed.

Repeated checks of the precision with which the milk formulae and water were measured by the mothers and the other food items by the case worker suggest that these errors did not exceed 1%. The sum of all random errors in the analyses for strontium-90, calcium, and phosphorus retention is believed to be no more than 10%.

SUMMARY

A long-term metabolic study in the home environment is described. Thirty-eight infants, aged about two months, participated in the study for an average of eight months. Data for approximately 250 infant periods of 28 d each are available. Participating in the study besides the infant and his mother were the family physician, our staff physician, and a case worker. Specific responsibilities were assigned to the various participants indicated. No additives, either stable or radioactive, were included with the intakes of the infants. Their exposure was only from environmental sources.

The system of laboratory analysis required adherence to strict quality control. Analyses included the determination of stable calcium, phosphorus, and strontium, and strontium-90, strontium-89, and the various gamma-emitting radionuclides encountered in environmental samples. Radium-226 analyses are planned.

It is believed that this study provides data on the dietary intake of infants of typical middle-class parents in the United States. From the analyses made, the intake of strontium-90, calcium, phosphorus and strontium will be reported subsequently as will information on the nutritional aspects of the diet.

This paper reviews the sources of error inherent in an extended home-environment metabolic study based on intake and excreta. Considered are the random errors associated with measurement and analysis of sample materials and the systematic errors associated with failure to recognize other pathways of intake and excreta. Random errors of analysis were estimated to result in retention values calculated within 10% for strontium-90, calcium and phosphorus. Errors in the analyses for stable strontium are expected to have been greater. The intake of strontium-90 through inhalation was computed. The estimate of losses through sweating and salivation sug-
<table>
<thead>
<tr>
<th>Substance</th>
<th>Intake</th>
<th>Gross excreta</th>
<th>Diaper † blank</th>
<th>Retention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Milk</td>
<td>Other food and water</td>
<td>Feces</td>
<td>Urine</td>
</tr>
<tr>
<td>Strontium-90, pc/period</td>
<td>121.0 ± 3.6</td>
<td>36.0 ± 1.7</td>
<td>(119.0 ± 3.6)</td>
<td>10.0 ± 0.6</td>
</tr>
<tr>
<td>Strontium, mg/period</td>
<td>12.2 ± 0.85</td>
<td>5.3 ± 0.44</td>
<td></td>
<td>16.0 ± 1.1</td>
</tr>
<tr>
<td>Calcium, g/period</td>
<td>12.9 ± 0.28</td>
<td>2.5 ± 0.26</td>
<td>3.7 ± 0.17</td>
<td>1.9 ± 0.34</td>
</tr>
<tr>
<td>Phosphorus, g/period</td>
<td>10.6 ± 0.21</td>
<td>2.3 ± 0.03</td>
<td>6.0 ± 0.12</td>
<td>3.5 ± 0.27</td>
</tr>
</tbody>
</table>

* Average values are based on infants No.1 to 5 for strontium-90, No.16 to 25 for strontium, and No.1 to 25 for calcium and phosphorus; infants and periods listed in Table I are not included. † Average diaper usage was divided 1/3 with feces and 2/3 with urine.
gest that they are small. If the systematic losses in feeding and excreta collection were as much as 5%, retention is overestimated by 22%. A study to determine the completeness of faecal collection by use of barium sulphate feeding is in progress.

From their experience with this study, the authors conclude that studies providing accurate intake information can be carried out in the home environment over long periods of time for the infant population consuming prepackaged food materials. Information on excretion is also available but is not believed to be as accurate because of failure to account for other excretary pathways (salivation, sweating) and systematic losses. The authors urge that studies be initiated to measure the amount of material excreted through these additional pathways. With this information it would be possible to re-evaluate excretion data from this study and others, and thus more accurately determine retention of radionuclides and stable chemicals by infants, children, and adults.

ACKNOWLEDGEMENTS

The success of this study depended upon the whole-hearted co-operation of the mothers of the infants and their family physician and this aid is gratefully acknowledged. In any protracted study lasting many years, many persons become associated with the project for various periods of time and it is impossible to single them out by name. These include persons involved in the preparation and analysis of samples, those responsible for counting the samples, and those who transferred much of the raw data to permit computer calculation and printing of the results. Without their diligent support the study could not have progressed as it did. To them the authors express their sincere gratitude. We would, however, wish to identify the case workers by name. They were Regina Weber, Ann Koors, Marva Pettus, Carole Matthews, and Freda Truman.

Finally, the authors must acknowledge the assistance received from and the interest expressed by the suppliers of the various items used in the study. They helped in many ways and provided information that is not generally made public. The generous contribution of Ross Laboratories of their product is particularly acknowledged.
### RHRA INFANT RETENTION STUDY - MOTHER'S WEEKLY RECORD

<table>
<thead>
<tr>
<th>Day</th>
<th>Input</th>
<th>Output</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Input**
- **Formula:**
- **Extra Water on:
- **Urinary Diapers:**
- **Fecal Diapers:**

**Output**
- **Input:**
- **Extra:**
- **Urinary Diapers:**
- **Fecal Diapers:**

**Note:**
- Use pencil
- Extra statement on back

---

**APPENDIX A - Page 1**

**C.F. STRAUB et al.**
<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
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<td>1</td>
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<td>3</td>
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<td>6</td>
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<td>7</td>
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<td></td>
<td></td>
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</tbody>
</table>
### INFANTS STUDY - WEEKLY USAGE

<table>
<thead>
<tr>
<th>ITEM CODE (12-15)</th>
<th>DESCRIPTION</th>
<th>GROSS WEIGHT g (16-20)</th>
<th>TARE WEIGHT g (21-25)</th>
<th>LOT (26-28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>080</td>
<td>SUGAR TYPE</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>090</td>
<td>VITAMINS - mis.</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>FAECAL DIAPERS (ODD #'s)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>TISSUES (EVEN #'s)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>URINARY DIAPERS (#'s &lt;50)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

### TOTALS NET TOTAL

| MILK TYPE | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUGAR TYPE | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| VITAMINS - mis. | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FAECAL DIAPERS (ODD #'s) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TISSUES (EVEN #'s) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| URINARY DIAPERS (#'s <50) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
### INFANT'S WEEKLY USAGE SUMMARY

<table>
<thead>
<tr>
<th>CASE NO.</th>
<th>REPORT PERIOD</th>
<th>WEEK BEGINNING</th>
<th>NAME</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>FORMULA</th>
<th>MILK</th>
<th>WATER</th>
<th>SUGAR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MILK</th>
<th>WATER</th>
<th>NET FOOD</th>
<th>TISSUE</th>
<th>DIAPERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LITRES</td>
<td>LOT NO.</td>
<td>LITRES</td>
<td>g</td>
<td>URINARY</td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EXTRA WATER</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### REFERENCES


W. GIESE: Commercially available milk was the main source of strontium-90 intake by infants and contributed largely to the 58 pc strontium-90 retained in the body per period. How do the retention values for strontium-90 in this experiment compare with those observed for breast-fed infants and what is your reaction to reports of a strontium loss rather than retention in breast-fed infants?

N. N. WELLMAN: You will note that data on two infants have been excluded from Table I of our paper because these infants were breast-fed. The only reason we collected these data at all was in order to obtain some idea of the amount of strontium-90 excreted by breast-fed infants. We did not have analyses of the breast milk, but the excretion of strontium-90 was far below that observed for infants fed on commercial milk. However, in both cases the amounts of strontium and strontium-90 in the infants' diapers were much greater than in the excreta, making satisfactory analysis impossible. There are other reports in the literature of negative strontium balance with breast-fed infants, but these data are open to question because of strontium in the diapers. Even with our new, low-strontium diapers we feel that the amount is still too great to permit adequate study of breast-fed infants. Reports of negative strontium balance in breast-fed infants should be meticulously scrutinized with regard to the methodology of excreta analysis.
ÉVALUATION DES CHARGES CORPORELLES
POUR LE STRONTIUM 90 ET LE RADIUM
CHEZ L'HOMME

P. WENGER ET K. SOUCAS
SERVICE CANTONAL DE CONTRÔLE DES IRRADIATIONS,
GENÈVE, SUISSE

Abstract — Résumé — Аннотация — Resumen

THE authors calibrated the Geneva whole-body counter for strontium-90, using the bremsstrahlung of the standards supplied by the International Atomic Energy Agency, i.e. source No. 3 (strontium-90 content - 10.55 µc on 26 February 1963), placed in the centre of a plaster of Paris shell.

The authors determined the conditions in which whole-body counting can be used to measure strontium-90, in the presence of radium, and the energy regions to which one must go in order to measure these two elements simultaneously. The radium standards consisted of sources containing 0.1, 0.2, 0.5 and 1 µc of radium-226 supplied by the National Bureau of Standards, United States Department of Commerce. In calibrating the whole-body counter the authors used either contaminated individuals or a phantom with the average absorption characteristics of these individuals. The 175-cm arc technique was used for the purpose of calibration. On the basis of the values obtained by the arc, the authors calibrated their tilting chair in order to carry out measurements more quickly. The methods of analysing data and interpreting measurements are described.

The cases measured with the whole-body counter were followed up for several months with a view to determining the amount of strontium-90 in urine excretion. These measurements enable the authors to present patterns of strontium-90 excretion as a function of the time which elapsed since chronic contamination ceased.

Blood measurements also make it possible to compare the total retention of strontium-90 by the body, as determined by the whole-body counter, with the level of activity in the blood and the rate at which it is excreted in the urine. With a view to improving the interpretation of results, the authors specify the chemical forms and the solubility of the contaminant, together with the mode of contamination. This work had not been done previously.

ÉVALUATION DES CHARGES CORPORELLES POUR LE STRONTIUM 90 ET LE RADIUM CHEZ L'HOMME.
Les auteurs ont étalonné l'anthropogammamètre (appareil pour le dosage de l'activité du corps humain) de Genève pour le dosage du strontium 90 en utilisant le rayonnement de freinage d'un étalon fourni par l'Agence internationale de l'énergie atomique, soit la source 3 contenant 10,55 µc de strontium 90 le 26 février 1963, placée au centre d'une couche de plâtre de Paris.

Ils ont défini les conditions de mesures du strontium 90 par anthropogammamétrie en présence de radium, ainsi que les bandes d'énergies nécessaires à l'évaluation simultanée de ces deux éléments. Les étalons de radium étaient constitués de sources de 0,1, 0,2, 0,5 et 1 µc de radium 226, fournies par le National Bureau of Standards, US Department of Commerce. Le réglage a été réalisé en utilisant, soit des sujets contaminés, soit un fantôme dont les caractéristiques d'absorption correspondaient à la moyenne des cas humains mesurés. La technique de l'arc de 175 cm a servi de base pour la calibration. En partant des valeurs obtenues par l'arc, les auteurs ont réglé leur fauteuil basculant pour permettre des mesures plus rapides. Ils décrivent les méthodes de dépouillement des données et l'interprétation des mesures.

Les cas mesurés par anthropogammamétrie ont été suivis depuis de nombreux mois pour leur exécration urinaire en strontium 90. Ces mesures permettent aux auteurs de présenter des schémas d'excrétion du strontium 90 en fonction du temps écoulé depuis la fin d'une contamination chronique.

Des mesures effectuées également au niveau du sang permettent de comparer la rétention totale du corps en strontium 90 définie par anthropogammamétrie, d'une part, et l'activité sanguine et le rythme de l'élimination urinaire, d'autre part. Pour améliorer l'interprétation des résultats, les auteurs définissent les formes chimiques et la solubilité du contaminant, ainsi que le mode de contamination. Ces travaux sont originaux.
ОПРЕДЕЛЕНИЕ СОДЕРЖАНИЯ СТРОНЦИЯ-90 И РАДИЯ В ОРГАНИЗМЕ ЧЕЛОВЕКА. Авторы калибровали женевский антропогаммаметр (счетчик для измерения активности всего организма) для определения содержания стронция-90, используя тормозное излучение всего организма) для определения содержания стронция-90, используя тормозное излучение стандартных источников, предоставленных Международным агентством по атомной энергии, т.е. источника №3, содержащего 10,55 миллиэкюри стронция-90 на 26 февраля 1963 года в гипсовом контейнере. Авторы определили условия измерения стронция-90 с помощью антропогаммаметрии в присутствии радиа, областей энергий, необходимых для одновременного определения этих двух элементов. Радиевые эталоны состояли из источников радиа-226 порядка 0,1; 0,2; и 0,5 и 1 миллиэкюри, предоставленных Национальным бюро стандартов США, департамент торговли. Калибровка проводилась либо на зараженных пациентах, либо на фантоме, характеристика поглощения которого соответствовала средним данным, полученными в результате измерений, произведенных у людей. Метод 157-см дуги служил основой для калибровки. Начальная с величин, полученных с помощью этой дуги, авторы откалибровали свое качающееся кресло с тем, чтобы проводить более быстрые измерения. Дается описание метода анализа данных и интерпретации измерений.

Наблюдение за выделением стронция-90 с мочой с помощью антропогаммаметрии проводилось в течение нескольких месяцев. Измерения позволяют авторам представить схемы выделения стронция-90 в зависимости от времени, прошедшего после окончания хронического заражения.

Измерения уровня активности позволяют сравнивать общую задержку в организме стронция-90, установленную с помощью антропогаммаметрии, с активностью в крови и ритмом выделения с мочой. Для улучшения интерпретации результатов, авторы определяют химическое строение и растворимость загрязнителя, а также способ заражения. Подобные работы проводятся впервые.

EVALUACIÓN DE LAS CARGAS CORPORALES CORRESPONDIENTES AL ESTRONCIO-90 Y AL RADIO EN EL HOMBRE. Los autores han calibrado el antropogammámetro de Ginebra (contador de la actividad del cuerpo humano entero), para determinar la acumulación del estroncio-90 utilizando la radiación de frenado del patrón proporcionado por el Organismo Internacional de Energía Atómica, a saber, la fuente № 3, que el 26 de febrero de 1963 contenía 10,55 μс de estroncio-90 colocados en el centro de una capa de yeso de París. Han definido las condiciones de medición del estroncio-90 por antropogammametría en presencia de radio y las bandas de energía necesarias para la evaluación simultánea de estos dos elementos. Los patrones de radio consistieron en fuentes de 0,1, 0,2, 0,5 y 1 μс de radio-226, proporcionadas por el National Bureau of Standards dependiente del US Department of Commerce. La calibración se ha efectuado utilizando bien individuos contaminados, o bien un modelo cuyas características de absorción correspondían a la media de los casos humanos investigados. La técnica del arco de 175 cm ha servido de base para la calibración. Fundándonos en los valores obtenidos por medio del arco, los autores han calibrado su silla basculante para poder efectuar mediciones más rápidas. Los autores exponen los métodos de análisis de los datos y la interpretación de los mismos.

Los casos estudiados por antropogammametría se han mantenido desde hace muchos meses en observación para vigilar su excreción de estroncio-90 por vía urinaria. Estas mediciones permiten a los autores presentar esquemas de excreción del estroncio-90 en función del tiempo transcurrido desde el final de una contaminación crónica.

Las mediciones efectuadas asimismo en la sangre permiten comparar la cantidad total de estroncio-90 retenida por el cuerpo, determinada por antropogammametría, con la actividad de la sangre y el ritmo de eliminación por vía urinaria. Para interpretar mejor los resultados, los autores definen las formas químicas y la solubilidad del contaminante, así como la modalidad de contaminación. Estos trabajos son originales.

I. ÉTALONNAGE DE L'ANTHROPOGAMMAMÈTRE DE GENÈVE POUR LA MESURE DU RADIUM 226

Introduction

Le radium déposé dans un organisme humain peut être mesuré par anthropogammmamétrie (Whole body counting) des Ra B et C.
ÉVALUATION DES CHARGES CORPORELLES

Principe général.

En raison de sa fixation au niveau des os et de sa longue période radioactive, le radium ne peut être administré volontairement à un organisme humain et il n'existe pas d'isotope qui puisse être ingéré à sa place.

La meilleure manière d'étalonner l'appareil consiste à choisir tout d'abord la technique de l'arc, proposée par Robley D. Evans. Pour réaliser la contamination radioactive, nous avons introduit momentanément une source de radium ponctuelle et calibrée dans le corps d'un sujet. Les valeurs trouvées pour l'arc peuvent ensuite être rapportées à la technique du fauteuil basculant de Miller, en utilisant un sujet suffisamment contaminé.

Pour l'arc, nous avons choisi une distance de 175 cm cristal-arc. Le fauteuil basculant a été décrit dans une publication antérieure [1].

Justification de l'utilisation d'une source intracorporelle

Pour pouvoir justifier l'utilisation d'une source intracorporelle ponctuelle de radium dans l'étalonnage, nous avons utilisé cette même technique pour étalonner l'appareil pour le $^{90}$Sr et le $^{137}$Cs. Dans ces derniers cas, nous avons également utilisé la contamination interne généralisée au moyen d'injections intraveineuses de $^{132}$Cs. Ceci nous a permis de comparer les deux méthodes. Les résultats sont indiqués au tableau I.

TABLEAU I

VALEUR EN cpm POUR 1 $\mu$C

<table>
<thead>
<tr>
<th>Source intracorporelle</th>
<th>Par injection intraveineuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{137}$Cs entre 75 et 275 keV</td>
<td>1044</td>
</tr>
<tr>
<td>$^{137}$Cs entre 275 et 375 keV</td>
<td>294</td>
</tr>
</tbody>
</table>

Les valeurs obtenues, compte tenu des erreurs statistiques, permettent de conclure à une équivalence des deux méthodes.

Nous avons ensuite placé la source à différentes places sur l'arc, dans un fantôme de pavatex correspondant à l'absorption humaine, afin de nous assurer de la réponse régulière du cristal.

Nous avons obtenu les chiffres suivants:

<table>
<thead>
<tr>
<th>Source de 1 $\mu$C placée</th>
<th>Entre 75 et 275 keV</th>
</tr>
</thead>
<tbody>
<tr>
<td>à une extrémité</td>
<td>2386</td>
</tr>
<tr>
<td>au milieu</td>
<td>2346</td>
</tr>
<tr>
<td>à une autre extrémité</td>
<td>2352</td>
</tr>
</tbody>
</table>
Nous avons ensuite fractionné la dose, pour la répartir sur l'arc. Nous avons obtenu les chiffres suivants:

<table>
<thead>
<tr>
<th>Sources</th>
<th>Entre 75 et 275 keV</th>
</tr>
</thead>
<tbody>
<tr>
<td>2х0,5 μc</td>
<td>2340</td>
</tr>
<tr>
<td>5х0,2 μc</td>
<td>2385</td>
</tr>
<tr>
<td>10х0,1 μc</td>
<td>2390</td>
</tr>
</tbody>
</table>

Nous constatons que le changement de position ou la répartition le long de l'arc ne modifie pas la réponse du cristal.

L'introduction d'une source ponctuelle de radium est donc justifiée au point de vue technique et sa durée de contact est trop brève pour présenter des dangers.

Mesure de radium

La quantité de radium présente dans le sujet est calculée en choisissant l'activité mesurée dans quatre bandes d'énergies bien déterminées. Ces bandes d'énergies sont: bande I de 75 à 275 keV, bande II de 275 à 375 keV, bande III de 525 à 675 keV et bande IV de 775 à 1275 keV. Le mouvement propre gamma de la chambre, ainsi que l'activité observée chez le sujet normal ou avant la contamination, sont soustraits pour chaque bande d'énergie respectivement (tableau II).

Comme étalon, nous avons choisi une source de 1,0 μc de radium, en équilibre avec ses produits de désintégration, provenant du US National Bureau of Standards.

**TABLEAU II**

<table>
<thead>
<tr>
<th>Sujet</th>
<th>Bande I</th>
<th>Bande II</th>
<th>Bande III</th>
<th>Bande IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cpm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L.W.</td>
<td>2460,0</td>
<td>737,4</td>
<td>406,9</td>
<td>336,9</td>
</tr>
<tr>
<td>D.E.</td>
<td>2482,9</td>
<td>760,7</td>
<td>430,3</td>
<td>373,3</td>
</tr>
<tr>
<td>L.W.</td>
<td>2499,2</td>
<td>780,5</td>
<td>420,2</td>
<td>336,5</td>
</tr>
<tr>
<td>Moyenne</td>
<td>2460±0,8%</td>
<td>760±2,9%</td>
<td>419±2,8%</td>
<td>349±5%</td>
</tr>
</tbody>
</table>

La source est placée d'une manière intracorporelle. Le sujet est mesuré sur un arc de 175 cm en décubitus dorsal et ventral. On prend la moyenne de ces deux mesures.
Technique du fauteuil basculant

Pour transposer les valeurs obtenues sur l'arc au fauteuil basculant, nous avons utilisé les résultats de mesures effectuées sur un sujet contaminé dans les deux positions.

Le résultat de ces mesures est indiqué au tableau III.

En multipliant les valeurs du tableau II obtenues pour l'arc par les rapports cpm fauteuil basculant/cpm arc pour chacune des bandes selon le tableau III, nous trouvons les résultats indiqués au tableau IV.

II. ÉTALONNAGE DE L'ANTHROPOGAMMAMÈTRE DE GENÈVE POUR LA MESURE DU STRONTIUM 90

Introduction

Le radiostrontium peut être mesuré par anthropogammamétrie en utilisant le rayonnement de freinage (Bremsstrahlung) résultant de son dépôt dans un organisme vivant.

L'anthropogammamètre de Genève a déjà été décrit [1]. Rappelons que nous utilisons un unique cristal cylindrique de NaI(Tl), ayant un diamètre de 203 mm et une hauteur de 102 mm.

Principe général

Dans un organisme vivant, la distribution interne d'un élément est particulière à cet organisme et joue un rôle important dans la géométrie de la mesure. Pour doser la quantité présente d'un radioisotope donné d'un certain élément dans un spectre anthropogammamétrique, la méthode la plus précise consiste à administrer au sujet une petite quantité supplémentaire exactement connue de ce même radioisotope et à mesurer l'effet de cet apport sur un spectre normal.

Si la période du radioisotope étudié est longue, si sa présence peut présenter un danger et si le radioisotope se désintègre en chaîne, on peut administrer à sa place l'un des produits dérivés, pourvu que l'allure du rayonnement émis ne soit pas modifiée et que la distribution interne soit la même, sinon des différences d'absorption fausseraient les mesures.

Pour le dosage du $^{90}\text{Sr}$ contenu chez l'homme, on peut utiliser $^{90}\text{Y}$, le Bremsstrahlung de $^{90}\text{Y}$ étant voisin de celui produit par le mélange de $^{90}\text{Sr}-^{90}\text{Y}$ à l'équilibre.

Sources étalons

Pour le $^{90}\text{Sr}$ et pour $^{90}\text{Y}$, nous avons utilisé des sources étalons provenant de l'Agence internationale de l'énergie atomique, à Vienne.
### TABLEAU III

**RAPPORT:** \( cpm \) DANS FAUTEUIL BASCULANT \\
\( cpm \) SUR ARC*

<table>
<thead>
<tr>
<th>Expérience n°</th>
<th>Bande I (75-275 keV)</th>
<th>Bande II (275-375 keV)</th>
<th>Bande III (525-675 keV)</th>
<th>Bande IV (775-1275 keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9,7773</td>
<td>9,7391</td>
<td>9,7826</td>
<td>10,7778</td>
</tr>
<tr>
<td>2</td>
<td>9,4449</td>
<td>9,3521</td>
<td>10,4419</td>
<td>10,5000</td>
</tr>
<tr>
<td>3</td>
<td>9,3822</td>
<td>9,0139</td>
<td>9,8182</td>
<td>10,7407</td>
</tr>
<tr>
<td>4</td>
<td>9,4068</td>
<td>9,5652</td>
<td>10,4524</td>
<td>11,1852</td>
</tr>
<tr>
<td>5</td>
<td>9,4749</td>
<td>8,8243</td>
<td>8,8571</td>
<td>11,5600</td>
</tr>
<tr>
<td>6</td>
<td>9,9727</td>
<td>9,3521</td>
<td>9,4285</td>
<td>11,3333</td>
</tr>
<tr>
<td>7</td>
<td>9,3712</td>
<td>8,8421</td>
<td>9,8298</td>
<td>9,7500</td>
</tr>
<tr>
<td>8</td>
<td>9,5808</td>
<td>8,1818</td>
<td>9,6669</td>
<td>10,5862</td>
</tr>
</tbody>
</table>

| Moyenne        | 9,5144               | 9,0137                 | 9,9111                 | 10,6786                |
| Facteur de transposition | 9,5 \( \pm \) 0,5 | 9,0 \( \pm \) 0,8 | 9,9 \( \pm \) 1,0 | 10,7 \( \pm \) 0,9 |

* Moyenne décubitus dorsal et ventral

### TABLEAU IV

**cpm POUR 1 \( \mu \)c Ra**

<table>
<thead>
<tr>
<th></th>
<th>Bande I</th>
<th>Bande II</th>
<th>Bande III</th>
<th>Bande IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>cpm pour 1 ( \mu )c Ra</td>
<td>23580 ( \pm ) 0,8%</td>
<td>6840 ( \pm ) 2,9%</td>
<td>4148 ( \pm ) 2,8%</td>
<td>3766 ( \pm ) 5,0%</td>
</tr>
</tbody>
</table>

1. **Radiostrontium**

Une source en plâtre de Paris (\( \text{CaSO}_4 \cdot 2\text{H}_2\text{O} \)), numérotée 3, et constituée de la manière montrée à la figure 1. Le 100\% du rayonnement \( \beta \) du \( ^{90}\text{Sr} \) et la majorité du rayonnement \( \beta \) de \( ^{90}\text{Y} \) sont absorbés dans le plâtre de Paris. Aucun rayonnement \( \beta \) ne sort de la couche de lucite. 

Rapport entre les 2 côtés: 1,00 
Activité: 10,55 \( \mu \)c \( ^{90}\text{Sr} \) le 26/2/1963, avec une précision de \( \pm \) 2\%. 
Période du \( ^{90}\text{Sr} \) annoncée: 29,3 a 
Calibration par le Bremsstrahlung entre 43,7 et 437 keV.
ÉVALUATION DES CHARGES-CORPORELLES

Figure 1
Source étalon n° 3 en plâtre de Paris pour $^{90}$Sr. Une goutte de solution de $^{90}$Sr a été évaporée sur chacune des faces d'un disque de 1,6 mm.

2. Radioyttrium

a) Une source en plâtre de Paris, numérotée 5, et constituée d'une manière analogue à la source de $^{90}$Sr (fig. 2).

Activité totale: 21,4 µc $^{90}$Y le 17/1/1964 à 12,00 MET.
Période du $^{90}$Y annoncée: 65,6 h.

Figure 2
Source étalon n° 5 en plâtre de Paris pour $^{90}$Y. Sur chacune des faces du disque de 1,6 mm il a été déposé environ 10 µc de $^{90}$Y.

b) Sept ampoules de Y(OH)$_3$ solubilisée par HCl 0,5 N, et diluée dans une solution tampon acide citrique plus NaOH 6 M pour avoir un pH de 3,5 avec une solution de citrate 0,8 M.

Chaque ampoule contenait 1,000 ± 0,005 g de cette solution (45 mg/g). Son activité était de 7,06 µc/g le 17/1/1964 à 12,00 MET, avec une précision de ± 2%.

Comparaison du rayonnement de freinage $^{90}$Sr - $^{90}$Y et $^{90}$Y.

Chacune des sources en plâtre de Paris a été placée à l'intérieur des patients placés sur un arc situé à 175 cm de la surface du cristal.

La comparaison des intensités du rayonnement de freinage par µc a été faite en comparant les activités obtenues dans deux bandes: l'une de 200 keV (entre 75 et 275 keV), l'autre de 100 keV (entre 275 et 375 keV). Les valeurs indiquées comprennent la moyenne des valeurs obtenues en décubitus dorsal et en décubitus ventral (tableau V).
### TABLEAU V

**SOURCES INTRA-CORPORELLES**

<table>
<thead>
<tr>
<th>Source</th>
<th>$^{90}$Sr (cpm/µc)</th>
<th>$^{90}$Y (cpm/µc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L. W.</td>
<td></td>
<td>L. W.</td>
</tr>
<tr>
<td>D. E.</td>
<td></td>
<td>D. E.</td>
</tr>
<tr>
<td>Bande I</td>
<td>41,9</td>
<td>43,1</td>
</tr>
<tr>
<td>(75 à 275 keV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bande II</td>
<td>3,9</td>
<td>3,9</td>
</tr>
<tr>
<td>(275 à 375 keV)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rapport $^{90}$Sr/$^{90}$Y pour L. W.: Bande I $\frac{41,9}{38,1} = 1,100$

Bande II $\frac{3,9}{3,7} = 1,05$

Rapport $^{90}$Sr/$^{90}$Y pour D. E.: Bande I $\frac{43,1}{39,0} = 1,105$

Bande II $\frac{3,9}{3,7} = 1,05$

Le rapport entre l'activité enregistrée pour 1 µc de $^{90}$Y et pour 1 µc de $^{90}$Sr sera appelé «facteur de correspondance».

Nous avons choisi pour les bandes I et II la valeur de 1,1.

**Vérification de la distribution.**

En plaçant le compteur à 40 cm d'un support horizontal et en choisissant 5 positions de mesure, séparées les unes des autres de 40 cm, nous avons tracé un profil de distribution de $^{90}$Y chez un sujet étendu sur le support. Nous avons également tracé un profil correspondant à la contamination Ra et $^{86}$Sr de ce même sujet.

La comparaison des profils nous indique que le dépôt osseux du Ra, $^{86}$Sr et Ra augmente un peu l'activité mesurée aux extrémités. Les mesures globales à l'arc et au fauteuil basculant restent comparables (fig. 3).

**Procédure et doses.**

Les sujets normaux et les sujets contaminés ont été mesurés chacun sur l'arc de 175 cm, pendant 20 minutes en décubitus dorsal et pendant 20 minutes en décubitus ventral, puis sur le fauteuil basculant de Miller pendant 20 minutes. Toutes ces mesures ont été effectuées avant et après l'absorption de $^{90}$Y.
ÉVALUATION DES CHARGES CORPORELLES

POUR Ra+90Sr: CONTAMINATION INTERNE PROFESSIONELLE
POUR 90Y : INJECTION INTRAVEINEUSE

Figure 3
Comparaison des profils du dépôt osseux.

Pour évaluer le Bremsstrahlung, nous avons choisi les deux bandes décrites précédemment, l'une de 200 keV (entre 75 et 275 keV), et l'autre de 100 keV (entre 275 et 375 keV).

Chacun des sujets a reçu par voie intraveineuse une dose de 90Y étonnée très exactement, par mesure à 40 cm du cristal, et comparée à la va-

TABLEAU VI
INTENSITÉ DES DOSES DE 90Y DONNÉES À CHACUN DES SUJETS ET CALCULÉES AU TEMPS ZÉRO*

<table>
<thead>
<tr>
<th>Sujets</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>L. W.</td>
<td>2,50 µc 90Y</td>
</tr>
<tr>
<td>D. E.</td>
<td>2,80 µc 90Y</td>
</tr>
<tr>
<td>S. E.</td>
<td>6,04 µc 90Y</td>
</tr>
</tbody>
</table>

* Les sujets n'ayant pas reçu l'yttrium au temps zéro, chacun d'eux a reçu pratiquement une dose inférieure à 2 µc.

leur moyenne des sept échantillons envoyés par l'Agence internationale de l'énergie atomique par une double mesure effectuée sur chacun d'eux. Les valeurs ont été rapportées au temps zéro qui a été choisi le 20 janvier 1964 à 9 h (tableau VI):

Une fraction de la dose étalon de 90Y a été introduite dans un flacon de teflon contenant 2 l d'eau dénommé «flacon étalon urinaire». Les activités de chaque flacon, y compris le flacon urinaire, ont été mesurées sur le support situé exactement à 40 cm de la surface du cristal.
Dans un autre flacon pareil, on a recueilli les urines de 24 heures de chaque sujet, gardées dès l'ingestion de $^{90}\text{Y}$, et leur volume a été égallement porté à 2 l. Les activités ont également été mesurées sur le support situé exactement à 40 cm de la surface du cristal. Après correction pour la décroissance radioactive, cette mesure a permis d'évaluer l'élimination urinaire en µc de $^{90}\text{Y}$. La même chose a été faite pour les selles. Ainsi, la rétention en $^{90}\text{Y}$ a pu être calculée, les autres voies d'élimination étant considérées comme négligeables et l'équilibre interne atteint après 24 heures. Les valeurs trouvées figurent dans le tableau VII.

Pour S. E., les mesures ont été faites 1 h après l'injection, avant toute élimination.

**TABLEAU VII**

**RÉTENTION DE $^{90}\text{Y}$ APRÈS 24 h EN µc ET EN %**

<table>
<thead>
<tr>
<th>Sujets</th>
<th>L. W.</th>
<th>D. E.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose donnée</td>
<td>µc</td>
<td>%</td>
</tr>
<tr>
<td>$^{90}\text{Y}$</td>
<td>2,500</td>
<td>100</td>
</tr>
<tr>
<td>Elimination urinaire de 24 h</td>
<td>0,200</td>
<td>8,00</td>
</tr>
<tr>
<td>Elimination fécale de 24 h</td>
<td>0,019</td>
<td>0,76</td>
</tr>
<tr>
<td>Rétention après 24 h</td>
<td>2,281</td>
<td>91,24</td>
</tr>
</tbody>
</table>

**Facteur de géométrie**

Le facteur de géométrie représente le rapport entre l'activité en cpm due à $^{90}\text{Y}$ enregistrée dans chacune des bandes I et II, et dans chacune des positions, arc et fauteuil basculant, pour une charge corporelle de 1 µc de $^{90}\text{Y}$ (tableau VIII). Il est obtenu en déduisant du spectre contaminé par $^{90}\text{Y}$, le spectre normal du même sujet, puis en divisant ces valeurs par la charge corporelle en $^{90}\text{Y}$. Les calculs sont faits en tenant compte de la correction pour la décroissance radioactive et les éliminations urinaires et fécales. Pour la technique de l'arc, les valeurs représentent la moyenne entre la mesure en décubitus dorsal et celle en décubitus ventral.

**Contenu corporel en $^{90}\text{Sr}$**

Le contenu corporel en $^{90}\text{Sr}$ peut être calculé au moyen de l'équation suivante pour chacune des bandes I et II et pour les positions de mesure arc et fauteuil basculant:

$$^{90}\text{Sr du sujet (µc)} = \frac{^{90}\text{Sr du sujet (cpm)}}{\text{Facteur de correspondance} \times \text{facteur de géométrie}}$$
ÉVALUATION DES CHARGES CORPORELLES 373

TABLEAU VIII

VALEURS EN cpm POUR 1 µc ⁹₀Y

<table>
<thead>
<tr>
<th>Sujets</th>
<th>Arc</th>
<th>Fauteuil basculant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bande I</td>
<td>Bande II</td>
</tr>
<tr>
<td>L.W.</td>
<td>25,3</td>
<td>3,1</td>
</tr>
<tr>
<td>D.E.</td>
<td>33,8</td>
<td>3,1</td>
</tr>
<tr>
<td>S.E.</td>
<td>34,6</td>
<td>8,1</td>
</tr>
<tr>
<td>Après 1h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L.W.</td>
<td>29,3</td>
<td>10,0</td>
</tr>
<tr>
<td>D.E.</td>
<td>36,7</td>
<td>5,2</td>
</tr>
<tr>
<td>Après 24h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moyenne:</td>
<td>31,9</td>
<td>5,9</td>
</tr>
<tr>
<td>Facteur de géométrie:</td>
<td>32±20%</td>
<td>6±66%</td>
</tr>
</tbody>
</table>

Les cpm correspondant à 1 µc de ⁹₀Sr seront calculés en posant:

\[ \text{Cpm de 1 µc } ⁹₀\text{Sr} = \text{Facteur de correspondance} \times \text{facteur de géométrie}. \]

Nous trouvons pour le fauteuil basculant:

\[ \text{Cpm pour 1 µc de } ⁹₀\text{Sr dans la bande I} = 341 \pm 7,5\% \]
\[ \text{Cpm pour 1 µc de } ⁹₀\text{Sr dans la bande II} = 45 \pm 20\% \]
\[ \text{Total} = 386 \]

Discussion

Si nous considérons que ⁹₀Y injecté n'est pas complètement déposé au niveau osseux, nous devons faire une correction, le Bremsstrahlung étant plus important au niveau osseux que dans les tissus mous.

Pour estimer cette correction nous avons comparé les valeurs de calibration obtenues en utilisant une injection de ⁹₀Y et celles résultant de l'application intracorporelle d'une source ponctuelle de ⁹₀Sr dans du calcium. Nous avons obtenu les résultats suivants dans la bande I:

\[ \text{Pour l'arc } \frac{⁹₀\text{Sr}}{⁹₀\text{Y}} = \frac{43,3}{35,2} = 1,25 \]

\[ \text{Pour le fauteuil basculant } \frac{⁹₀\text{Sr}}{⁹₀\text{Y}} = \frac{433,7}{341} = 1,25 \]

Ce rapport de 1,25 semble valable. Il faut donc considérer pour ⁹₀Sr, entre 75 et 375 keV, un facteur de calibration de 495 cpm par µc.
III. MÉTHODES D'ÉVALUATION DU DÉPÔT INTRACORPOREL DE STRONTIUM 90

Introduction

Nous avons décrit dans le premier chapitre la méthode utilisée pour étalonner l'anthropogammamètre de Genève pour la mesure du strontium 90. Nous avons montré que chez un sujet placé dans la position du fauteuil basculant, le Bremsstrahlung de 1 µc de $^{90}\text{Sr}$ donnait une activité de $341 \pm 7,5\%$ cpm dans une bande de 200 keV entre 75 et 275 keV, et $45 \pm 20\%$ cpm dans une bande de 100 keV entre 275 et 375 keV.

Les spectres de nos sujets contaminés comprennent, une fois le mouvement propre déduit, une activité correspondant à celle d'un spectre normal, plus celle due à la contamination du radium 226 et plus celle due à la contamination du strontium 90.

Pour évaluer la contamination due au $^{90}\text{Sr}$, nous avons choisi deux techniques:

1. l'analyse par épuration du spectre; et
2. l'analyse par utilisation d'une matrice.

Nous allons décrire ces techniques.

Analyse par épuration du spectre

Pour trouver l'activité du $^{90}\text{Sr}$, nous avons choisi quatre bandes d'énergie:

- Bande I, de 75 à 275 keV, soit 200 keV
- Bande II, de 275 à 375 keV, soit 100 keV
- Bande III, de 525 à 675 keV, soit 150 keV
- Bande IV, de 775 à 1275 keV, soit 500 keV.

Dans les bandes I et II, nous trouvons l'influence du spectre normal, de celui du $^{226}\text{Ra}$ et de celui du $^{90}\text{Sr}$. Dans les bandes III et IV, seuls le radium et le normal apparaissent.

En déduisant le normal, il reste donc dans les bandes I et II: $^{226}\text{Ra} + ^{90}\text{Sr}$ et, dans les bandes III et IV: $^{226}\text{Ra}$.

Les bandes III et IV nous permettent donc d'évaluer le dépôt intracorporel de $^{226}\text{Ra}$.

Une fois la valeur du $^{226}\text{Ra}$ connue, il est possible de calculer son activité en cpm dans les bandes I et II, le rapport entre les bandes I, II, III, IV étant constant pour le $^{226}\text{Ra}$.

La bande I, épurée du spectre normal et de celui du radium, nous donnera les cpm correspondant à l'activité due au $^{90}\text{Sr}$. Il sera donc possible de calculer le dépôt intracorporel de $^{90}\text{Sr}$.

Comme spectre normal, nous choisissons celui d'un sujet non contaminé ayant le même sexe, le même poids, la même hauteur que le sujet contaminé et mesuré dans les mêmes conditions à la même époque.

Pour le $^{226}\text{Ra}$, nous avons, entre les activités des différentes bandes, un équilibre résultant des valeurs trouvées au paragraphe II, soit:
ÉVALUATION DES CHARGES CORPORELLES

<table>
<thead>
<tr>
<th>Bande</th>
<th>cpm pour 1 μc $^{226}$Ra</th>
<th>Rapport entre bandes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>23 560</td>
<td>6,256</td>
</tr>
<tr>
<td>II</td>
<td>6 840</td>
<td>5,680</td>
</tr>
<tr>
<td>III</td>
<td>4 148</td>
<td>1,000</td>
</tr>
<tr>
<td>IV</td>
<td>3 766</td>
<td>1,000</td>
</tr>
</tbody>
</table>

Résultats

Nous donnons ci-après les valeurs en $^{226}$Ra et en $^{90}$Sr du sujet GE 03, calculées par éruption de 12 spectres enregistrés sur le fauteuil basculant.

<table>
<thead>
<tr>
<th>N° du spectre</th>
<th>μc $^{226}$Ra</th>
<th>μc $^{90}$Sr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1433</td>
<td>0,0704</td>
<td>1,695</td>
</tr>
<tr>
<td>2007</td>
<td>0,0685</td>
<td>1,716</td>
</tr>
<tr>
<td>2014</td>
<td>0,0693</td>
<td>1,607</td>
</tr>
<tr>
<td>2051</td>
<td>0,0680</td>
<td>1,610</td>
</tr>
<tr>
<td>2065</td>
<td>0,0682</td>
<td>1,552</td>
</tr>
<tr>
<td>2073</td>
<td>0,0714</td>
<td>1,431</td>
</tr>
<tr>
<td>2078</td>
<td>0,0680</td>
<td>1,610</td>
</tr>
<tr>
<td>2089</td>
<td>0,0659</td>
<td>1,607</td>
</tr>
<tr>
<td>2101</td>
<td>0,0722</td>
<td>1,405</td>
</tr>
<tr>
<td>2176</td>
<td>0,0725</td>
<td>1,589</td>
</tr>
<tr>
<td>2192</td>
<td>0,0741</td>
<td>1,246</td>
</tr>
<tr>
<td>2230</td>
<td>0,0728</td>
<td>1,387</td>
</tr>
</tbody>
</table>

Moyennes: $0,0701 \pm 5,8\%$, $1,538 \pm 15,3\%$

Rappelons que les valeurs $^{226}$Ra mesurées par anthropogammamétrie ne représentent que les 30% environ du dépôt corporel total.

Analyse par utilisation d’une matrice [2]

Le spectre étant constitué de trois éléments, le radium, le strontium 90 et le normal, nous avons constitué un système de trois équations à trois inconnues:

$$a_1 \text{Ra} + b_1 \text{Sr} + c_1 \text{N} = \text{cpm bande I} + \text{II}$$
$$a_2 \text{Ra} + b_2 \text{Sr} + c_2 \text{N} = \text{cpm bande III}$$
$$a_3 \text{Ra} + b_3 \text{Sr} + c_3 \text{N} = \text{cpm bande IV}$$

Pour les valeurs de $a$, $b$ et $c$, nous avons choisi les pour-cents relatifs calculés à partir des valeurs de 1 μc pour le $^{226}$Ra et le $^{90}$Sr, ainsi que celles du spectre normal. Nous obtenons les chiffres suivants.

Pour le $^{226}$Ra:

<table>
<thead>
<tr>
<th>Bande</th>
<th>cpm 1 μc</th>
<th>μc $^{226}$Ra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bande I+II</td>
<td>30 400</td>
<td>a = 0,7934</td>
</tr>
<tr>
<td>Bande III</td>
<td>4 148</td>
<td>a = 0,1083</td>
</tr>
<tr>
<td>Bande IV</td>
<td>3 766</td>
<td>a' = 0,0983</td>
</tr>
</tbody>
</table>

Total 38 314 $1,0000$
Pour le $^{90}$Sr:

<table>
<thead>
<tr>
<th>Bande</th>
<th>$\text{cpm}$</th>
<th>$\mu$C</th>
<th>$%$</th>
</tr>
</thead>
<tbody>
<tr>
<td>I + II</td>
<td>386</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>386</td>
<td></td>
<td>1,0000</td>
</tr>
</tbody>
</table>

Pour le normal:

<table>
<thead>
<tr>
<th>Bande</th>
<th>$\text{cpm}$</th>
<th>$%$</th>
</tr>
</thead>
<tbody>
<tr>
<td>I + II</td>
<td>391,9</td>
<td>$c_1 = 0,6935$</td>
</tr>
<tr>
<td>III</td>
<td>140,4 - 0</td>
<td>$c_2 = 0,2485$</td>
</tr>
<tr>
<td>IV</td>
<td>32,8</td>
<td>$c_3 = 0,0580$</td>
</tr>
<tr>
<td>Total</td>
<td>565,1</td>
<td>1,0000</td>
</tr>
</tbody>
</table>

Avec ces trois éléments, nous pouvons constituer une matrice:

\[
\begin{pmatrix}
226\text{Ra} & 90\text{Sr} \\
\text{Normal}
\end{pmatrix}
\]

\[
\begin{pmatrix}
0,7934 & 1,0000 \\
0,1083 & 0 \\
0,0983 & 0
\end{pmatrix}
\]

Et si nous calculons l'inverse de cette matrice, nous pouvons évaluer la quantité de cpm attribuable à chacun des constituants.

Matrice inversée:

\[
\begin{pmatrix}
226\text{Ra} & 90\text{Sr} & \text{Normal}
\end{pmatrix}
\]

\[
\begin{pmatrix}
I + II & III & IV
\end{pmatrix}
\]

\[
\begin{pmatrix}
0 & -3,2044 & +13,7293 \\
1,0000 & -1,2265 & -6,7459 \\
0 & +5,4309 & -5,9834
\end{pmatrix}
\]

d'où

\[
\text{cpm Ra} = -3,2044 \cdot \text{cpm (III)} + 13,7293 \cdot \text{cpm (IV)}
\]

\[
\text{cpm Sr} = \text{cpm (I + II)} - 1,2265 \cdot \text{cpm (III)} - 6,7459 \cdot \text{cpm (IV)}
\]

\[
\text{cpm normal} = 5,4309 \cdot \text{cpm (III)} - 5,9834 \cdot \text{cpm (IV)}
\]

En divisant les cpm obtenus pour chacun des constituants par les valeurs correspondant à 1 µC ou au spectre normal, nous obtenons l'activité en µC pour le $^{226}$Ra et le $^{90}$Sr, ainsi que la divergence par rapport au normal.

Résultats

Nous donnons ci-après les valeurs de dépôt intracorporel de $^{226}$Ra et de $^{90}$Sr du sujet GE 03, calculées par inverse de matrice sur les mêmes spectres que précédemment:
ÉVALUATION DES CHARGES CORPORELLES

N° du spectre | µc Ra | µc Sr | N
---|---|---|---
1433 | 0,0721 | 1,771 | 0,84
2007 | 0,0664 | 1,699 | 1,27
2014 | 0,0678 | 1,591 | 1,20
2051 | 0,0676 | 1,635 | 1,07
2065 | 0,0678 | 1,536 | 1,08
2073 | 0,0715 | 1,448 | 1,02
2078 | 0,0673 | 1,619 | 1,11
2089 | 0,0646 | 1,596 | 1,17
2101 | 0,0711 | 1,381 | 1,16
2176 | 0,0710 | 1,518 | 1,20
2192 | 0,0732 | 1,228 | 1,14
2230 | 0,0736 | 1,326 | 0,94

Moyennes: 0,0695 ± 6,5% 1,529 ± 18%

Commentaires

Pour que la matrice soit valable, il faut que le spectre normal soit choisi avec soin et corresponde vraiment au cas contaminé.

Les résultats obtenus tant par la méthode d'épuration que par l'utilisation d'une matrice sont comparables:

<table>
<thead>
<tr>
<th>Analyse</th>
<th>µc 226Ra</th>
<th>µc 90Sr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Par épuration</td>
<td>0,0701 ± 5,8%</td>
<td>1,538 ± 15,3%</td>
</tr>
<tr>
<td>Par matrice</td>
<td>0,0695 ± 6,5%</td>
<td>1,529 ± 18%</td>
</tr>
<tr>
<td>Après correction pour l'os</td>
<td>—</td>
<td>1,25</td>
</tr>
</tbody>
</table>

Pour tenir compte de la variation de la teneur en 137Cs au cours du temps, nous avons établi une matrice à quatre variables, 226Ra, 90Sr, 137Cs et 40K, et quatre bandes d'enregistrement. Cette matrice fera l'objet d'une prochaine publication.

IV. COURBES D'ÉLIMINATION URINAIRE DU STRONTIUM 90

Introduction

Nous présentons trois cas de contamination au 90Sr, dont nous avons suivi l'élimination urinaire pendant une longue période en vue d'établir l'allure des courbes d'élimination.

Il s'agit de contaminations provoquées par une absorption chronique de 90Sr incorporé à des peintures luminescentes. La contamination a duré environ trois ans et s'est terminée en 1957 pour les deux cas codés GE. Pour le cas SO, la contamination a été interrompue plus récemment, mais avant le début des analyses.

Procédure

Les analyses ont été effectuées sur les urines de 24 h selon une technique précédemment décrite [3].
Les courbes d'élimination ont été établies en partant d'une équation de la forme

\[ E = A \cdot t^x \]

où

- \( E \) = taux d'élimination au temps \( t \) (j),
- \( A \) = élimination au temps initial,
- \( x \) = pente de la droite de régression.

Résultats

Nous avons obtenu les résultats indiqués aux tableaux IX, X et XI. Ces résultats nous donnent la droite de régression (fig. 4)

\[ E_{GE \ 03} = A \cdot t^{-0.086} \]

la droite de régression (fig. 5)

\[ E_{GE \ 05} = A \cdot t^{-0.083} \]

et la droite de régression (fig. 6)

\[ E_{SO \ 01} = A \cdot t^{-0.254} \]

Commentaires

Nous n'indiquons pas les valeurs de \( A \). Nous les évoquerons ultérieurement dans un travail comparatif entre l'élimination, la rétention et la dose accumulée.

Pour l'instant, nous nous contenterons de souligner que pour les deux cas GE, cas ayant subi une contamination au même moment et ayant les mêmes conditions d'existence, étant mari et femme, la pente est approximativement semblable.

\[ E_{GE \ 03} = A \cdot t^{-0.086} \]
\[ E_{GE \ 05} = A \cdot t^{-0.083} \]

Pour le cas SO, de contamination plus récente, la valeur

\[ E_{SO \ 01} = A \cdot t^{-0.254} \]

se rapproche des valeurs de rétention tirées de la littérature et citées par MAYS et coll. [4].

\[
\begin{align*}
\text{Homme} \quad &\{0,52 \ t^{-0.22} \ &\text{Bishop} \\
&0,52 \ t^{-0.18} \ &\text{Cohn} \\
\text{Chien} \quad &\{0,68 \ t^{-0.21} \ &\text{Mays} \\
&0,71 \ t^{-0.20} \ &\text{Stover} \\
\text{Souris} \quad &0,80 \ t^{-0.32} \ &\text{Finkel}
\end{align*}
\]
<table>
<thead>
<tr>
<th>Nombre de jours écoulés depuis le début de la recherche</th>
<th>Activité de l'urine de 24 h en 10^5 μc de 90Sr</th>
<th>Nombre de jours écoulés depuis le début de la recherche</th>
<th>Activité de l'urine de 24 h en 10^5 μc de 90Sr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90.19</td>
<td>364</td>
<td>55.14</td>
</tr>
<tr>
<td>49</td>
<td>55.59</td>
<td>371</td>
<td>06.44</td>
</tr>
<tr>
<td>91</td>
<td>135.48</td>
<td>378</td>
<td>20.60</td>
</tr>
<tr>
<td>98</td>
<td>117.55</td>
<td>285</td>
<td>75.94</td>
</tr>
<tr>
<td>105</td>
<td>137.50</td>
<td>292</td>
<td>21.43</td>
</tr>
<tr>
<td>119</td>
<td>97.87</td>
<td>412</td>
<td>04.86</td>
</tr>
<tr>
<td>147</td>
<td>26.44</td>
<td>450</td>
<td>96.81</td>
</tr>
<tr>
<td>154</td>
<td>94.58</td>
<td>457</td>
<td>85.88</td>
</tr>
<tr>
<td>161</td>
<td>148.31</td>
<td>484</td>
<td>96.17</td>
</tr>
<tr>
<td>188</td>
<td>112.96</td>
<td>441</td>
<td>85.41</td>
</tr>
<tr>
<td>178</td>
<td>84.71</td>
<td>448</td>
<td>86.08</td>
</tr>
<tr>
<td>189</td>
<td>92.21</td>
<td>455</td>
<td>55.18</td>
</tr>
<tr>
<td>199</td>
<td>51.65</td>
<td>469</td>
<td>98.21</td>
</tr>
<tr>
<td>204</td>
<td>81.35</td>
<td>469</td>
<td>54.48</td>
</tr>
<tr>
<td>217</td>
<td>112.82</td>
<td>476</td>
<td>58.66</td>
</tr>
<tr>
<td>280</td>
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<td>450</td>
<td>96.95</td>
</tr>
<tr>
<td>294</td>
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<td>457</td>
<td>66.76</td>
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<td>301</td>
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<td>538</td>
<td>76.91</td>
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<tr>
<td>308</td>
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<td>555</td>
<td>58.75</td>
</tr>
<tr>
<td>318</td>
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<td>582</td>
<td>59.97</td>
</tr>
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<td>329</td>
<td>59.99</td>
<td>619</td>
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</tr>
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<td>399</td>
<td>58.92</td>
<td>546</td>
<td>61.90</td>
</tr>
<tr>
<td>362</td>
<td>55.51</td>
<td>583</td>
<td>90.38</td>
</tr>
<tr>
<td>556</td>
<td>111.86</td>
<td>540</td>
<td>67.64</td>
</tr>
<tr>
<td>557</td>
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<td>567</td>
<td>61.70</td>
</tr>
<tr>
<td>Nombre de jours écoulés depuis le début de la recherche</td>
<td>Activité de l'urine de 24 h en $10^{5}$ pC de $^{90}$Sr</td>
<td>Nombre de jours écoulés depuis le début de la recherche</td>
<td>Activité de l'urine de 24 h en $10^{5}$ pC de $^{90}$Sr</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>------------------------------------------------------</td>
<td>--------------------------------------------------------</td>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>1</td>
<td>48.88</td>
<td>367</td>
<td>55.14</td>
</tr>
<tr>
<td>46</td>
<td>90.00</td>
<td>354</td>
<td>54.07</td>
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<td>85.82</td>
<td>373</td>
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</tr>
<tr>
<td>96</td>
<td>72.73</td>
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</tr>
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<td>390</td>
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</tr>
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<td>164</td>
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<tr>
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<td>452</td>
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</tr>
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<td>460</td>
<td>55.62</td>
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<tr>
<td>217</td>
<td>35.26</td>
<td>465</td>
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</tr>
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<td>61.03</td>
<td>476</td>
<td>26.07</td>
</tr>
<tr>
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<td>77.88</td>
<td>490</td>
<td>44.02</td>
</tr>
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</tr>
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</tr>
<tr>
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<td>60.85</td>
<td>553</td>
<td>43.28</td>
</tr>
<tr>
<td>366</td>
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<td>580</td>
<td>40.02</td>
</tr>
<tr>
<td>378</td>
<td>102.46</td>
<td>587</td>
<td>33.19</td>
</tr>
<tr>
<td>384</td>
<td>55.86</td>
<td>574</td>
<td>56.10</td>
</tr>
<tr>
<td>380</td>
<td>77.70</td>
<td>581</td>
<td>41.12</td>
</tr>
</tbody>
</table>
TABLEAU XI

ÉLIMINATION URINAIRE DE $^{90}$Sr DE SO 01 PAR FRACTION DE 24 h AU COURS DU TEMPS

<table>
<thead>
<tr>
<th>Nombre de jours écoulés depuis le début de la recherche</th>
<th>Activité de l'urine de 24 h en $10^{-5}$ µc de $^{90}$Sr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>95,98</td>
</tr>
<tr>
<td>125</td>
<td>118,80</td>
</tr>
<tr>
<td>261</td>
<td>72,50</td>
</tr>
<tr>
<td>268</td>
<td>87,47</td>
</tr>
<tr>
<td>275</td>
<td>98,10</td>
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<td>282</td>
<td>93,31</td>
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<td>296</td>
<td>72,92</td>
</tr>
<tr>
<td>303</td>
<td>68,48</td>
</tr>
<tr>
<td>310</td>
<td>35,61</td>
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<td>26,99</td>
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<td>331</td>
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<td>352</td>
<td>18,81</td>
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<td>21,68</td>
</tr>
<tr>
<td>373</td>
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<tr>
<td>380</td>
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</tr>
<tr>
<td>387</td>
<td>13,43</td>
</tr>
<tr>
<td>394</td>
<td>14,81</td>
</tr>
<tr>
<td>401</td>
<td>12,65</td>
</tr>
</tbody>
</table>

Figure 4
Droite de régression.
Cas GE 03.
V. COMPARAISON ENTRE LA RÉTENTION ET L’ÉLIMINATION DU STRONTIUM 90

Cette comparaison sera limitée à trois cas, GE 03, GE 05 et SO 01, pour lesquels nous avons pu établir des courbes d'élimination (paragraphe IV) et des valeurs de rétention (paragraphe III) d'une manière statistique.
ÉVALUATION DES CHARGES CORPORELLES

<table>
<thead>
<tr>
<th>Date</th>
<th>Sujet</th>
<th>Elimination urinaire en µc ⁹⁰Sr</th>
<th>Rétention en µc ⁹⁰Sr</th>
<th>Rapport rétention/élimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov. 1963</td>
<td>GE 03</td>
<td>0,00068</td>
<td>1,25</td>
<td>2000</td>
</tr>
<tr>
<td>Mai 1963</td>
<td>GE 05</td>
<td>0,00049</td>
<td>0,79</td>
<td>1600</td>
</tr>
<tr>
<td>Avril 1964</td>
<td>SO 01</td>
<td>0,00038</td>
<td>1,04</td>
<td>2600</td>
</tr>
</tbody>
</table>

D'après ces résultats, on peut estimer que l'élimination urinaire quotidienne de ⁹⁰Sr dans une phase d'équilibre correspondant à plus d'un millier de jours après la fin de la contamination, représente environ la 2000 à 2300e partie de la rétention corporelle.

RÉFÉRENCES


BIBLIOGRAPHIE


Wenger, P. et Soucas, K., Anthropogammamètre (Whole Body Counter) de Genève — Etalonnage pour le potassium naturel et Variation de la teneur en potassium naturel en fonction du poids du sujet, Helvetica Chimica Acta (à paraître).
BODY BURDEN AND EXCRETION OF STRONTIUM FOLLOWING INGESTION

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HEALTH PHYSICS DIVISION,
JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
IBARAKI, JAPAN

Presented by N. Yamagata

Abstract — Résumé — Аннотация — Resumen

BODY BURDEN AND EXCRETION OF STRONTIUM FOLLOWING INGESTION. Retention and excretion of strontium-85 following a single ingestion in a normal man have been measured up to about 200 d. Assuming the fraction of Sr passing from the GI tract to the blood is 0.25, total body retention (q) and urinary excretion (u) are best expressed as a sum of three exponentials.

\[
q = 14.1 e^{-0.693 t} + 6.1 e^{-0.111 t} + 4.6 e^{-0.069 t}
\]

\[
u = 3.6 e^{-0.693 t} + 3.5 e^{-0.111 t} + 0.0055 e^{-0.069 t}
\]

\[
e = \frac{3}{2} \frac{dq}{dt} \quad t = 3,
\]

where \(e\) shows total excretion.

Using the formulae obtained, it is possible to evaluate the body burden on urinalysis if the time between exposure and analysis is known. When the time is not known, urinalysis must be performed several times at suitable intervals to determine the time.

In the case of chronic exposure like the daily intake of strontium-90 by fallout, it is found that the formulae are also useful to estimate the body burden and excretion from the pattern of daily intake. In this study, for example, it is assumed that the level of daily intake increased linearly from 1956 (almost 0 pc/d) to 1960 (about 7 pc/d) for four years, but stopped increasing thereafter and kept the level (about 7 pc/d) till 1962 for two years. The calculated body burden (240 pc) and daily urinary excretion (1 pc/d) at a given time (August 1962) are in good agreement with those measured. The daily urinary excretion (U) at that time may be related to the body burden (Q) by a simple equation according to exponential function model as follows,

\[
U = \frac{2}{3} \times \frac{0.693}{T_b} \times Q
\]

where \(T_b\) is a representative biological half-life of the nuclide. In this case, it is concluded that a half-life of about 100 d must be used instead of each value of the three components (1.8, 8 and 600 d) in the above formulae. The value of \(T_b\) changes according to the pattern and duration of exposure. For instance, if exposure has occurred at a constant level for two years, \(T_b\) of 73 d must be adopted.

CHARGE CORPORELLE ET EXCRÉTION DE STRONTIUM APRÈS INGESTION. L'auteur a mesuré la rétention et l'excrétion de strontium 85 chez l'homme normal jusqu'à 200 j après une ingestion unique. Si l'on admet que la fraction du strontium qui passe de l'appareil gastro-intestinal dans le sang est de 25% de la quantité totale, on obtient de bonnes expressions de la rétention corporelle totale q et de l'excrétion urinaire u en appliquant les formules suivantes, qui se présentent comme des sommes de trois exponentielles:

\[
q = 14.1 e^{-0.693 t} + 6.1 e^{-0.111 t} + 4.6 e^{-0.069 t}
\]

\[
u = 3.6 e^{-0.693 t} + 3.5 e^{-0.111 t} + 0.0055 e^{-0.069 t}
\]

\[
e = \frac{3}{2} \frac{dq}{dt} \quad t = 3,
\]

where \(e\) shows total excretion.

Using the formulae obtained, it is possible to evaluate the body burden on urinalysis if the time between exposure and analysis is known. When the time is not known, urinalysis must be performed several times at suitable intervals to determine the time.

In the case of chronic exposure like the daily intake of strontium-90 by fallout, it is found that the formulae are also useful to estimate the body burden and excretion from the pattern of daily intake. In this study, for example, it is assumed that the level of daily intake increased linearly from 1956 (almost 0 pc/d) to 1960 (about 7 pc/d) for four years, but stopped increasing thereafter and kept the level (about 7 pc/d) till 1962 for two years. The calculated body burden (240 pc) and daily urinary excretion (1 pc/d) at a given time (August 1962) are in good agreement with those measured. The daily urinary excretion (U) at that time may be related to the body burden (Q) by a simple equation according to exponential function model as follows,
M. FUJITA

\[
\begin{align*}
  u &= 3,6 e^{-\frac{t}{18}} + 3,5 e^{-\frac{t}{600}} + 0,0035 e^{-\frac{t}{600}} \\
  \epsilon &= \frac{3}{2} u = \frac{du}{dt} \quad t \geq 3,
\end{align*}
\]

où \( \epsilon \) indique l'excrétion totale.

A l'aide de ces formules, il est possible de déterminer la charge corporelle à partir du résultat d'une analyse d'urine si l'on connaît le temps \( t \) qui s'est écoulé entre l'exposition et l'analyse. Si l'on ne connaît pas \( t \), il faut procéder à des analyses d'urine plusieurs fois à des intervalles convenables pour déterminer cette grandeur.

En cas d'exposition chronique, par exemple une absorption quotidienne de strontium 90 résultant d'une re-tombée radioactive, les formules permettent également d'évaluer la charge corporelle et l'excrétion si l'on connaît les caractéristiques de cette absorption. Dans l'étude qui fait l'objet du mémoire, par exemple, on admet que l'absorption quotidienne a augmenté régulièrement de 1956 (environ 0 \( \mu \)c/j) à 1960 (environ 7 \( \mu \)c/j), soit pendant 4 a, et qu'elle est ensuite restée stationnaire au chiffre de 7 \( \mu \)c/j environ jusqu'à 1962, c'est-à-dire pendant 2 a. La charge corporelle (240 \( \mu \)c) et l'excrétion urinaire quotidienne (1 \( \mu \)c/j) obtenues par le calcul à une époque donnée (août 1962) concordent bien avec les valeurs mesurées. L'excrétion urinaire quotidienne \( U \) à cette époque peut être exprimée d'une manière très simple en fonction de la charge corporelle sur le modèle d'une fonction exponentielle. On a

\[
U = 2 \frac{0,963}{3} \cdot T_b \cdot Q,
\]

\( T_b \) étant un coefficient qui représente la période biologique du radioélément considéré. Dans le cas qui nous occupe, on peut en déduire que l'on doit prendre une valeur unique voisine de 100 \( j \) représentant la période au lieu de conserver les trois composantes (1,8, 8 et 600 \( j \)) qui figuraient dans les formules. La valeur de \( T_b \) varie selon la forme et la durée de l'exposition. Par exemple, si l'exposition a lieu à un niveau constant pendant deux ans, on prendra pour \( T_b \) une valeur égale à 73 \( j \).

СОДЕРЖАНИЕ СТРОНЦИЯ И ВЫДЕЛЕНИЕ ЕГО ИЗ ОРГАНИЗМА ПОСЛЕ ПРИЕМА.

Содержание стронция и выделение его из организма после приема.

Задержка и выделение стронция-85 после однократного приема измерялись в течение 200 дней у здорового человека. Если принять фракцию стронция, попавшую из желудочно-кишечного тракта в кровь за 0,25, то общая задержка в организме (\( q \)) и выделение с мочой (\( u \)) лучше всего выражаются суммой трех экспоненциальных величин

\[
q = 14,1 e^{-\frac{t}{3,6}} + 6,1 e^{-\frac{t}{600}} + 4,6 e^{-\frac{t}{600}} ;
\]

\[
u = 3,6 e^{-\frac{t}{3,6}} + 3,5 e^{-\frac{t}{600}} + 0,0035 e^{-\frac{t}{600}} ;
\]

где \( \epsilon \) обозначает общее выделение.

С помощью полученной формулы можно определить содержание элемента в организме путем анализа мочи, если известно время между облучением и временем анализа. Если время не известно, анализ мочи следует делать несколько раз через соответствующие интервалы для определения времени.

В случае хронического облучения, например, при ежедневном поглощении стронция-90 при радиоактивных осадках, оказывается, что формула также может быть использована для определения содержания элемента в организме и его выделения на основе характеристик суточного поглощения. При этом исследовании, например, допускается, что уровень суточного поглощения повышался линейно с 1956 (почти 0 \( \mu \)кмк/сут) до 1960 (почти 7 \( \mu \)мкмк/сут) в течение четырех лет. Но после этого повышение прекратилось, и величина поглощения сохранилась на данном уровне (около 7 \( \mu \)мкмк/сут) в течение двух лет до 1962 года. Вычисленные величины содержания в организме (240 \( \mu \)мкмк) и суточного выделения с мочой (1 \( \mu \)мкмк/сут) в данное время (август, 1962) хорошо соответствуют измеренным величинам. Уровень суточного выделения с мочой (\( U \)) в это время может быть
An understanding of the relationship between the excretion and retention of a radionuclide is necessary for the estimation of body burden from excretion analysis.

Several investigators have studied the urinary excretion of Sr$^{90}$ following single accidental intakes [1 - 3]. The variation of the daily urinary excretion
with time was expressed by the sum of two or three exponential terms. However, it was not possible in these cases to measure directly the body retention. On the other hand, the retention of strontium has been studied in patients by whole-body counting using Sr\(^{85}\) as a tracer, without paying much attention to the excretion. The retention following a single dose was also represented as a sum of three exponentials \([4, 5]\). The retention or excretion may be shown by a power function as well, but here only the exponential function model is taken into account, because of the ease of mathematical treatment.

Simultaneous measurements of the retention and excretion of Sr\(^{85}\) following a single intravenous injection have been made by BISHOP et al. \([6]\). They expressed the results of the daily excretion as the sum of three exponentials and, considering that the retention was dose minus cumulative excretion, the retention was given as a constant minus a sum of three exponential terms.

The behaviour of Sr\(^{85}\) in a normal man following a single oral administration has been studied by SUGURI et al. for the retention \([7]\), and by FUJITA et al. for the absorption and excretion \([8]\). Using the experimental data on the single oral administration, in this report, formulae which are composed of three exponential terms are derived to represent the variation with time of the retention and excretion.

By comparing the derived formulae with the observed values reported by many workers, the universality of the derived formulae was examined.

Further, in the case of continuous exposure, if the levels of the daily intake are known, the retention as well as the excretion can be predicted by integration of the derived formulae. As the dietary levels of fall-out Sr\(^{90}\) have been known in Japan \([9-11]\), it was attempted in this paper to calculate the body burden and daily excretion expected in the middle of 1961 and 1962. The calculated values almost agreed with observation.

It is discussed lastly that the estimation of strontium body burden from excretion data is not always possible when the pattern of the intake is unknown, which usually occurs.

2. EMPIRICAL FORMULAE OF RETENTION AND EXCRETION FOR A SINGLE ORAL ADMINISTRATION

The results of the retention and excretion of Sr\(^{85}\) in a normal man following a single oral administration are shown in Fig. 1 \([7, 8]\). The formulae below, representing these data, were fitted by eye on the condition that the derivative of the retention formula was equal to the excretion, i.e., the daily decrease of the body burden was the daily elimination from the body. (Elimination through sweating was not taken into account here, assuming its amount was small.)

\[
q = 7.7 e^{-0.693 t} + 3.3 e^{-0.693 t} + 2.5 e^{-0.693 t} \quad (\% \text{ dose}) \quad (1)
\]

\[
\epsilon = 2.96 e^{-0.693 t} + 0.286 e^{-0.693 t} + 0.00289 e^{-0.693 t} \quad (\% \text{ dose/d}) \quad (2)
\]
where $q$, $e$, and $u$ show the retention, daily total excretion (urine + faeces), and daily urinary excretion, respectively. In this derivation, body burden obtained by whole-body counting was used because of its reliability, instead of that obtained from dose minus excretion.

These formulae were obtained when the fraction of ingested strontium reaching the blood was $0.136$ [8]. It has been shown that absorption varies
with individuals [12, 13]. According to the report of ICRP [14], the fraction of the absorption, $f_1$, of the standard man is 0.3, but SAMACHSON [12] has reported 0.2 as the mean value of $f_1$. Accordingly, 0.25 was assumed here to be the most probable figure of the absorption fraction. Therefore, the value of 0.136 in the above formulae was replaced by 0.25 to derive the more generalized formulae shown below.

$$
q = 14.1 \times e^{0.693 \times t} + 6.1 \times e^{0.693 \times t} + 4.6 \times e^{0.693 \times 600 \times t} \quad \text{(\% dose)} \tag{5}
$$

$$
u = 3.6 \times e^{0.693 \times t} + 0.35 \times e^{0.693 \times t} + 0.0035 \times e^{0.693 \times 600 \times t} \quad \text{(\% dose/d)} \tag{6}
$$

$$
\epsilon = \frac{3}{2} u = -\frac{dq}{dt}, \quad t \geq 3. \tag{7}
$$

These formulae may be used in general to estimate the body burden in a single ingestion from urinalysis. When the time of exposure or the time, $t$, between the exposure and urinalysis is known, the problem is very simple and the body burden can be easily estimated by using the formulae. Even if the time of exposure is not known, the urinalysis data obtained at suitable intervals will permit the determination of the time and subsequently the estimation of the body burden.

### 3. UNIVERSALITY OF THE DERIVED FORMULAE

To examine the universality of the derived formulae, comparison was made with experimental results of single intakes reported by many authors. BISHOP et al. have studied, as stated above, the retention and excretion following a single intravenous injection [6]. It was here assumed that the results of injection correspond to 100% absorption in oral administration. After dividing the data by four to obtain the values corresponding to 25% absorption, the divided values were plotted on a semi-logarithmic scale in Fig. 2, together with the derived empirical formulae shown by the solid lines. Both agree satisfactorily. Figure 2 shows also the retention data following single intravenous injection reported by MacDONALD, although in this case the results of the excretion could not be utilized [15]. Again the results of injection were modified in the Figure to those of oral administration, where $f_1$ was 0.25. It may be said that the data agree with the solid line (the empirical formula).

The retention of Sr$^{85}$ following a single oral administration has been studied for about 160 d by FURCHNER et al. [5]. The biological half-life for the longest component was about 200 d. However, the data themselves are not so different from the formula if it is assumed that the absorption fraction did not always correspond to 0.25. (In the three cases reported, the data were best fitted to the formula if $f_1 = 0.25$, 0.36, and 0.60). According to COHN et al. [4], the retention of Sr$^{85}$ following a single injection was expressed by a similar formula which is the sum of three exponentials.
Comparison of the derived empirical formulae with experimental data

- Body retention, oral (normal subject)
  SUGURF et al. [7]
- Body retention, I.V. (normal subject)
  BISHOP et al. [6]
- Body retention, I.V. (patient)
  MacDONALD [15]
- Urine, oral (normal subject)
  FUJITA et al. [8]
- Urine, I.V. (normal subject)
  BISHOP et al. [6]

The solid lines represent formula (5) of body retention (upper line) and formula (6) for urinary excretion (lower line). The dashed lines show formulae (9) and (10).

That is,

\[
Retention = a_1 e^{-0.693 \frac{t}{2.5}} + a_2 e^{-0.693 \frac{t}{18.7}} + 24.5 e^{-0.693 \frac{t}{843}}, \quad \text{(% dose)}
\]  

(8)

where \(a_1\) and \(a_2\) are constants.

The biological half-life for the long-lived component, 843 d, was higher than the 600 d obtained in this study. The value shown in the above formula, 24.5, was 1.5 times higher than the present value of 18.4, obtained by multiplying 4.6 (given in the derived formula for retention) by 4 allowing for the assumed absorption of 25%.
On the other hand, two cases of urinary excretion of Sr$^{90}$ following accidental intakes were reported by STEWART et al. [2]*. Further data on the urinary excretion after a single accidental inhalation of Sr$^{90}$Cl$_2$ and Sr$^{90}$CO$_3$ are reported by COWAN et al. [1] and by RUNDO et al. [3], respectively. These data have been obtained for ingestion, while the derived formulae come from the data for ingestion. Therefore, it may be a problem to make a comparison between them, particularly if the isotope does not easily transfer from the lung into the blood. In addition, the excretion data have not accompanied, unfortunately, precise data on the body burdens. This does not permit expressing the excretion in per cent dose per day. Nevertheless, it was attempted to make a comparison between these data and the derived formula, because the data were obtained over several hundreds of days.

It is possible to fit well the urinary data to the derived formula during the first 25 d, but after that time they deviate gradually from the formula, and after 100 d they are about 1.8 times higher than the values of the formula (Fig. 3). Accordingly, it was tried to elaborate an-

![Fig. 3](image_url)

Comparison of urinary data with two empirical formulae

\[ 
\begin{align*} 
\Delta & \quad \text{COWAN et al. (inhalation of Sr$^{90}$Cl$_2$) [1]} \\
\circ & \quad \text{STEWART et al. (Sr$^{90}$) [2]} \\
\times & \quad \text{RUNDO et al. (inhalation of Sr$^{90}$CO$_3$) [3]} 
\end{align*} 
\]

The dashed line is fitted to the data by eye, and it equals relatively formula (10). The solid line derived from formula (6) is drawn so as to fit to the data during the first 25 d.

other set of formulae for the urinary excretion and the body retention on the three conditions that: (1) the urinary excretion predicted by the new formula decays parallel to that of the previous one during the first 25 d, (2) the absorption fraction is 0.25, for convenience of comparison with the ingestion data, and (3) the ratio of urine to the total excretion is 2/3. The urinary excretion formula was fitted to the data by eye, and the retention formula

* The chemical form of strontium and the route of entry are not clear.
RETENTION AND EXCRETION OF STRONTIUM

was obtained from the excretion formula by integration. These new formulae are shown as follows:

\[
\text{Retention} = 16.5 e^{-2.5t} + 3.33 e^{-12.5t} + 5.17 e^{-400t}, \quad (\% \text{ dose}) \quad (9)
\]

\[
\text{Urine} = 3.05 e^{-2.5t} + 0.123 e^{-12.5t} + 0.006 e^{-400t}, \quad (\% \text{ dose/d}) \quad (10)
\]

The half-lives of the first two terms in the above formulae, 2.5 and 12.5 d, are almost in accord with those given by COHN et al. [4]. The formulae are shown graphically by the dashed lines in Fig. 2. It appears that the new retention formula agrees with the higher data on the retentions, and the previous one shown by the solid line is in agreement with their lower values.

Examining the fitness of the two sets of derived formulae with the data on retention and excretion reported by many workers, it may be concluded that both the derived formulae can afford the means of assessment of the body burdens from urinalysis data with considerable accuracy.

However, as the experimental data have not been obtained over a period longer than 1 or 2 years, it must be noted here that the biological half-life of strontium may vary with time after long periods of time as suggested by COHN et al. [4], and the present formulae may be inapplicable for such long periods of time.

4. CALCULATION OF TOTAL BODY BURDEN AND DAILY URINARY EXCRETION CAUSED BY CONTINUOUS EXPOSURE TO FALL-OUT STRONTIUM-90 FROM THE SINGLE EXPOSURE FORMULAE

Using the derived formulae of a single exposure, the body burden and daily urinary excretion for continuous exposure to strontium can be calculated from the daily intakes on the assumption that each single intake does not influence the metabolism of other intakes.

Fortunately, the daily dietary levels of Sr\textsuperscript{90} have been measured since 1957 in Japan as shown in Fig. 4 [9–11]. Introducing these daily levels in the formulae, the body burden and the daily urinary excretion in the middle of 1961 and 1962 were calculated by integration and the results were compared with measurements.

4.1. Body burden

For convenience of calculation, it was assumed that the dietary intake increased linearly for four years from 1956 (0 pc/d) to 1960 (8 pc/d) and thereafter kept level (8 pc/d) for two years until 1962, as shown by the dashed line in Fig. 4. The total intake was divided into two parts, i.e., the first linearly increased intake, \( I_1 \), from 1956 to 1960 and the second constant level intake, \( I_2 \), after 1960. When the body burden, \( q_s \), in a single ingestion is expressed by \( q_s = a_1 e^{-\lambda_1 t} + a_2 e^{-\lambda_2 t} + a_3 e^{-\lambda_3 t} \), the body load, \( Q_1(t_2) \), which is observed at \( t = t_2 \) due to the first intake, will be expressed in the following
Estimated by multiplying the average concentration of Sr$^{90}$ in various foods by average daily consumption of these foods by individuals in Tokyo [9]

Measurement of the duplicate of the daily diet in Tokyo [10]


The dashed line shows the dietary levels assumed for calculation.

way, under the condition that the intake increased from $t = 0$ to $t = t_1$ but stopped at time $t = t_1$ and thereafter the body radioactivity decayed until $t = t_2$,

$$ Q_1(t_2) = \lambda_1 \left\{ \frac{a_1}{1 - \lambda_2 t_1} \left( 1 - e^{-\lambda_1 t_1} \right) e^{-\lambda_1 (t_2 - t_1)} + \frac{a_2}{\lambda_2} \left( 1 - \frac{1}{\lambda_2 t_1} \right) (1 - e^{-\lambda_2 t_1}) \right\} e^{-\lambda_2 (t_2 - t_1)} + \frac{a_3}{\lambda_3} \left( 1 - \frac{1}{\lambda_3 t_1} \right) (1 - e^{-\lambda_3 t_1}) \right\} e^{-\lambda_3 (t_2 - t_1)} \right\}, \quad (11) $$

where $I_1'$ is the rate of linear increase of the dietary intake (pc/d per day). The derivation of this formula has been given by McNEILL and TROJAN [16].

The body load, $Q_2(t_2)$, produced by the second intake of constant level from $t_1$ to $t_2$ is expressed as follows [14],

$$ Q_2(t_2) = \frac{a_1}{\lambda_1} (1 - e^{-\lambda_1 (t_2 - t_1)}) + \frac{a_2}{\lambda_2} (1 - e^{-\lambda_2 (t_2 - t_1)}) + \frac{a_3}{\lambda_3} (1 - e^{-\lambda_3 (t_2 - t_1)}) \right\}, \quad (12) $$

The total body load $Q(t_2)$ produced by the sum of the two intakes ($I_1$ and $I_2$), is the sum of the two body loads calculated above.

$$ Q(t_2) = Q_1(t_2) + Q_2(t_2). \quad (13) $$

Now, actual values of the dietary intakes from the fallout Sr$^{90}$ can be substituted in formulae (11) and (12). As already shown, the daily intake
from 1960 to 1962 was 8 pc/d. Therefore, \( I \) is 8 pc/d. The rate of increase, \( I' \), is \( 8/(365 \times 4) \) pc/d per day as the daily intake increased linearly for four years from 0 to 8 pc/d. From the derived empirical formula (5) for the body retention in a single ingestion the following figures are obtained:

\[
a_1 = 0.141, \quad a_2 = 0.061, \quad a_3 = 0.046, \quad \lambda_1 = 0.693/1.8, \quad \lambda_2 = 0.693/8, \quad \lambda_3 = 0.693/600. \tag{14}
\]

The calculated body loads in the middle of 1961 and 1962 are as follows:

\[
Q_1 \text{ (in 1961)} = 110 \text{ pc}, \quad Q_2 \text{ (in 1961)} = 120 \text{ pc}, \quad Q \text{ (in 1961)} = 110 + 120 = 230 \text{ pc}; \tag{16}
\]

\[
Q_1 \text{ (in 1962)} = 72 \text{ pc}, \quad Q_2 \text{ (in 1962)} = 193 \text{ pc}, \quad Q \text{ (in 1962)} = 72 + 193 = 265 \text{ pc}. \tag{17}
\]

Similar figures are obtained by using formula (9). (See column (b) in Table I.)

According to Saiki et al., the average Sr\(^{90}\) concentration in rib bones of adults (more than 20 years of age) in Tokyo was 0.39 pc/g Ca in 1961, and 0.40 pc/g Ca in 1962. Assuming that the ratio of Sr\(^{90}\) concentration in the rib to that in the whole skeleton is 1.4 [18], the body burden of Sr\(^{90}\) in the whole skeleton (or in the whole body) was calculated as 220 pc in 1961 and 290 pc in 1962.

### Table I

**COMPARISON BETWEEN THE BODY BURDENS CALCULATED FROM DIETARY INTAKE AND THOSE CALCULATED FROM CONCENTRATION IN RIB**

<table>
<thead>
<tr>
<th>Year</th>
<th>Total body burden of Sr(^{90}) (pc)</th>
<th>Sr(^{90}) concentration in rib (pc/g Ca)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Calculated from dietary intakes</td>
<td>Calculated from Sr(^{90}) concentration in rib</td>
</tr>
<tr>
<td>1961</td>
<td>230</td>
<td>200</td>
</tr>
<tr>
<td>1962</td>
<td>285</td>
<td>224</td>
</tr>
</tbody>
</table>

(a) Using formula (5).
(b) Using formula (9).
(c) Assuming ratio of Sr\(^{90}\) concentration in rib to concentration in the whole skeleton, rib/whole skeleton, is 1.4 [18].
(d) Assuming rib/whole skeleton is 1.1 [19].
(e) Average values of the concentration in rib bones sampled in Tokyo [17]. The figure in parentheses is number of samples.
230 pc in 1962. The details of the calculation are given in the Appendix. The body burdens calculated from dietary intakes and those from rib concentrations are summarized in Table I. It may be said that although some uncertainties are involved in the estimation of the daily ingestion, the calculated body burdens are in good agreement with measurements.

4.2. Urinary excretion

Urinary excretion resulting from continuous ingestion can be calculated from the dietary intakes by the same procedure as that for body burden using the empirical formulae (6) or (10) for a single ingestion. According to formula (6), the daily urinary excretion expected from the intake \( I_1 \) is 0.055 pc/d, and that from the intake \( I_2 \) is 1.22 pc/d in the middle of 1962. The total daily urinary excretion from the two intakes is the sum of the two values. That is, \( u = 1.28 \) pc/d. Similarly from formula (10), \( u = 0.05 + 1.25 = 1.30 \) pc/d in the middle of 1962.

The observed values for four persons in the middle of 1962 ranged between 0.8 and 1.2 pc/d, and the average value was 1.0 pc/d. In the urinary excretion too, the calculated value almost agrees with observation.

5. SOME PROBLEMS IN THE ASSESSMENT FROM URINALYSIS DATA OF BODY BURDEN FOR CONTINUOUS EXPOSURE

According to the simple exponential law, the body burden can be estimated from the data of urinalysis by using the following formula:

\[
\text{body burden (µc)} = \frac{\text{urine (µc/d)}}{\lambda_b(1/d) \times f_u},
\]

where \( \lambda_b \) is the biological decay constant of strontium and equals \( 0.693/T_b \) (\( T_b \) is the biological half-life), and \( f_u \) is the ratio of urine to the total excretion (urine plus faeces) of endogenous origin [21].

For the practical use of the formula, values of \( \lambda_b \) (or \( T_b \)) and \( f_u \) must be known beforehand. Judging from the experiment carried out with Sr\(^{85} \) [8], \( f_u \) seems to be \( 2/3 \) and is probably independent of time. However, the value of \( T_b \) changes according to the pattern and duration of exposure. For instance, the biological half-life for the continuous exposure of the fall-out Sr\(^{90} \) from 1956 to 1962 becomes 96 d from the values of the body burden (265 pc) and the urinary excretion (1.28 pc/d). \([265 = 1.28 \times (3/2) \times (T_b/0.693), \text{and } T_b = 96]\). However, provided an exposure started two years ago and continued at a constant level for the subsequent two years, the biological half-life is 73 d.

In the routine sampling of urine, we usually do not know the pattern of exposure. Even if an internal contamination is found by urinalysis, the

---

* It is also possible to obtain the urinary excretion at time \( t \) by multiplying \( f_u(2/3) \) by the total excretion (of endogenous origin) which is the daily decrease or the derivative of the body burden at the time.

** It was likely that the four subjects examined consumed ordinarily 5 to 7 pc of Sr\(^{85} \) per day, which was less than 8 pc/d assumed in this calculation [20].
simple formula of a single exponential term cannot be used for the estimation of the body burden from the value of the 24-h urine sample, since the biological half-life to be used does not take a definite value as shown above. If contamination has occurred, the variation of daily urinary excretion must be followed as long as possible after the cessation of further exposure. The urinary excretion curve obtained by plotting the data against time may be resolved into three components on the assumption that the activity eliminated per day is the sum of three parts, each of which decreases according to one of the three biological half-lives, i.e. 1.8, 8 and 600 d. From the three components of the urinary excretion, the corresponding body burdens which are the parts of the total body burden can be estimated by substituting their own biological half-lives in the above simple exponential formula (18). The total body burden is then obtained as the sum of the three partial body burdens.

However, it may happen in some cases that the low activities involved in the urine samples do not permit accurate determination at later stages of the sampling period, even if the activities at the earlier stages can be determined. Under these conditions, the component of the longest half-life of the urinary excretion is likely to be missed, and the partial body burden which must be evaluated from this longest half-life component may not be obtained. Unfortunately, this part occupies, in general, a major portion of the total body burden at the later stages. Therefore, it is impossible to assess accurately total body burden even though the other minor partial burdens for the shorter half-lives may be estimated.

This trouble does not occur in nuclides which have single biological half-lives according to the simple exponential law. In these nuclides we can estimate the body burden at any time from the urinalysis data using their own biological half-lives. In nuclides which have two or more biological half-lives, the difficulty described above occurs inevitably in the estimation of the body burden.

Similar discussions about the limitation of the urinalysis of radium as a measure of radium body burden have been reported by HURSH [22], and a mathematical analysis of the estimation of a body burden of plutonium from urinalysis data has been given by SNYDER according to the power function model [23].

6. CONCLUSIONS

In a single exposure of strontium through ingestion, both sets of derived empirical formulae can afford the means of evaluation of the body burden from urinalysis data.

In the case of continuous exposure, provided the pattern of the daily levels is known, the body burden at a point is calculated by integration of the derived formula.

When the pattern of intake is not known, as usually occurs, it is not possible to estimate the body burden at a point from urinalysis data at the point only, since the biological half-life to be used changes with the pattern and duration of exposure. If such an internal exposure is found, the urinalysis must be followed as long as the determination of strontium is possible.
in order to resolve the obtained urinary excretion curve into three components to which the three biological half-lives are assigned. From each of the three components, the corresponding partial body burden can be estimated using its own biological half-life, and the total body burden is obtained as the sum of the three partial body burdens.

Sometimes, however, it may not be possible to find out the component of the longest half-life in urinary excretion curve, because of the low activities involved in the urine samples at later stages. In these cases, large errors cannot be avoided in the evaluation of the total body burden.

APPENDIX

CALCULATION OF THE TOTAL BODY BURDEN OF Sr	extsuperscript{90} FROM THE CONCENTRATION OF RIB BONE IN STRONTIUM UNITS

According to the data of SAIKI et al., the mean Sr	extsuperscript{90} activity in rib bone of adults in Tokyo in 1962 [17] was 0.40 pc/g Ca. Since it is given that the ratio of Sr	extsuperscript{90} concentration in the rib bone to the concentration in the whole skeleton is 1.4 [18], the concentration in the whole skeleton becomes 0.29 pc/g Ca (=0.40 pc/g Ca/1.4).

Now, it is necessary to know the total amount of Ca in the whole skeleton in order to obtain the Sr	extsuperscript{90} body burden in the whole skeleton. According to the report of ICRP [14], the amount of Ca in bone is 0.148 g/g of wet bone. The weight of the whole skeleton of the standard man in Japan is 5.4 kg on the assumption that the total body weight is 54 kg [24] and that the whole skeleton occupies one tenth of the body weight [14]. The total amount of Ca is, therefore, 800 g (=0.148 g/g of wet bone x 5400 g) in the whole skeleton.

Consequently, the body burden of Sr	extsuperscript{90} in the whole skeleton is 230 pc (=0.29 pc/g Ca x 800 g Ca). As the amount of Sr	extsuperscript{90} in soft tissues is very small compared with that in bone [14], the level in the total body is practically equal to that of the whole skeleton (230 pc).

REFERENCES

DISCUSSION

G.W. DOLPHIN: I am interested by the low value of $f_1$ reported in this paper. The transfer of strontium across the gut wall is a passive process but can be influenced by the amount of stable strontium and stable calcium in the diet. Has Dr. Yamagata any data on the stable strontium and calcium in the diet in Japan?

N. YAMAGATA: Data has been obtained for the stable strontium content of the diet in Japan, but I do not have the information here.

J. MUELLER: In considering the proportion of strontium-89 or strontium-90 absorbed from the gastro-intestinal tract after a single oral administration, it is important to determine whether the subject has eaten before strontium was administered or whether a period without food preceded administration. Dr. Volf, of the Institute of Industrial Hygiene and Occupational Diseases in Prague, compared absorption in rats which had been starved for 24 h with that in rats which had been given a normal diet. The difference in absorption is very significant.
HUMAN INTERNAL CONTAMINATION WITH STRONTIUM-90 TITANATE

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Abstract — Résumé — Аннотация — Resumen

HUMAN INTERNAL CONTAMINATION WITH STRONTIUM-90 TITANATE. Strontium-90 has been used in multikilocurie quantities recently as a heat source for thermoelectric generators. The titanate was carefully selected for this purpose as the chemical form which best met requirements including inertness to corrosive attack in the event of accidental release to the environment. An industrial accidental exposure of one worker on 26 June 1963 to strontium-90 titanate powder, originally in the form of particles of about 120 μm and less, provided an opportunity to attempt the assessment of the human body burden of this supposedly highly insoluble compound.

Because of the physical and biological behaviour of the particles, it was assumed that the actual particle size which was dispersed and ingested and/or inhaled by the exposed person was in the range of 1 to 30 μm. Three techniques were used to estimate the body burden. Whole-body radiation counting carried out by Dr. Charles E. Miller at Argonne National Laboratory, which only gave an upper limit because of the non-specific bremsstrahlung spectrum from strontium-90, yttrium-90 indicated an initial total-body burden of 4.8 μc. The second method, total urinary and faecal output collection, totalled 5.0 μc for the first 20 d. Combining that amount with an estimate of the amount retained in the body, an initial total-body burden of 5.2 μc was obtained. The third technique, blood radioactivity determination, indicated an initial total-body burden of 6 μc.

The ratio of faecal to urinary output in the first 20 d was 15 to 1, and 94% of the total strontium-90 excretion was via the gastro-intestinal tract. It is of interest, however, that a significant fraction was evidently soluble. By the 20th post-incident day, it was estimated that the retained body burden was only 5% of the total intake. Methods used in that period to enhance faecal excretion by MgSO4 and urinary excretion by a combination of Ca-gluconate and NH4Cl are described. Subsequent excretion patterns and the current estimate of the retained body burden are presented.

CONTAMINATION INTERNE DU CORPS HUMAIN PAR LE TITANATE DE STRONTIUM 90. Le strontium 90 a été récemment utilisé en quantités de l'ordre de plusieurs kilocuries comme source de chaleur pour des générateurs thermoelectriques. Après une étude approfondie, on a choisi à cette fin le titanate comme étant la forme chimique dont les propriétés satisfont le mieux aux exigences de la situation et qui notamment résiste bien à la corrosion en cas de libération accidentelle dans l'environnement. À la suite de la contamination accidentelle d'un ouvrier par du titanate de strontium 90 en poudre — à l'origine sous forme de particules d'environ 120 μm au maximum — le 20 juin 1963, on a pu tenter d'évaluer la charge corporelle de ce composé, considéré comme très peu soluble.

D'après le comportement physique et biologique des particules, on a supposé que la dimension effective des particules dispersées puis absorbées par voie digestive ou respiratoire, ou par l'une et l'autre à la fois, était comprise entre 1 et 30 μm. Trois techniques différentes ont été utilisées pour l'évaluation de la charge corporelle. En recourant à l'anthropogammamétrie, qui en raison de la non-specificité du spectre du rayonnement de freinage du strontium 90 - yttrium 90 n'a donné qu'une limite supérieure, Dr. Charles E. Miller, du Laboratoire national d'Argonne, a évalué la charge corporelle totale initiale à 4,8 μc. Avec la deuxième méthode, fondée sur la collecte de la totalité des excréta éliminés par voie urinaire et fécale, la charge corporelle totale a été évaluée à 5,0 μc pour les 20 premiers jours. En additionnant cette radioactivité à celle que l'on estime avoir été retenue par l'organisme, on a obtenu une charge corporelle totale initiale de 5,2 μc. Avec la troisième méthode, c'est-à-dire la détermination de la radioactivité dans le sang, on a obtenu une charge corporelle initiale totale de 6 μc.

Le rapport élimination fécale/élimination urinaire a été, pendant les 20 premiers jours, de 15 à 1, 94% de la quantité totale de strontium 90 éliminée a été évacuée par l'intermédiaire du tractus gastro-intestinal.
Il y a lieu toutefois de noter qu’une fraction significative de cette quantité était manifestement soluble. Vingt jours après l’accident, on a calculé que la rétention ne représentait que 5% de la radioactivité totale absorbée. Les auteurs décrivent les méthodes qui ont été utilisées au cours de cette période pour stimuler l’élimination fécale au moyen de MgSO₄ et l’élimination urinaire en combinant le gluconate de calcium et NH₄Cl. Ils donnent des indications sur le régime ultérieur de l’élimination et sur les dernières évaluations de la rétention.

CONTAMINACIÓN INTERNA DEL CUERPO HUMANO CON TITANATO DE ESTRONCIO-90. Recientemente el estroncio-90 viene utilizándose en cantidades de multikilocuries como fuente térmica para generadores termoeléctricos. El titanato fue cuidadosamente elegido para este propósito como la forma química que reúne las mejores condiciones, incluyendo la resistencia a la corrosión, para el caso de una liberación accidental al medio ambiente. El accidente sufrido por un obrero de la industria el 26 de junio de 1963 al exponerse a la acción de polvo de titanato de estroncio-90, originalmente en forma de partículas de unas 120 μm o menos, brindó la oportunidad de determinar la carga corporal de este compuesto, que se considera como altamente insoluble.

Debido al comportamiento físico y biológico de las partículas, se supuso que el tamaño real de las mismas, que se dispersaron y fueron ingeridas o inhaladas, era del orden de 1 a 30 μm. Se utilizaron tres técnicas diferentes para estimar la carga corporal. La antropogammagrafía llevada a cabo por el Dr. Charles E. Miller en el Laboratorio Nacional de Argonne, que sólo proporcionó un límite superior debido a la inespecificidad del espectro de la radiación de frenado (Bremsstrahlung) del estroncio-90 - itrio-90, indicó una cantidad total de 4,8 μc para la carga corporal inicial. El segundo método, basado en la recolección de toda la orina y heces, indicó un total de 5,2 μc en los 20 primeros días. Al combinar esta cantidad con una estimación de la que quedaba retenida en el organismo, se obtuvo una carga inicial de 6 μc. La tercera técnica, esto es, la determinación de radiactividad en la sangre, indicó una carga inicial de 6 μc.

La relación de contenidos en heces y orina fue, durante los primeros 20 días, de 15 a 1, realizándose la excreción del 94% de la totalidad del estroncio-90 por el tracto gastrointestinal. Es de destacar, sin embargo, que una buena parte era soluble. Al vigésimo día del accidente, se calculó que la cantidad presente en el cuerpo era solamente un 5% del total inicial. Se describen los métodos empleados durante aquel período para...
Contamination With Strontium-90 Titanate

I. Introduction

Strontium-90 has been used in multikilocurie quantities since 1961 as a heat source for thermoelectric generators which supply power for automatic remote weather stations and ocean light buoys. The titanate was carefully selected for this purpose in an extensive USAEC-sponsored research programme which began in 1958. It is the chemical form which best met requirements for high strontium content, long-term stability at high temperatures, good thermal conductivity and inertness to corrosive attack in the event of accidental release to the environment [1, 2]. Studies of strontium-90 titanate in sea water showed a reassuringly low solution rate [3]. An industrial accidental exposure of one worker on 26 June 1963 to air-borne strontium-90 titanate powder provided the first opportunity to attempt the assessment of a human body burden of this supposedly highly insoluble compound.

II. Exposure Incident

The incident involved the probable inhalation and ingestion of fine particles of air-borne strontium-90 titanate by one worker (D.D.). It occurred as the employee was in the process of transferring three vials containing a total of 20 c of strontium-90 titanate from their inner shipping container into a shielded storage area. Each vial contained particles of a different size range.

The material had a density of approximately 5 g strontium-titanate (SrTiO₃) per cm³. Its specific activity was 40 c Sr⁹⁰ per gram SrTiO₃. The Sr⁹⁰ was processed into the titanate form about one year prior to the incident.

On the afternoon of 25 June 1963, D.D. placed an unopened shipping container in an aluminium prefabricated shed which was adjacent to, but not attached to the Radiochemistry Area. The shed was used for the shipment and receipt of radioactive materials and had no mechanical ventilation.

On the morning of 26 June 1963, D.D., wearing the standard laboratory coat and gloves, transferred the vial containing particles in the range 74-125 μm into a lead transfer container. The lead container was transferred into a glove box in the High Level Radiochemistry Laboratory. D.D. then checked his gloves for contamination. The following readings were observed with a thin-window G-M survey meter (approximate calibration factor on contact (0.003 μc Sr⁹⁰/cm²)/(mr/h)) : 0.06 μc/cm² on face and near nostrils; 0.06 μc/cm² on gloves, and 0.03 - 0.06 μc/cm² on facial tissue which was used to remove activity from D.D.'s face.

D.D. proceeded to take a shower with his clothes on. At about this time the company's medical consultant was called and then D.D. took a second
shower and at the same time started to remove his clothes. Following the second shower, he was monitored and spots of contamination were noted for the third and final shower. While he was showering, the area around the outdoor shed was checked for contamination. An air sample was taken at approximately the same time. Neither showed any Sr$^{90}$ contamination. The areas where D.D. had walked from the shed, to the glove box, to the laboratory monitor were all found to be contaminated, including the laboratory monitor itself.

At 4 p.m. the same day, D.D. was seen in the doctor's office and an independent check was made for radioactive contamination by smear, mucous, nostril, saliva and meter survey and the only areas of significant contamination were a spot in the hair and right knuckle which were easily decontaminated by washing.

All excreta were collected following the accident. The presence of radioactivity in the urine and faecal specimens indicated the presence of internal radioactivity. Magnesium sulphate was given as a cathartic to enhance clearing of the gastro-intestinal tract. When the rate of decrease in urinary radioactivity slowed on the third and fourth day after the accident, it was decided to attempt enhancement of strontium excretion by use of intravenous calcium gluconate and oral ammonium chloride. This combined therapy, developed by SPENCER, SAMACHSON, KABAKOW and LASZLO [4] and recently reviewed by SPENCER [5], attempts to block strontium deposition in bone by increasing the blood level of ionic calcium. The metabolic acidosis produced by the ammonium chloride serves to demineralize bones beginning with the most recently deposited elements, and therefore reduces the likelihood that the strontium-90 will be incorporated into the crystalline matrix. An alteration of the expected urinary excretion curve during the 5-d treatment period suggested that enhancement of strontium excretion was occurring and the method was repeated, therefore, for another 5-d period beginning on the fifteenth day after the accident (see Fig. 1). The detailed results of this therapy will be reported elsewhere [6]. There was no clinical evidence of injury throughout the period during which D.D. was under observation following the accident.

III. EXCRETA AND BODY MEASUREMENT

After the accident all excreta were collected for 40 d without interruption. At that time, 5 August, the daily excreta activity levels were approaching the minimum detectable levels for the counting equipment, and daily collection was stopped in favour of weekly urine checks. At the end of August, weekly urine checks were stopped and D.D. was placed on the standard bio-assay monitoring programme of his company which involves quarterly urine checks.

On 30 June, 2, 3 and 12 July, 10-ml blood samples were obtained. The blood was fractionated into plasma and red cell fractions and the activity of the separate fractions was determined.

From 26 June to 4 July, individual activity determinations were made on each individual urine and faecal specimen excreted; from 5 July to 5 August the daily output was cumulated and determinations were made on
CONTAMINATION WITH STRONTIUM-90 TITANATE

Aliquots. The procedure for the bio-assay of the urine samples was as follows:

A 10-ml aliquot of the urine sample was taken and wet-ashed to destroy the organic component. The sample was counted in a Nuclear-Chicago Model D-47 gas flow proportional counter. Another aliquot was measured for $K^{40}$ activity by the flame photometer method. This value was subtracted from the proportional counter measurement to give a net beta-activity value. The limit of sensitivity of this procedure is 500-1000 dpm per litre of urine. A specific radionuclide analysis for $Sr^{90}$ was used to check the net beta-activity determinations and the results agreed within the statistical counting error. The lower detection limit for $Sr^{90}$ by this technique is approximately 5 dpm per litre.

Faecal analysis: The entire faecal sample was wet-ashed and a 200-mg aliquot of ash was counted, $K^{40}$ activity subtracted and net beta activity determined.

The growth of activity in the urine was determined in six samples which were collected in the first six days after the incident. In all the samples the activity grew to approximately twice the initial value. This result suggests that the yttrium daughter is retained by the body and only the strontium is excreted in the urine. At secular equilibrium the $Y^{90}$ daughter activity would contribute the same amount of beta activity as the $Sr^{90}$, which would double the initial activity. In two faecal samples which were collected on the 1st and 2nd of July the growth of activity was followed to equilibrium. In these samples the growth was not as pronounced, increasing to only approximately 1.5 times the initial value. This would indicate that the faecal samples were partially in equilibrium when they were initially counted.

Table I summarizes all the urine and faecal data which have been collected up to the present time. No significant activity has been detected in the urine by the net beta technique since 22 August. A specific analysis
### TABLE I

**SUMMARY OF EXCRETION DATA ON D.D.**

<table>
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<th>Day</th>
<th>Treatment</th>
<th>$I_0$ (dpm/ml)</th>
<th>$Q$ (ml)</th>
<th>$I$ (dpm)</th>
<th>$S_I$ (μCi/d)</th>
<th>$E_f$ (μCi)</th>
<th>$E_{f+I}$ (μCi)</th>
<th>$E_{f+I+II}$ (μCi)</th>
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<td>$I$ (dpm)</td>
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<td>$Sf$ (µC)</td>
<td>$E_{u}+Sf$ (µC)</td>
<td>$C_{u}^{Eu}$ (dpm/ml)</td>
<td>$C_{u}^{Eu}$ (dpm/ml)</td>
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CONTAMINATION WITH STRONTIUM-90 TITANATE

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<th>In</th>
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<th>I</th>
<th>En</th>
<th>Ef</th>
<th>Ef+En</th>
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Iu : Disintegrations per minute per millilitre (dpm/ml)  
Q : Volume of urinary output in millilitres (ml)  
I : Total disintegrations per minute in urine (dpm)  
En : Daily urinary excretion rate in microcuries per day (mC/d)  
Ef + En : Total daily excretion rate in microcuries (mC)  
Cplasma : Activity of plasma fraction of blood in (dpm/ml)  
CRBC : Activity of red blood cell fraction of blood in (dpm/ml)
for Sr\(^{90}\) on 14 October gave a value for the output in the urine on that day of 93 pc of Sr\(^{90}\).

The urine and faeces daily output data are plotted on semi-logarithmic graph paper in Figs.1 and 2. The urine output per day (\(E_u\)) decreased with a half-life of five days, assuming a one-compartment biological model. Integrating this curve over the 40 d in which total urine output was collected gave an output of 0.24 \(\mu\)c and the actual measured output was 0.33 \(\mu\)c. If a two-compartment model is used to fit the points, then integration of the two lines gives a value which overestimates the output in comparison with that observed. From the 10th d onward this line fits the points more accurately and integration to the 40th d gives a total output of 0.060 \(\mu\)c. The actual output in this time interval was 0.056 \(\mu\)c. The first 10 d post-incident covered the period in which one might anticipate difficulties in fitting a curve to the data because of the medical treatment.

The faecal output accounted for 94% of the total observed output up to the 40th d post-incident. There is a considerable scatter of points in the plot of the faecal output and any attempt to compartmentalize must be looked at with some scepticism. A visual fit gave three lines with half-lives of approximately 0.3 d, 3 d and 144 d. On 27 July there was an anomalously high faecal output which was 100 times the faecal outputs of the preceding and succeeding days. If this was not a laboratory error, it may have been due to (a) inhalation of more radioactive material, or (b) a particle of the original high specific activity material may have been dislodged from the lung, causing that particular faecal sample to contain more radioactivity. The faecal data was also plotted on log-log graph paper but the points did not appear to fit the data any better than on semi-log paper. The power function expression for the excretion curve after the 20th d was \(A = 0.74\).
In Fig. 3 the cumulative excretion data is plotted on a linear scale. The anomalous output on 27 July causes a discontinuity in an otherwise smooth curve. This graph is useful in estimating the initial total body burden after the period of rapid excretion of the first few days is over.

Due to the initial large output in the faeces and the unknown biological behaviour of SrTiO₃ an estimate of D.D.'s body burden was attempted by whole-body counting through the co-operation of the Argonne National Laboratory on 29 June. Dr. Charles Miller of that institution used the standard Argonne Tilting Chair Method to obtain the spectrum shown in Fig. 4. Analysis of the spectrum by Dr. Miller indicated that the patient contained (a) 139 g normal potassium, (b) 0.015 μC Cs¹³⁷, (c) 0.04 μC Zn⁶⁵, (d) 0.03 μC
Co$^{60}$, (e) 0.07 μc 1.25, and (f) less than 0.42 μc Sr$^{90}$. The value for Sr$^{90}$ is an upper limit determined by attributing all gamma rays in the energy interval from 150 keV to 300 keV to Sr$^{90}$ bremsstrahlung. Use of the standard stripping technique, made difficult in this case by the low-energy gamma rays present, yields a value of 0.16 μc Sr$^{90}$. Since that time D.D. has excreted 0.33 μc Sr$^{90}$, but if one discounts the 0.104 μc faecal output on 27 July, then a value of 0.2 μc output is not incompatible with the 0.16 μc Sr$^{90}$ body burden estimated by the stripping technique.

On four occasions blood samples were obtained and the plasma and red cell fractions were counted for Sr$^{90}$ activity. The ratio of concentration of activity in urine to concentration of activity in plasma varied from 6.2 to 18.8, while the ratio of concentration of activity in urine to concentration in red blood cell fraction varied from 8 to 28.5. The former ratio for the four determinations remained relatively constant while the latter ratio varied to a much greater extent. This was an attempt to determine which of the blood fractions might determine the urinary output level. These results may indicate that the plasma pool is the determining compartment.

IV. ESTIMATES OF INITIAL AND PRESENT BODY BURDEN

Initially in accident analysis, the most important question which must be answered is how much activity has been retained in the body. Medical management is facilitated by such estimates. The first estimate of retained activity, based on an initial total body output of 2.5 μc and a half-life of 6.6 d, was 29 μc. This was made on 28 June, only two days after the incident, and represented an upper limit.

By 3 July more data had been obtained and a complete analysis of the initial body burden was attempted based on the techniques reported by BISHOP, HARRISON, RAYMOND, SUTTON and RUNDO [7]; and RUNDO and WILLIAMS [8]. The first technique involved the use of the whole-body counter data. Since at first we did not have any calibration factor for conversion of the whole-body counts into μc Sr$^{90}$, a calibration factor given by RUNDO [8] of 1 μc Sr$^{90}$/250 cpm was utilized. The counts in the channels 4 to 120 (15 keV-730 keV) gave a total of 1250 counts/40 min = 31.3 cpm. These counts are based on the assumed bremsstrahlung spectrum which is drawn in Fig. 4. This indicates a retained body burden of 0.128 μc Sr$^{90}$ on 29 June. If one adds to this value the 4.649 μc which had been excreted up to that time, one obtains an initial body burden, q₀ = 4.774 μc. Using the 0.16 μc Sr$^{90}$ as estimated by Dr. Miller, a q₀ = 4.81 μc is obtained.

The second method employed was the empirical relationship derived by BISHOP [7], and used by RUNDO [8] in an accidental Sr$^{90}$CO₃ inhalation. This equation is:

$$ q = 0.65 E_u^{0.33} + 0.06, $$

$$ q = \text{body burden (μc)}, $$

$$ E_u = \text{μc/d urine output}. $$
With \( q \) the body burden and \( \frac{1}{t} \sum_{0}^{t} E_{u+f} \), it is possible to estimate the initial body burden, \( q_0 = q_1 + \frac{1}{t} \sum_{0}^{t} E_{u+f} \). The results are presented in Table II. After the high faecal excretions of the first three days, the estimate of \( q_0 \) in-

### Table II

**ESTIMATES OF \( q \) AND \( q_0 \) BY BISHOP'S EMPIRICAL RELATIONSHIP**

\( (q = 0.65 E_{u}^{0.33} + 0.06) \)

<table>
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<th>Day</th>
<th>Eu (( \mu )c/d)</th>
<th>q (( \mu )c)</th>
<th>( \frac{1}{0} E_{u+f} ) (( \mu )c)</th>
<th>( q_0 ) (( \mu )c)</th>
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<tr>
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<td>0.0353</td>
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<td>0.251(2)</td>
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<td>0.0209</td>
<td>0.240(2)</td>
<td>5.001</td>
<td>5.24(2)</td>
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(\( q \) by WBC 0.1-0.2 \( \mu \)c)  
(\( q_{AVG} \) = 0.25 \( \mu \)c)  
(\( q_{0AVG} \) = 5.2 \( \mu \)c)

- \( E_u \): Daily urinary excretion rate in microcuries per day
- \( q \): Body burden on day, \( t \)
- \( q_0 \): Initial body burden, \( t = 0 \)
- \( E_{u+f} \): Total daily excretion rate in microcuries

Increases by only 0.3 \( \mu \)c; in fact, the \( q = 5.2 \( \mu \)c predicted by the measurements on 1, 2 and 3 July equals the total output 40 d after the inhalation. This is the more remarkable since the empirical formula was originally based on injected soluble Sr\(^{85}\). Rundo has also found this formula to give values of \( q_0 \) in good agreement with values of \( q_0 \) estimated by different techniques. In the case of a Sr\(^{85}\)CO\(_3\) inhalation he reported the formula gave a mean value of \( q_0 = 0.459 \( \mu \)c and the estimated value by whole-body counting was 0.4 \( \mu \)c. In our case, on 29 June the formula estimates \( q = 0.24 \( \mu \)c. Our estimate by whole-body counting on that day is \( q = 0.13 \( \mu \)c and Argonne estimates \( q = 0.16 \( \mu \)c. These values are in good agreement considering the uncertainties in the derivation.

Another technique used by Rundo and Williams to estimate \( q \) was based on the activity in the blood plasma. For D.D., the estimated body fluid volume was 11.51. The total plasma activity was \( 11.51 \times 0.00293 \( \mu \)c/l = 0.0338 \( \mu \)c. HARRISON [9] found only 2.7% of the original amount of strontium injected in the plasma and extra-cellular fluid on the sixth day after an intravenous
TABLE III

ESTIMATES OF BODY BURDEN ON t = 0 AND t = 3 d POST-INCIDENT BY THREE DIFFERENT METHODS

<table>
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<th>Method</th>
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<th>qt = 0 (µc)</th>
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<tr>
<td>Urine activity</td>
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<td>4.9</td>
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<tr>
<td>Plasma activity</td>
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<td>5.8</td>
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qt = 3 d: Body burden on 3rd day post-incident
qt = 0: Initial body burden

injection. Therefore, q0 = (0.0338 µc/0.027 =) 1.25 µc + 4.52 µc + 5.77 µc. The 4.52 µc is the faecal excretion on the two days immediately after the incident and probably represents material most or all of which was never in the body strontium pool and available for circulation.

In Table III the various estimates of q0 and qt=3d are summarized. Based on these results, it appears that the time is approaching when one can estimate the radioisotope body burden in man with a fair degree of accuracy. This helps to give one confidence when dealing with an accident case in the first few days after exposure.

An estimate of q for D.D. at the present time is important, as it may affect his future employment in the nuclear industry. Two methods were used to make this estimate and they agreed within 50% of each other.

In the first method, use was made of the formula of Bishop to estimate q. The specific Sr90 analysis on 14 October 1963 gave an output on that day of 9.3X10⁻⁵ µc. If this is taken as Eu in Bishop's formula, q = 0.1 µc Sr90, retained body burden on that date.

The second method involved determining Eu+f from the output data and integrating over infinite time to obtain an estimate of q. The last eight daily Eu+f values from 29 July to 5 August were averaged to obtain an Eu+f = 9.1X10⁻⁴ µc/d. A biological half-life of 144 d was assumed as this is the faecal output half-life for its long-term component. The above average Eu+f was taken as the Eu+f0 in the equation q = \( \bar{E}(u + f)_0 \exp(-\lambda t_{df}) \) which gave a value of 0.2 µc Sr90. The estimates of D.D.'s present body burden by these two methods therefore are in fairly close agreement. If one assumes q = 0.15 µc, the average of the two estimates, this is 7.5% of the maximum permissible body burden of 2 µc for Sr90 with bone as the critical body organ.

V. FIFTY-YEAR LIFETIME DOSE

It is also important to determine the lifetime dose from this inhaled isotope to assess the overall hazard which D.D. has incurred in the accident.
It is not easy to determine in what site of the body the remaining Sr\textsuperscript{90}–Y\textsuperscript{90} is retained. If one takes bone as the retention site with a biological half-life of 144 d, this results in a 50-yr bone dose of 2 rem which will be inconsequential compared to the 50-yr upper radiation protection guide level of 1500 rem for bone. If the total body is taken as the critical body organ, then a 50-yr dose of only 0.2 rem will be received. This dose might be compared with a 50-yr radiation protection guide level of 250 rem for the total body.

All these calculations must be taken with some degree of caution. We know of no other human exposure to strontium titanate at this initial level of activity. There is very little biological data available concerning its long-term fate in the various body organs. However, if the faecal and urinary output data are a good criterion, the body burden of strontium titanate seems to be reduced rapidly to negligible quantities despite an initial body burden of about 5.2 μc Sr\textsuperscript{90}.

VI. SUMMARY AND CONCLUSIONS

In transferring a vial containing approximately 7 c of strontium-90 titanate, a worker, D.D., inhaled and ingested approximately 5.2 μc Sr\textsuperscript{90}: In the first four days following the incident 4.745 μc Sr\textsuperscript{90} and 0.1558 μc Sr\textsuperscript{90} were excreted in the faeces and urine respectively. This constituted 94% of the total quantity taken in. Medical therapy with intravenous calcium gluconate and oral ammonium chloride on the 4th to 8th day post-incident and again on the 15th to 19th day post-incident appeared to enhance elimination of the material. From the 10th day post-incident to the 40th day, the urine excretion curve is described by equation

\[ E_u = 0.0085 \exp\left(-\frac{0.693}{5 \text{ d}} t\right) \mu\text{c/d}. \]

The observed faecal output from the 10th day onward followed the equation

\[ E_f = 480 \exp\left(-\frac{0.693}{0.3 \text{ d}} t\right) + 0.022 \exp\left(-\frac{0.693}{3 \text{ d}} t\right) + 0.0017 \exp\left(-\frac{0.693}{144 \text{ d}} t\right). \]

Bishop's empirical equation: \( q = 0.65 E_{0.33}^{0.33} + 0.06 \), indicated a body burden of 0.24 μc on the 4th day post-incident, whole-body counting suggested 0.1 – 1.2 μc and the total observed output from the 5th to the 40th day was 0.3 μc. The initial body burden was 2.5 times the maximum permissible body burden recommended by the Committee II of ICRP for Sr\textsuperscript{90}, but in the particle size range and chemical form encountered in this accident Sr\textsuperscript{90} was considerably less hazardous because of its rapid elimination than it would have been in the more soluble chemical forms upon which the present limits are based.
CONTAMINATION WITH STRONTIUM-90 TITANATE

REFERENCES


DISCUSSION

J. RUNDO: I would like to ask Dr. Bradley one question, followed by one comment and one suggestion. Firstly, I would like to ask whether you have any information on the possible effects of radiation on the chemical composition of strontium titanate.

F. J. BRADLEY: No, I do not.

J. RUNDO: Very well. My comment concerns the use of the empirical equation for estimating retention ($R_{uc}$) from daily urinary excretion ($U_{uc}$)

$$R = 0.65 U_{uc} + 0.06.$$ 

I was very surprised that it gave reasonable results in this case, as it was derived from two cases of injection with 0.5 $\mu$C. According to this equation, if you had a case of suspected strontium-90 contamination and found no strontium-90 in the urine, then the man's content would be 0.06 microcuries; if you found 10 microcuries in the urine, this would imply that his content was 1.46 microcuries; if you found 1000 microcuries, it would imply that his content was 6.6 microcuries. This is clearly nonsensical.

I think that one should not use this equation at all. Dr. Harrison, who originally derived this equation, has other equations with more general application.

My suggestion is that the excretion data presented would seem to be just those one would expect for lung clearance of an insoluble particulate deposit.

F. J. BRADLEY: The retention equation was used initially only to get a rough estimate of the body burden and was used in conjunction with two other independent bioassay techniques, i.e. whole-body counting and plasma activity.

Moreover, as indicated in my summary, the equation gave a body burden of 0.24 $\mu$C on day 4 after the incident and the total observed output from day 5 to day 40 was 0.3 $\mu$C. This may be fortuitous but it is what we observed, and the results are in the range on the basis of which the equation was originally developed.
I am grateful to you for pointing out the limitations of the formula. We should perhaps make it clear that it is valid only where \( R \) is between 0.1 and 0.7 \( \mu \)c and where \( U \) is much less than 1.

Your suggestion concerning the excretion data is probably true but very little human data is available on this point. In your case of Sr\(^{90}\)CO\(_3\) inhalation\(^*\) no faecal output was obtained until five days after the incident, and followed consecutively only until day 24. To predict a priori what human output pattern will develop is very difficult and greatly dependent on the individual's breathing habit and the characteristics of the dust, such as particle size, chemical form, concentration and solubility in lung and body fluids.

S. PRÊTRE: I would like to put three questions to Mr. Bradley. Firstly, when you speak of ingestion do you mean solely the ingestion of particles inhaled and trapped in the upper respiratory organs or are you also thinking of direct ingestion through the mouth?

Secondly, do you know whether the person involved in the accident normally breathes through the nose or the mouth?

Thirdly, I do not quite understand what is the position regarding the granulometric spectrum of the particles. In your paper you refer to sizes between 74 and 125 microns, but in the abstract you speak of "actual particle size" between 1 and 30 microns.

F. J. BRADLEY: By ingestion I also include particles which may have passed into the mouth and right down the oesophagus without entering the respiratory tree.

This leads into the second question, whether or not this person breathes through the mouth. From the large quantity that did get into the lung and the gastro-intestinal tract, I suspect that he probably breathes through the mouth or that he had his mouth open during part of the exposure.

With regard to your third question, the exposed person was handling a vial containing particles which were originally sized for particles in the range 74 microns to 125 microns in diameter. Since the approximate specific activity and density of the materials was known we estimated that particles in this range would have an activity range of 42.4 \( \mu \)c to 204 \( \mu \)c. But monitoring at the time of the incident indicated, using the same specific activity and density, that the person was exposed to particles that were probably less than 12 microns in diameter, and therefore potentially in the size range of particles which would be retained by the lung.

TRITIUM
(Session 13)
THE RADIATION HAZARD TO WORKERS USING TRITIATED LUMINOUS COMPOUNDS

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Abstract — Résumé — Аннотация — Resumen

THE RADIATION HAZARD TO WORKERS USING TRITIATED LUMINOUS COMPOUNDS. The traditional radioactive constituent of luminous compounds has been radium, a substance of potentially great hazard. In recent years, suitable alternatives to radium have been sought and in the UK and elsewhere official encouragement has been given to the use of tritiated compounds. We have for some time been monitoring the urine of users of these tritiated compounds and have made complementary measurements of tritium in air. The stability of the compounds themselves has also been investigated.

Eight compounds have been tested but work has been concentrated on the two which are in actual use in British industry. Urine from employees of seven firms has been monitored but only four of these firms are large-scale users of tritiated compounds.

Interpretation of the results is complicated because the ICRP recommends two different maximum permissible body burdens for tritiated water, 2 mc and 1 mc. The corresponding concentrations of tritium in urine, assuming the body to contain 4.3 x 10^4 ml of water, are 4.7 x 10^{-2} and 2.3 x 10^{-2} µc/ml respectively.

Employees at all four major factories were found to have tritium in their urine, one person attaining a concentration of over six times the lower maximum permissible level. A number of operators at two factories are still maintaining concentrations of 1-2 times the maximum permissible level.

The main hazard appears to be due to the inhalation of tritiated water-vapour when the compound is mixed with its solvent and adhesive. A new test for the stability of the compounds in moist air has therefore been devised. Under the conditions of the test, the two compounds in major use lose 0.1 and 0.5% of their tritium respectively in the first 2 1/2 h, mainly as tritiated water.

The biological half-life of the tritiated water in two luminizers was found to be 12.1 and 13.4 d respectively, which is in reasonable agreement with the 12 d assumed by the International Commission on Radiological Protection (ICRP).

The significance of these results is discussed.
H. G. JONES and B. E. LAMBERT

composés en atmosphère humide. Dans les conditions de l'essai, les deux composés les plus utilisés perdent respectivement 0,1 et 0,5% de leur tritium durant les 150 premières minutes, essentiellement sous forme d'eau tritiée.

Chez deux ouvriers, la période biologique de l'eau tritiée était de 12,1 et 13,4 j respectivement, ce qui n'est pas très éloigné de la période de 12 j admise par la CIPR.

Les auteurs discutent les résultats obtenus.

RADIAÇÃOONÁ DE RABOЧИХ, РАБОТАЮЩИХ С СВЕТЯЩИМИСЯ СОСТАВАМИ. Традиционным радиоактивным компонентом светящихся составов является радий, вещество, обладающее высокой потенциальной опасностью. В последние годы велось поиска заменителя радия, после чего в Соединенном Королевстве и других странах предпочли использовать триитированные соединения. Некоторое время производилась дозиметрия мочи лиц, работающих с этими триитированными соединениями, и дополнительно измерялись содержание трития в воздухе. Изучалась также стабильность этих соединений.

Исследовано 8 соединений, но основная работа проводилась с двумя наиболее ходовыми в британской промышленности соединениями. Производилась дозиметрия мочи у служащих 7 фирм, но лишь 4 из этих фирм используют триитированные соединения в большом масштабе.

Интерпретация результатов осложняется тем, что МКРЗ рекомендует две различные величины максимально допустимого содержания в организме триитированной воды — 2 и 1 милликрюри. Соответствующие концентрации трития в моче при содержании в организме $4,3 \times 10^4$ мл составляют $4,7 \times 10^{-2}$ и $2,3 \times 10^{-2}$ микрокюри/мл соответственно.

У служащих всех четырех главных заводов был обнаружен тритий в моче, у одного человека концентрация его в шесть раз превышала нижний уровень максимально допустимой дозы. У ряда рабочих на двух заводах до сих пор держится концентрация порядка 1—2 максимально допустимых уровней.

Очевидно основная опасность связана с вдыханием паров триитированной воды, где соединение смешано с растворителем и связывающим веществом. Поэтому был поставлен новый опыт на устойчивость соединений во влажном воздухе. В условиях этого опыта два наиболее часто используемых соединения теряют 0,1 и 0,5% своего трития соответственно в первые 2,5 часа, главным образом в форме триитированной воды.

Период полувыведения триитированной воды у двух рабочих, работавших со светящимися составами, равнялся 12,1 и 13,4 дням соответственно, что примерно отвечает норме 12 дней, установленной МКРЗ.

Обсуждается значение этих результатов.

RIESGOS RADIOLÓGICOS INHERENTES AL TRABAJO CON COMPUESTOS LUMINOSOS TRITIADOS. Como constituyente radiactivo de los compuestos luminosos se acostumbraba anteriormente utilizar el radio, elemento cuyo empleo supone grandes riesgos. En los últimos años se ha procurado hallar sustitutos apropiados y en el Reino Unido y otros países se ha recomendado oficialmente el uso de los compuestos triitados con ese fin. Los autores han venido controlando la orina de las personas que trabajan con dichos compuestos y han efectuado mediciones complementarias de la concentración de tritio en el aire. Además, investigaron la estabilidad de los propios compuestos.

Hicieron ensayos con ocho compuestos, pero dedicaron mayor atención a los dos que se aplican efectivamente en la industria británica. Controlaron la orina de los empleados de siete empresas, de las cuales solamente cuatro utilizan en gran escala compuestos triitados.

El hecho de que la CIPR recomiende dos valores distintos para la carga corporal máxima admisible de agua triitada, a saber, 2 mcuries y 1 mcurie, complica la interpretación de los resultados. Suponiendo que el cuerpo humano contiene $4,3 \times 10^4$ ml de agua, las correspondientes concentraciones de tritio en la orina serían $4,7 \times 10^{-2}$ y $2,3 \times 10^{-2}$ uc/ml, respectivamente.

Se comprobó la presencia de tritio en la orina de los empleados de las cuatro fábricas más importantes y en una persona la concentración registrada fue más de seis veces mayor que el valor umbral fijado para la concentración máxima admisible. En muchos trabajadores de dos de las fábricas las concentraciones observadas oscilan entre la máxima admisible y el doble de la misma.

El riesgo principal consiste, al parecer, en la inhalación del vapor de agua triitada durante la mezcla del compuesto con el disolvente y con el adhesivo. Por lo tanto, se ha ideado un nuevo ensayo de estabilidad de los compuestos en aire húmedo. En las condiciones indicadas para este ensayo, los dos compuestos más usados pierden en las primeras dos horas y media 0,1 y 0,5 por ciento del tritio contenido, principalmente en forma de agua triitada.
HAZARD OF TRITIATED LUMINOUS COMPounds

Se comprobó que el período biológico del agua trituida en los dos compuestos luminiscientes es de 12.1 y 13.4 d, respectivamente, valores que concuerdan razonablemente con el de 12 d adoptado por la Internacional Comisión de Protección Radiológica (ICPR).

Los autores interpretan los resultados obtenidos.

1. INTRODUCTION

Luminous compounds or paints have been used in the watch and clock industry for many years. The basic constituents of these compounds consist of a radioactive substance and a scintillator, usually zinc sulphide. Traditionally, the radioactive substance used has been radium, a substance of potentially great hazard. Thus, a number of luminizers who worked in the industry during the first quarter of this century sustained severe illness or death in later years because of the radium they had ingested. However, successive legislation has improved conditions in the industry and cases of this type have not occurred amongst persons who were engaged in luminizing after this period [1].

The traditional luminous watch or clock dial, which contained radium has been reported to contain very approximately about 0.2 μc of radium and to deliver to the gonads of its wearer, a radiation dose of about 1 m r per year [1]. However, there was considerable variation in the quantity of radium to be found on any individual watch. More recently, another survey by the Medical Research Council has reported that more modern watches contain rather less radium [2]. The original figure of 1 m r per year represents about 1% of the average background radiation dose to the gonads of the British population and although very small, is finite.

In recent years suitable alternatives to radium have been considered including Sr90, Pu239, Am241, Pm147 and tritium. Objections have been raised to the first three and Pm147 is not at present in significant use in the United Kingdom. During the last year or so, certain compounds of tritium have been produced which may be incorporated into luminous paints and in the United Kingdom, as elsewhere, official encouragement has been given to the use of these compounds. Tritium seemed to be an ideal nuclide for the purpose for two reasons. Firstly it emits an extremely weak beta particle ($E_{\text{max}} = 0.018$ MeV) which is absorbed completely by the outer case of a watch or clock. Secondly, in considering the radiation hazard to luminizing workers, it has an extremely short biological half-life (12 d) if it is assumed that the absorbed tritium is in the form of tritiated water in the body [3]. In this latter context, it compares very favourably indeed with radium, which has a biological half-life in bone of $1.6 \times 10^4$ d [3].

However, consideration of the hazard to persons exposed to an atmosphere containing tritium is complicated because the International Commission on Radiological Protection (ICRP) recommends two maximum permissible body burdens for tritiated water. Other compounds of tritium are not considered at all [3]. One ICRP recommendation considers the critical organ after absorption of tritiated water to be the whole body. The tritiated water is considered to be evenly distributed throughout the 70 kg of body mass of the "standard man" and the quantity which delivers an annual radiation dose to the whole body of 5 rem is calculated. This quantity is 1.96 mc.
In a second calculation the critical organ is considered to be "body tissue". For the purpose of this calculation, the tritiated water is considered to be evenly distributed throughout the 43 kg of body water in the "standard man". The quantity of tritiated water which delivers 5 rem per year to this body water is calculated to be 1.20 mc.

In the normal way these two figures were issued in the ICRP recommendations as whole numbers, i.e. 2 mc and 1 mc respectively. As it is assumed in both cases that the tritiated water becomes evenly distributed throughout body water, it is a simple matter to calculate the concentrations in urine which correspond to the two body burdens. They are 0.046 and 0.023 µc/ml urine respectively. Throughout this paper these two latter figures have been referred to as higher and lower maximum permissible levels of tritiated water in urine.

For some time, the Radiological Protection Service has been monitoring for tritiated water the urine of luminizing workers from seven factories which use tritiated luminous compounds. Several factories have only recently relinquished radium in favour of tritium but at least two have used the tritiated compounds for about a year. It is now possible, therefore, to draw certain conclusions from the results obtained to date.

2. METHODS

2.1. Sampling

The workers being monitored were asked to provide a spot sample of about 100 ml of urine at appropriate intervals. As a routine this interval was a fortnight but in those cases where the urine contained one half the higher maximum permissible level or more, samples were taken weekly. In the case of two workers, the biological half-life of the tritium they contained was estimated. For this purpose, they were rested temporarily from their normal work and provided urine samples daily. All urine samples were acidified with 2-3 drops of concentrated hydrochloric acid before being sent to the laboratory.

2.2. Estimation of tritiated water in urine

Each urine sample was distilled, 1 ml of the distillate added to 10 ml of scintillator mixture and the sample counted by means of a liquid scintillation counter. The scintillator used was NE 572 (Nuclear Enterprises Ltd.) in dioxane solution and the counter was of the twin photomultiplier tube type with coincidence circuit (Isotope Developments Ltd.), which counted tritiated water with an efficiency of 11%. The counter was calibrated against a standard source of n-hexadecane-1, 2-T, the specific activity of which was known to within ±4% (Radiochemical Centre, Amersham).

2.3. Estimation of atmospheric tritiated water

The tritiated water content of the atmosphere in the luminizing rooms of two factories was estimated by pumping a stream of the air through a
tube immersed in a solid CO₂/ethanol cooling mixture. The resulting ice was collected, thawed and counted in the scintillation counter in the manner described for the urine samples. The water content of the air in the room was estimated by means of a whirling hygrometer.

2.4 Stability tests on tritiated luminous compounds

The stability of the tritiated luminous compounds was investigated by drawing a stream of air, saturated with water vapour, at a rate of 44 ml/min over a mixture of the compound and its adhesive lacquer. The sample consisted of 25 mg of luminous compound mixed with 50 mg of lacquer and spread out over an area of 0.5 in² on a nickel dish. The tritiated water and other condensable substances which were given off the mixture, were frozen out in a trap immersed in a solid CO₂/ethanol freezing mixture. In the earlier experiments the trap was washed out with water but it was discovered that all the tritium was not extracted from the trap by this method. Subsequently the water was replaced by acetone. For some experiments the effluent stream of gas was also passed through a tube containing heated copper oxide, to oxidize any elementary tritium which it contained. The tests were also carried out using 25 mg of luminous compound alone, with no added lacquer.

3. RESULTS

3.1 Urine monitoring

The details of the monitoring programme as it relates to the three heaviest users are set out in Table I. Factory A uses an imported compound (compound 1) exclusively, factory B uses only a compound made in the United Kingdom (compound 2). Factory C uses compound 2 almost exclusively but occasionally uses small amounts of compound 1. The other, smaller users of the compounds use one or other or both of these two compounds. Several other compounds are available on the British market but none is used commercially to any significant extent up to the present time.

The number of employees in factories A, B and C who are monitored continually is shown in Table I. Other employees in the same firms are monitored occasionally. Each factory is subject to a certain turnover of labour.

The number of employees who have absorbed a significant quantity of tritium is shown in Table II. The second column shows the number of employees who have absorbed quantities of tritiated water exceeding an arbitrary warning level corresponding to one-fifth of the lower of the two maximum permissible levels. Columns 3 and 4 show the number of employees whose urine contained at some time quantities greater than the two maximum permissible levels. The final column in Table II shows the highest single result found at each factory in terms of the lower maximum permissible level.

Table III shows the number of occasions on which these three levels have been exceeded at each factory. The results vary with the task per-
TABLE I

MONITORING PROGRAMME AT THREE MAJOR FACTORIES

<table>
<thead>
<tr>
<th>Factory</th>
<th>Compound used</th>
<th>Quantity of compound used (c/week)</th>
<th>No. of employees monitored continually</th>
<th>No. of times monitored</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>25</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>12-25</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>C</td>
<td>1+2</td>
<td>10-15</td>
<td>5</td>
<td>19</td>
</tr>
</tbody>
</table>

TABLE II

NUMBER OF EMPLOYEES IN WHOM SIGNIFICANT FRACTIONS OF A MAXIMUM PERMISSIBLE LEVEL OF TRITIATED WATER IN URINE OCCURRED

<table>
<thead>
<tr>
<th>Factory</th>
<th>&gt;1/5 Lower MPL</th>
<th>&gt;Lower MPL</th>
<th>&gt;Higher MPL</th>
<th>Highest result as fraction of lower MPL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>B</td>
<td>8</td>
<td>5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>2/3</td>
</tr>
</tbody>
</table>

TABLE III

NUMBER OF OCCASIONS ON WHICH SIGNIFICANT FRACTIONS OF A MAXIMUM PERMISSIBLE LEVEL OF TRITIATED WATER IN URINE OCCURRED

<table>
<thead>
<tr>
<th>Factory</th>
<th>&gt;1/5 Lower MPL</th>
<th>&gt;Lower MPL</th>
<th>&gt;Higher MPL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>91</td>
<td>37</td>
<td>.13</td>
</tr>
<tr>
<td>B</td>
<td>50</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>14</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

formed. Some employees show a variation in their body content of tritiated water, whereas the luminizing machine operators in factories A and B maintain a fairly constant level except for short periods after a holiday or other
rest period. In both factories the urine of the two machine operators contains regularly more than the lower maximum permissible level of tritiated water. One operator in each of these two factories maintains regularly just below one higher maximum permissible level.

Apart from the two machine operators who still present a problem, the position at factory A has improved considerably over the last few months. Various improvements to ventilation, room size and working techniques have meant that employees, other than the two machine operators, now exceed the arbitrary warning level on few occasions. They never acquire a lower maximum permissible level. The highest figure of six times the lower maximum permissible level occurred before these improvements were carried out.

3.2. Environmental monitoring

The tritiated water content of the air in the luminizing room in factory A was measured by the method described in section 2.3, before and after the improvements mentioned in the last paragraph were carried out. On the first occasion an attempt was also made to measure the total tritium content of the air at various points in the room by means of a portable gas monitor type N.I.S.221 (AWRE). The latter did not prove sensitive enough to measure the general level of tritium in the room but was able to demonstrate pockets of higher concentration at various points.

Before the improvements were made the general concentration of tritiated water in the luminizing room was found to be $5 \times 10^{-6} \mu c/cm^3$ which is exactly the lower maximum permissible concentration in air recommended by ICRP for a 40-h working week [3]. At that time one person was working continuously in the room and her urine contained about one higher maximum permissible level of tritiated water. The gas monitor, sampling the air at a distance of 2 in from the pot in the luminizing machine, which held about 3 c of the luminous compound, gave a reading of $8 \times 10^{-4} \mu c/cm^3$.

After the improvements were carried out, the general concentration of tritiated water in the room was $5.7 \times 10^{-7} \mu c/cm^3$. In the meantime, the concentration of tritiated water in the urine of employees who spent part of their working day in the luminizing room had lessened considerably. By this time the tritiated water content of the machine operators (now increased to two in number), had decreased but was still in excess of a lower maximum permissible level. The results seem to imply that the machine operators were probably subjected to local high concentrations of tritium.

The general level of tritiated water was also estimated in the luminizing room of factory C. It was found to be $6.4 \times 10^{-8} \mu c/cm^3$.

3.3. Biological half-life of the absorbed tritium

Two employees in factory A who contained more than a lower maximum permissible body burden of tritiated water were removed from the luminizing room for ten days. The tritiated water content of their urine was measured daily and the results are shown in Fig.1. In both cases, the tritiated water content declined exponentially with a half-life of 12.1 d in the case of Miss B.
and 13.4 d in the case of Mrs. L. Both these figures agree well with that quoted as the biological half-life of tritiated water by ICRP[3].

3.4. Stability of the luminous compounds

The only recognized test for the stability of these compounds was a soak test for the finished luminous dials and hands [4]. The results of the monitoring survey seemed to indicate an inhalation hazard rather than one involving ingestion, so the tests described in section 2.4 were devised. These tests were carried out on a number of compounds either alone or mixed with lacquers of various types. The results for the two compounds in major use in British industry are set out in Table IV. Under the conditions of the tests both compounds give off significant quantities of tritium; compound 1 more than compound 2. Several lacquers had an effect upon the stability of compound 2 and one lacquer in particular had a marked effect on both compounds. It is probable that the conditions of these tests are more extreme than those existing in industrial practice.

When the effluent gases from the above tests were passed over heated copper oxide, the condensate contained no extra tritium, suggesting that no significant proportion of elementary tritium is given off the compounds. As acetone was a better solvent for the condensate than water, it also seems that the tritium given off the compound does not consist entirely of tritiated water.

4. DISCUSSION

4.1. Monitoring results

When tritiated luminous compounds were introduced, it was not anticipated that luminizers would absorb regularly the quantity of tritium found
HAZARD OF TRITIATED LUMINOUS COMPOUNDS

TABLE IV

QUANTITY OF TRITIUM LOST BY COMPOUND 1 (471 μc/mg) AND COMPOUND 2 (210 μc/mg) WHEN SUBJECTED TO A STREAM OF MOIST AIR FOR 20 min

<table>
<thead>
<tr>
<th>Compound</th>
<th>Added lacquer (code No.)</th>
<th>H³ removed μc/mg compound</th>
<th>% H³ removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>1.89</td>
<td>0.40</td>
</tr>
<tr>
<td>1</td>
<td>RC2</td>
<td>2.08</td>
<td>0.44</td>
</tr>
<tr>
<td>1</td>
<td>RE</td>
<td>2.71</td>
<td>0.57</td>
</tr>
<tr>
<td>1</td>
<td>KCH</td>
<td>4.70</td>
<td>1.00</td>
</tr>
<tr>
<td>1</td>
<td>38</td>
<td>2.94</td>
<td>0.62</td>
</tr>
<tr>
<td>1</td>
<td>91</td>
<td>1.96</td>
<td>0.42</td>
</tr>
<tr>
<td>1</td>
<td>85</td>
<td>1.64</td>
<td>0.35</td>
</tr>
<tr>
<td>1</td>
<td>SGE</td>
<td>2.18</td>
<td>0.46</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>0.32</td>
<td>0.15</td>
</tr>
<tr>
<td>2</td>
<td>RE</td>
<td>0.64</td>
<td>0.31</td>
</tr>
<tr>
<td>2</td>
<td>KCH</td>
<td>1.10</td>
<td>0.52</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>0.30</td>
<td>0.15</td>
</tr>
<tr>
<td>2</td>
<td>91</td>
<td>0.46</td>
<td>0.22</td>
</tr>
<tr>
<td>2</td>
<td>85</td>
<td>0.36</td>
<td>0.17</td>
</tr>
<tr>
<td>2</td>
<td>SGE</td>
<td>0.48</td>
<td>0.23</td>
</tr>
</tbody>
</table>

in some people during the monitoring programme. During the last few months improvements have been made in factories A and B, particularly in the former. However, the hard core of the problem remains at these two factories. They use different luminous compounds but in both factories two luminizing machine operators maintain between a higher and a lower maximum permissible level more or less continuously.

The hopeful fact is that not one employee in factory C approaches even a lower maximum permissible level. Yet this factory uses nearly as much compound, in terms of radioactivity, as the other two. The explanation of this apparent contradiction is probably complex but two factors seem very important. Firstly, the employees in factory C operate the machines in turn whereas the other factories employ full-time machine operators. Secondly, factory C is air-conditioned and the standards of ventilation are considerably higher than in a normal factory. With regard to this second point, it is interesting that factory C, unlike factory A, has not enclosed its machines in separate enclosures which are exhausted. It relies entirely upon an extremely efficient evacuation of air from the room as a whole. This seems to be further evidence in support of the hypothesis that the main hazard to the machine operators consists of local high concentrations of tritiated water vapour or other vapour heavier than tritium gas.
H. G. JONES and B. E. LAMBERT

It is therefore reasonable to assume that given a sufficiently efficient exhaust system, tritium luminous compounds may be used under reasonably satisfactory conditions. However, this might prove rather expensive where these conditions do not already exist.

4.2. Chemical form of tritium absorbed

The greatest hazard to luminizers probably occurs at a time when the compound is mixed with its lacquer. Under these conditions it seems unlikely that much of the tritium which reaches the lungs of the luminizers is in the form of elementary tritium. Elementary tritium might well be given off the compounds initially and then become oxidized to or exchanged with water vapour. These reactions are not thought to proceed at a very fast rate in the absence of a catalyst [5] but it has been reported that such reactions are induced by a radiation field produced by beta rays from tritium itself if the specific activity is sufficiently high [6-8]. However, whether these reactions occur or not, the main hazard to luminizers is likely to be due to tritiated water and certainly the half-life of the tritium in the urine of two of the luminizers studied corresponded very accurately with that for tritiated water, i.e. 12 d.

It is possible, however, that other tritium compounds are given off by the luminous paint while drying. Thus the fact that acetone is a better solvent than water for the condensates from the tests described in section 2.4 is evidence for this. There is also some preliminary evidence that tritium may exchange into the molecules of organic solvents to some extent, at least under the conditions of the tests. No information is available concerning the metabolism of these labelled solvent molecules in humans or their radiological significance.

4.3. Radiation hazards due to tritium and radium luminous compounds

In this laboratory, both active and retired luminizers are measured for radium content by a whole-body counter and by measurements of radon in breath. During the last year 34 current luminizers from private industry were measured, about half the total labour force. Ten were found to contain more than one-fifth of a maximum permissible body burden of radium, five exceeded one-third and three had body burdens of 82%, 84% and 100% of the maximum permissible [9]. However, much of the radium contained in these current luminizers is likely to be retained for a short time only. Thus the employee who had a maximum permissible body burden of radium ceased luminizing and four months later contained only one-half of that quantity [9].

A group of 41 persons who luminized between 1945 and 1960 were also measured. Of these, six had greater than one-fifth of a maximum permissible body burden, four exceeded one-third and the highest result was 45% [9].

A comparison between the relative hazards of tritium and radium luminous compounds is therefore not easy. A consideration of external radiation dose to the general public favours tritium. The introduction of tritium has not, however, been an unmixed blessing to the luminizers themselves. Thus
the fractions of the corresponding maximum permissible body burden found in routine monitoring tend to be higher in the case of tritium, although they are not negligible in the case of radium. Secondly, tritium emits a $\beta$ particle of such low energy that environmental monitoring for tritiated water is not feasible. This means that a programme of urine monitoring has to be instituted, a situation which is disliked by some of the people involved. Thirdly, it is not certain that the hazard is due only to tritiated water and if other tritium-containing molecules are being absorbed, no appropriate maximum permissible body burdens are as yet available.

On the other hand, it should be argued that since the biological half-life of tritiated water is short, a maximum permissible body burden of the substance soon decreases when the person is removed from a contaminated atmosphere. This is not true of a high proportion of any radium absorbed. A maximum permissible body burden for tritiated water, as in the case of any other radioactive material, is based on the concept of a constant body content. This condition is unlikely to occur if the person concerned is being monitored continually. Secondly, radium luminizers are subjected to a possible dose of external radiation, an additional hazard which is absent in the case of tritium. Finally, research into tritiated luminous compounds continues and it is possible that compounds which are more stable under factory conditions will be produced.

REFERENCES


DISCUSSION

N. A. TAYLOR: Have you estimated the adsorbed radiation dose to soft tissues for the exposed persons and compared it with the permissible 5 rem/yr to total body or gonads? I consider this preferable to referring to body burdens in the case of isotopes with a short effective half-life, and it also has the advantage of avoiding the "problem" of the two quoted maximum permissible body burdens.

H. G. JONES: No, we have not done that. Incidentally, the U. K. A. E. A. use yet another figure for the maximum permissible level of tritiated water
in urine, namely the MPCW for tritiated water. This gives a working figure between the two I described.

S. JACKSON: In your oral presentation you mentioned that the concentration of tritiated water in urine corresponding to the maximum permissible body burdens was different from the concentration recommended in the paper by Jackson and Taylor*, namely the lower figure recommended for MPCU by ICRP Committee II (1959): It is my belief that the difference between MPCU and the lower figure you calculated is entirely due to the rounding-off in the calculations made by ICRP Committee II.

H. G. JONES: Yes, that is true.

W. LANGHAM (Chairman); As Chairman, I would like to comment on the question of two maximum permissible body burdens. It is unfortunate that the picture is confused by two values. There should be only one, but the ICRP could not agree on what should be considered the critical tissue. As far as I can see, it is difficult to rationalize the body water as a critical tissue, so the value for the total body would seem more logical.

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* JACKSON, S., and TAYLOR, N.A., "A survey of the methods used in the United Kingdom Atomic Energy Authority for the determination of radionuclides in urine", these Proceedings.
ASSESSMENT OF TRITIUM IN PRODUCTION WORKERS

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Abstract — Résumé — Аннотация — Resumen

ASSESSMENT OF TRITIUM IN PRODUCTION WORKERS. The tritium bioassay programme at the Savannah River Plant is geared for rapid urinalysis of large numbers of samples. More than 300,000 urine samples have been analysed in the past ten years.

A liquid scintillation counting procedure currently used for analysis of urine samples is described. Untreated samples containing as little as 1 μc of tritium per litre can be assayed in one minute. The detection limit for distilled urine is 5 × 10⁻⁴ μc of tritium per litre. Automation of equipment, optimum scintillation mixture and sample volumes, selection of reagents and counting containers, and elimination of interfering radionuclides are discussed.

Empirical studies of biological half-life are summarized. In 310 cases where the initial tritium concentrations in urine ranged from 20 to 118 μc/l, the average biological half-life was 9.5 d. The half-life varied inversely with ambient temperature and age of employees.

EVALUACIÓN DEL TRITIO EN EL PERSONAL DEDICADO A LA PRODUCCIÓN DE ESTE ISÓTOPO. En la planta del río Savannah se ha organizado un programa de determinación del tritio basado en el análisis rápido de gran cantidad de muestras de orina. En los diez últimos años se han analizado más de 300,000 de estas muestras.
Se describe un método de recuento, basado en un centelleador líquido, que se utiliza corrientemente para el análisis de las muestras de orina. El método permite determinar en 1 min muestras sin tratar que sólo contienen 1 μc de tritio por litro. El límite de detección, en el caso de la orina destilada, es de $5 \times 10^{-4}$ μc de tritio por litro. Se examina la automatización del equipo, la mezcla de centelleo y los volúmenes de muestras óptimos, la selección de reactivos y de recipientes de recuento, y la eliminación de radionúclidos susceptibles de interferir.

Se resumen los estudios empíricos realizados sobre el período biológico. En 310 casos en que la concentración inicial de tritio en la orina estuvo comprendida entre 20 y 118 μc/l, el período biológico medio fue de 9,5 d. El período biológico varió en relación inversa a la temperatura ambiente y a la edad de los individuos.

1. INTRODUCTION AND SUMMARY

The Savannah River Plant (SRP) is the major centre of tritium production in the United States. Quantities of tritium sufficient to present a health hazard to operating personnel are produced in SRP reactors by irradiation of lithium and by neutron absorption in the heavy-water moderator [1]. Tritium is also a minor product of fission [2]. Recent papers describe the procedures for controlling tritium health hazards at SRP [3], the analytical methods for assaying tritium in various media [4], and the uptake of tritium by SRP personnel [5]. This paper describes the methods currently used for the assessment of tritium in production workers.

The external radiation hazard from tritium is negligible, but radiological protection is complicated by two factors: (a) the low average energy of tritium beta particles (5.7 keV), and (b) the ease with which tritium oxide is assimilated. All of the oxide which enters the body is absorbed and equally distributed in body fluids [6]; therefore, urinalysis is an accurate method for determining the body burden of tritium.

The tritium bio-assay programme at SRP is geared for rapid urinalysis of large numbers of samples; approximately 60,000 urine samples from production workers are currently analysed each year. Employees who are exposed to tritium during a work day submit urine samples at the end of the work day. Since there is a time lapse between exposure and equilibrium in urine, an interval of at least 45 min is normally maintained between the last exposure and the submission of samples.

A liquid scintillation counting procedure, described in this paper, is used for rapid analysis of urine samples. An untreated sample containing as little as 1 μc of tritium (as HTO) per litre of urine can be counted in one minute. The International Commission on Radiological Protection recommends 1000 μc (23 μc of HTO per litre of urine) as the maximum permissible body burden; therefore, a detection limit of 1 μc per litre is adequate for monitoring the exposure of workers. The detection limit can be lowered to $5 \times 10^{-4}$ μc per litre by distilling the urine and extending the counting time.

Several improvements have been made in the liquid scintillation procedure during six years of routine use at SRP. Various reagents and counting containers have been tested, optimum scintillation mixtures and optimum spike and sample volumes have been determined, equipment for dispensing spikes and scintillation mixtures has been automated, and methods of detecting and eliminating interfering radionuclides have been developed.
The tissue dose from assimilated tritium is considered as whole-body irradiation and is added to the occupational gamma dose. In cases where the initial tritium concentration in urine is less than 20 μc per litre, a biological half-life of 12 d is assumed. In 310 cases where the initial concentrations ranged from 20 to 100 μc per litre, the average biological half-life was 9.5 d. The half-life varied inversely with ambient temperature and age of employees.

2. EXPERIMENTAL

Liquid scintillation counting is used most successfully to determine low-energy radionuclides in compounds soluble in organic solvents. Analysis of aqueous samples is less sensitive because of their limited solubility in scintillation mixtures and because of quenching. Quenching, or attenuation of pulses, causes appreciable reduction in absolute counting efficiency. A number of experiments were conducted to determine the optimum procedure for liquid scintillation analysis of urine samples. Since the amount of quenching varies in urine samples due to differences in solids content and colour, distilled water was used during much of the development work.

2.1. Apparatus

Samples were counted in a "Tri-Carb" liquid scintillation spectrometer (Model 314, Packard Instrument Company) equipped with an automatic sample changer and an 8-channel tape printout system. The instrument was modified to contain a specially designed "Lucite" chamber which is optically coupled with selected photomultiplier tubes (DuMont 6292 and E.M.I. 9536B). The freezer temperature was 4°C. Each instrument must be adjusted individually; typical high voltage is 1100 V, and typical discriminator settings are 5 to 50 V (analyser channel) and 50 V to infinity (monitor channel).

A specially designed automatic dispenser (Fig.1) fills each of 100 counting containers with 15 ml of scintillation mixture. The containers are held in a standard "Tri-Carb" turntable, which stops automatically after the last container is filled.

2.2. Reagents

Scintillation-grade PPO (2,5-diphenyloxazole) and POPOP (p-bis [2-(5-phenyloxazolyl)] benzene) were used as primary and secondary scintillators. Two qualities of p-dioxane were used as the primary solvent: one for routine analyses (Eastman Organic Chemicals, melting point 10.5-11.0°C) and the other for special samples which require lower detection limits (Mathieson-Coleman-Bell, spectro-quality). Naphthalene recrystallized from alcohol was used as a secondary solvent. To ensure that reagents are of consistent quality, each batch of scintillation mixture should be tested before use for urinalysis.
2.3. Selection of counting container

The ideal counting container is free of radioactive contamination, is an efficient transmitter of light, and is inexpensive. Of several container materials tested, polyethylene best meets all three requirements. Tests of polyethylene containers showed a blank sample count only about 5 cpm higher than background and a light transmission efficiency about 10% greater than that of glass containers. A 17-ml polyethylene vial which costs about $0.04 was selected for use at SRP. Each vial is used only once, to eliminate cross-contamination.

2.4. Effect of sunlight and fluorescent light

Figure 2 shows the effect of sunlight and fluorescent light on counting rates. Blank samples (consisting of distilled water and scintillation mixture), in vials of polyethylene, low K\textsuperscript{40} glass, and quartz, were cooled and then counted before and after a 10-s exposure to direct sunlight. The counting rate increased to several thousand counts per minute for each sample after exposure. Phosphorescence diminished with an initial half-
life of 1 to 2 min; re-establishment of the original counting rates required more than 6 h. One sample in a polyethylene vial was exposed to bright fluorescent light for 3 min; an hour was required to re-establish the original counting rate. DAVIDSON and FEIGELSON [7] obtained similar results for glass vials; they attributed the slow decay of phosphorescence to glass rather than to scintillation solution, and they reported that phosphorescence is lower with incandescent light.

2.5. Optimum scintillation mixture

The ingredients usually contained in scintillation mixtures for aqueous samples are p-dioxane, PPO, POPOP, and naphthalene [7, 8]. Screening tests were made (Fig. 3) to determine what mixture of these ingredients gives the highest counting efficiency with a spike of HTO. The optimum mixture
(No. 21) contained 4 g of PPO, 0.05 g of POPOP, and 120 g of naphthalene, all dissolved in 1000 ml of p-dioxane. Although additional mixtures were prepared with several other primary solvents and primary and secondary phosphors, none excelled mixture 21.

Eastman dioxane yielded a fourfold increase in absolute counting efficiency over other qualities of dioxane (except the more expensive spectro-quality), probably because it contained lesser amounts of the substances classified as quenchers [7, 9].

2.6. Optimum volumes of samples and scintillation mixture

The volumes of scintillation mixture and urine were varied, within the 17-ml capacity of the polyethylene vials, to determine optimum volumes for each. Results of these tests are shown in Fig. 4, together with results of similar tests for distilled water. (The urine and the water were spiked at different concentrations.)

![Fig. 4](image)

Optimum volumes of urine, water, and scintillation mixture

Maximum counting rates were obtained with 1 ml of urine and 15 ml of scintillation mixture, and with 3 ml of water and 13 ml of scintillation mixture. Tests with 25-ml polyethylene containers showed the optimum volumes to be 2 and 23 ml for urine and 4 and 21 ml for water. The total count increased about 25% with the larger container, but this gain was partially nullified by higher background count and greater expense.

2.7. Internal spiking of urine samples

The scintillation counting efficiencies of individual urine samples were inconsistent because of variations in solids content and colour. OKITA et al. [10] solved this problem by decolourizing each urine sample prior to analysis. The counting efficiency for each sample was determined by adding internal tritium standard and recounting the urine. WERBIN et al. [11] obtained good counting efficiency by distilling urine with benzene prior to analysis.
At the Savannah River Plant, untreated urine was assayed for tritium by counting before and after the addition of a small volume of tritium spike. For example, the initial count rate for a mixture of 1 ml of urine and 15 ml of scintillation mixture was 854 cpm, and the count rate after addition of 50 μl of distilled water containing 0.05 μc of tritium (equivalent to 50 μc of HTO per litre of urine) was 20854 cpm. The average count rate for blank urine is 54 cpm. By using the following formulae, it was determined that the original urine sample contained 2 μc of HTO per litre.

\[
\text{cpm with spike - original cpm = cpm due to spike}
\]

\[
\frac{\text{cpm due to spike}}{\mu c \text{ HTO per litre equivalent}} = \text{cpm/μc per litre due to spike}
\]

\[
\frac{\text{Original cpm - blank cpm}}{\text{cpm/μc per litre due to spike}} = \mu c \text{ HTO per litre of sample}
\]

Since the internal tritium spike is itself an aqueous solution which contributes to quenching, the influence of spike volume on the final urine assay was determined. A urine sample which contained 36 μc of HTO per litre was counted. Samples were internally spiked with 0.05 μc of HTO, added in volumes of 50, 100, 150, and 200 μl. The results of triplicate analyses for each spike volume are shown in Table I. The 50-μl spike volume resulted in an assay 3% higher than the known value, while the 200-μl spike yielded a result 15% high.

<table>
<thead>
<tr>
<th>Volume of spike (μl)</th>
<th>HTO (μc/l)</th>
<th>% high</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actual</td>
<td>Determined</td>
</tr>
<tr>
<td>50</td>
<td>36</td>
<td>37.0</td>
</tr>
<tr>
<td>100</td>
<td>36</td>
<td>37.8</td>
</tr>
<tr>
<td>150</td>
<td>36</td>
<td>39.5</td>
</tr>
<tr>
<td>200</td>
<td>36</td>
<td>41.3</td>
</tr>
</tbody>
</table>

These tests indicate that the internal spike should be in the minimum volume practical for routine analysis. A Gilmont micropipette-burette was found best for dispensing 50 μl of spike. Less time was required and greater accuracy was obtained with this pipette than with manual dispensers.

2.8. Effects of contaminating nuclides and acidity

The presence in urine of microcurie quantities of fission products other than tritium is very unlikely. Nevertheless, any significant quantities of
nuclides other than tritium can easily be detected with the liquid scintillation procedure. Previous work in this laboratory [12] showed that 17 other nuclides are counted more efficiently than tritium - some at 100%. Even other low-energy radionuclides; such as Ni63 and Cl4, can be detected by comparing the ratio of counts in the analyser and monitor channels. The spectrometer is adjusted so that 90% of the tritium pulses are registered in the low-energy analyser channel. The majority of counts due to other radionuclides fall in the monitor channel.

Unusually acidic urine samples may also reduce counting efficiency and cause a downward shift in counting spectra. Any discrepancy in the normal 9:1 ratio for tritium is easily detected. Any sample exhibiting such a discrepancy should be neutralized, distilled, and re-analysed.

2.9. Final procedure

The liquid scintillation procedure for determining tritium in urine samples is as follows: Dispense 1 ml of urine into a polyethylene bottle containing 15 ml of scintillation mixture (see Fig. 3 for optimum mixture). Eliminate all direct sunlight and use a minimum of artificial lighting during sample preparation. Place the sample in position in the automatic changer table. Let the sample cool for at least 30 min and count for 1 min. Spike the sample internally, recount for 0.5 min, and calculate the result (see section 2.7).

In routine work, groups of 100 bottles are filled by the automatic dispenser and precooled. The desired sensitivity is 1 μc of HTO per litre, and internal spiking is not performed unless the sample count is greater than 4000 cpm (equivalent to about 10 μc per litre). Analyser-to-monitor ratios are observed on the readout to verify that counts are due to tritium.

3. RESULTS AND DISCUSSION

The liquid scintillation procedure for tritium urinalysis has been in routine use at the Savannah River Plant for six years. The procedure is unmatched by other published methods of tritium urinalysis for accuracy, sensitivity, rapidity, and low cost per sample.

The previous method of analysis at SRP [13], which required more than 15 min per sample, consisted in generating tritium-hydrogen gas and measuring the current by the potential-drop Vibrating-Reed-Electrometer (VRE) method. This procedure yielded inaccurate results at concentrations near 1 μc of HTO per litre, because of background current fluctuations; however, the accuracy was good for activity above 10 μc per litre. Sixty-eight urine samples, each assaying higher than 10 μc of HTO per litre, were analysed by both methods. The over-all average result was 20.0 μc of HTO per litre by the VRE method and 19.8 μc of HTO per litre by the liquid scintillation method.

Urine samples can be assayed for tritium at levels below 1 μc of HTO per litre by extending the counting period to more than 1 min. For maximum sensitivity, a replicate method is used after distilling the urine. The optimum volumes of distilled urine and scintillation mixture are 3 and 13 ml,
respectively. In the replicate method, three or more aliquots of low-level sample, distilled water (blank sample), and low-level spike are distributed in large groups. The samples are counted on a 10-min cycle over a period of 2 to 3 d so that the total counting time for each type of sample is at least 300 min. Samples are then internally spiked and the HTO concentration is calculated.

The counting efficiency is 18% for routine urinalysis (1 and 15 ml) and 14% for the replicate method (3 and 13 ml). For comparison, the counting efficiency for water (3 and 13 ml) is 18%. Fifty spikes, each containing $4 \times 10^{-4}$ μc of HTO per litre of water, have been counted during the past two years by the replicate method; these spikes assayed $4 \times 10^{-4}$ μc per litre (120 tritium units) with a relative standard deviation of less than 25%. Because of the lower counting efficiency of distilled urine, its detection limit is about $5 \times 10^{-4}$ μc of HTO per litre.

KINARD [14] introduced a system for comparing scintillation procedures. In his system, the figure of merit for a particular procedure is the product of the percentage of water in a mixture and the counting efficiency. The figure of merit for routine urinalysis at SRP is 130, and the merit for replicate urinalysis is 250. For comparison, the water merit is 330.

4. ASSESSMENT OF BIOLOGICAL HALF-LIFE

More than 300,000 urine samples have been analysed for tritium since start-up of the Savannah River Plant some ten years ago. Only through urinalyses for tritium can the effectiveness of radiological controls in Plant manufacturing areas be accurately determined. The tissue dose from assimilated tritium is considered as whole-body irradiation and is added to the occupational gamma dose. The tritium dose ($D$) is estimated by the following equation

$$D \text{ (mrem)} = 0.73 \ T^*_B,$$

where $T^*_B$ = effective (biological) half-life, days;

$B$ = initial concentration of tritium in urine, μc/l.

A 12-d effective or biological half-life is assumed when the concentration of tritium in urine is less than 20 μc per litre. When the concentration exceeds 20 μc per litre, the effective half-life for the individual employee is determined. Data were examined from 310 cases where uptakes were 20 μc per litre or greater. The average effective half-life was found to be $9.5 \pm 4.1$ d (90% confidence limit) for ad libitum water intake. The distribution of half-lives over the range from 4 to 18 d is shown in Fig. 5. BUTLER [5] compared earlier results at SRP with those found by other investigators. In seven previous studies with deuterium oxide or tritium oxide at other locations, the biological half-lives ranged from 4 to 14 d.

Factors that affect the biological half-life were studied. Tritium retention is a function of body water turnover, which in turn is very much influenced by ambient temperature. Figure 6 shows the inverse correlation between biological half-life and temperature at the time of assimilation.
The mean temperature over the past six years for each month is plotted, together with the average half-life for that month. (Better correlation might be expected in a controlled study.) From these data the following comparisons can be made between ambient temperature and half-life:

- 45 to 60°F - 10.1 d.
- 60 to 70°F - 9.2 d.
- 70 to 80°F - 8.1 d.

The age of the employee also influences the biological half-life. Figure 7 shows the reduction in half-life with increasing age. The higher body water turnover rate for older individuals is thought by some investigators to be due to decreasing production of antidiuretic hormone [15]:

ACKNOWLEDGEMENT

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REFERENCES


DISCUSSION

W. N. SAXBY: I was interested to see your inverse correlation of tritium biological half-life with ambient temperature. In the United Kingdom,
where our temperatures are low, the mean biological half-life from a small number of cases of which I have knowledge is about 10 d, and this figure correlates well with your data. Dr. Jones' two cases, presented earlier*, also provide consistent data. The range of the UK half-lives now runs from about 6 to 12 d.

I should also like to ask whether you have found any evidence of a second long half-life component in the excretion data from any of your cases—such a component might be expected if there is any exchange with hydrogen well bound in tissue constituents.

F.E. BUTLER: No, we have not. We have followed many cases for a number of weeks, and I think it is amazing that we find consistency in the biological half-life between, say, the first two results and results several weeks later. I know of no tailing off of the half-life which might indicate organically bound tritium released at a lower rate.

H.G. JONES: I wish to ask two short questions. Firstly, did you find any sex difference in biological half-life? Secondly, I find no reference to the acidification of urine samples in your paper; did you acidify your samples and, if not, did you experience any trouble with the precipitation of phosphate and other solids?

F.E. BUTLER: The 310 cases studied were male production workers so we do not have data for females.

Urine is not routinely acidified. On occasion, salts have precipitated from the mixture, but with no resultant loss in counting efficiency.

P. HENRY: Was the exposure to tritium at a constant level or did the level vary?

F.E. BUTLER: The level of exposure to the production workers is not constant. All the cases are either accidental or deliberate, timed exposures.

P. HENRY: How often are the urine checks made on the workers?

F.E. BUTLER: They are sampled each day they are exposed to tritium.

W. LANCHAM: I would like to ask whether you investigated the drinking and eating habits of those individuals showing extremes of 4 and 18 d in the biological half-life of tritium water. This seems important in view of the fact that tritium half-life reflects the rate of replacement of the body water.

F.E. BUTLER: We do not at the moment have sufficient information available regarding individuals.

* JONES, H.G. and LAMBERT, B.E.: "The radiation hazard to workers using tritiated luminous compounds", these Proceedings.
THORIUM
(Session 14)
GAMMA-SPECTROMETRIC AND HISTO-AUTORADIOGRAPHIC INVESTIGATIONS ON THE DISTRIBUTION AND EXCRETION OF THORIUM AND ITS DAUGHTERS IN THOROTRAST PATIENTS*

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Abstract — Résumé — Аннотация — Resumen

GAMMA-SPECTROMETRIC AND HISTO-AUTORADIOGRAPHIC INVESTIGATIONS ON THE DISTRIBUTION AND EXCRETION OF THORIUM AND ITS DAUGHTERS IN THOROTRAST PATIENTS. The estimation of the internal radiation dose from thorium and its daughters in thorotrast patients presupposes the knowledge of the distribution of the nuclides of the thorium series within the organism. Moreover, the knowledge of the excretion of the thorium daughters with faeces, urine and exhalation is of importance.

At a series of cases of a ThO₂ incorporation 10-20 yr ago mainly two kinds of distribution patterns could be observed:

(a) Deposition of thorium-232 and its daughters mainly within the organs liver and spleen (and bone marrow);

(b) Simultaneous deposition of the X-ray contrast medium at the spot of the former injection.

The thorotrast deposits were analysed quantitatively in vivo and localized with the Frankfurt Nal (Tl)-total body γ-ray spectrometer (HUCO). In addition it was possible from excretion measurements to estimate the radioactive equilibrium state between thorium-232 and its daughters in the physiological steady state. Parallel analyses of section materials of former thorotrast patients showed similar results.

Mainly the question of the radioactive equilibrium state between thorium-232 and its daughters radium-228 and thorium-228 was investigated. The thorium-232 and thorium-228 content of different samples of soft tissue (liver, spleen), bone marrow and marrow-free bone were determined with the so-called mixing method and the obtained thorium-228 activities compared with results of γ-spectrometric analyses.

The observed activity ratios thorium-232/thorium-228 served as a base for calculations of both the thorium-232 and thorium-228 content of samples by histo-autoradiographic investigations.

Both methods and the results of the γ-spectrometric and histo-autoradiographic investigations are discussed in detail.

* This study is based on work supported in part by funds provided by the Bundesministerium für Wissenschaftliche Forschung, Federal Republic of Germany.
Des dosages faits parallèlement des coupes de tissus prélevées sur des malades ayant autrefois absorbé du thorotrast, ont donné des résultats similaires.

L’étude a surtout porté sur l’état d’équilibre radioactif, entre le thorium 232 et ses produits de filiation, le radium 228 et le thorium 228. Par la méthode dite de mélange, l’auteur a déterminé la teneur en thorium 232 et thorium 228 de divers échantillons de tissus mous (foie, rate), de moelle osseuse et d’os sans moelle, et il a comparé les chiffres obtenus pour l’activité de thorium 228 aux résultats de dosages par spectrométrie gamma.

Les rapports entre les activités observées pour le thorium 228 et le thorium 228 ont servi de base à la détermination de la teneur d’échantillons en thorium 232 et thorium 228 par histo-autoradiographie.

L’auteur étudie en détail les deux méthodes et les résultats des recherches par spectrométrie gamma et histo-autoradiographie.

**Gamma-Spectrométrische und Histio-Autoradiographische Untersuchungen der Verteilung von Thorium und seiner Tochterprodukte**

A. KAUL

L’étude a surtout porté sur l’état d’équilibre radioactif, entre le thorium 232 et ses produits de filiation, le radium 228 et le thorium 228. Par la méthode dite de mélange, l’auteur a déterminé la teneur en thorium 232 et thorium 228 de divers échantillons de tissus mous (foie, rate), de moelle osseuse et d’os sans moelle, et il a comparé les chiffres obtenus pour l’activité de thorium 228 aux résultats de dosages par spectrométrie gamma.

Les rapports entre les activités observées pour le thorium 228 et le thorium 228 ont servi de base à la détermination de la teneur d’échantillons en thorium 232 et thorium 228 par histo-autoradiographie.

L’auteur étudie en détail les deux méthodes et les résultats des recherches par spectrométrie gamma et histo-autoradiographie.

**Gamma-Spektrometrische und Histio-Autoradiographische Untersuchungen der Verteilung von Thorium und seiner Tochterprodukte**

A. KAUL

L’étude a surtout porté sur l’état d’équilibre radioactif, entre le thorium 232 et ses produits de filiation, le radium 228 et le thorium 228. Par la méthode dite de mélange, l’auteur a déterminé la teneur en thorium 232 et thorium 228 de divers échantillons de tissus mous (foie, rate), de moelle osseuse et d’os sans moelle, et il a comparé les chiffres obtenus pour l’activité de thorium 228 aux résultats de dosages par spectrométrie gamma.

Les rapports entre les activités observées pour le thorium 228 et le thorium 228 ont servi de base à la détermination de la teneur d’échantillons en thorium 232 et thorium 228 par histo-autoradiographie.

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L’auteur étudie en détail les deux méthodes et les résultats des recherches par spectrométrie gamma et histo-autoradiographie.
INTRODUCTION

For the proper understanding of the clinical-radiological data from persons with a body burden of thorium in the state of colloidal ThO₂ (thorotrast), as it was used in diagnostic medicine between 1930 and 1945, a knowledge of the internal radiation dose delivered by Th²³² and its daughters is required. Colloidal thorium dioxide, however, behaves quite differently from soluble thorium compounds, and rather complicated redistribution and self-absorption problems make dosimetry difficult.

An estimation of the internal radiation dose presupposes the knowledge of a series of parameters to be discussed in detail: (1) Evaluation of both the amount and distribution of Th²³² and its daughters by in vivo whole-body counting; (2) Determination of the steady-state activity ratios between Th²³² and its daughters years after the incorporation of thorotrast; and (3) Determination of the excretion of the Th²³² daughters in faeces, urine and exhalation.

1. ANALYSIS OF Th²³² DAUGHTERS BODY BURDEN BY WHOLE-BODY COUNTING FOR DIFFERENT DISTRIBUTION PATTERNS OF Th²³² AND ITS DAUGHTERS

Investigations of both the amount and distribution of Th²³² and its daughters within the bodies of thorotrast patients were carried out with the Frankfurt total-body γ-ray spectrometer "HUGO". The device, consisting of a non-collimated 8-in×4-in NaI(Tl) crystal, was designed and constructed in the same way as the one at the Argonne National Laboratories (Argonne, Ill., USA) [1]; the counter's construction is described in detail elsewhere [2, 3, 4].

As Th²³² and its daughters, after incorporation in the state of colloidal ThO₂, will be deposited in the liver, spleen and bone marrow of the reticuloendothelial system (RES) or, simultaneously, at the site of the injection, similar distribution patterns were imitated in a phantom for calibration of the spectrometer. This phantom consisted of a plexiglass cover, filled up with a tissue equivalent substance, and a real skeleton as described earlier [2, 3]. By variation of the position of even the uncollimated crystal in steps...
along the axis of a patient under the same conditions as in phantom calibration, both the amount and deposition of the incorporation could be determined.

The calibration of the spectrometer, however, presupposed the knowledge of the distribution of the thorium decay products in the liver and spleen. In a series of cases this question could be answered by total-body counting before and after extirpation of the spleen, or by analysis of section samples (liver and spleen). In agreement with RUNDO [5] the results showed that about 75% of Th\textsuperscript{232} and its daughters Ra\textsuperscript{228} and Th\textsuperscript{228} in the liver and spleen are deposited in the liver, whereas about 25% are to be found in the spleen.

In the same cases a comparison of the results of total-body measurements and analysis of autopsy and biopsy material was possible. The analysis of whole-body measurements before and after extirpation of the spleen or a perivascular deposit led to the same results as did the subsequent examination of the biopsy material and samples of tissue obtained at operation or autopsy. The results agreed within ±10% (on the average) (Table I) which was shown to be the accuracy of the in vivo determinations of the total-body thorium burden.

### Table I

**COMPARISON OF RESULTS BY DIRECT IN VIVO MEASUREMENT AND ANALYSIS OF AUTOPSY AND BIOPSY MATERIAL**

<table>
<thead>
<tr>
<th>Case</th>
<th>Ra\textsuperscript{228} activity (C)</th>
<th>Δ(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>In vivo (whole-body counting)</td>
<td>Autopsy biopsy</td>
</tr>
<tr>
<td>Bu. (parav. inf.)</td>
<td>5.0 \times 10^{-9}⁺</td>
<td>5.5 \times 10^{-9}</td>
</tr>
<tr>
<td>Wa. (spleen)</td>
<td>1.4 \times 10^{-8}**</td>
<td>1.2 \times 10^{-8}</td>
</tr>
<tr>
<td>Sc. (spleen)</td>
<td>9.7 \times 10^{-9}⁺</td>
<td>8.2 \times 10^{-9}</td>
</tr>
<tr>
<td>Sz. (spleen)</td>
<td>1.5 \times 10^{-7}⁺</td>
<td>1.6 \times 10^{-7}</td>
</tr>
</tbody>
</table>

Average: ~±10%

* Direct in vivo whole-body measurement. Before and after extirpation.
** Activity ratio: A(Ra\textsuperscript{228}) (liver)/A(Ra\textsuperscript{228}) (spleen) assumed to be 0.75:0.25.
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In Fig. 1 the analysis of three different distribution patterns with the body counter is demonstrated by means of three cases:

While in case Sz, Th$^{232}$ and its daughters are deposited exclusively in the liver and spleen, in the two other cases there is a simultaneous deposition of contrast medium at the site of the injection (perivascular deposit in neck or arm). In cases where the predominant deposits of colloidal ThO$_2$
are in the liver and spleen, a quantitative determination of the Th\(^{232}\) daughters body burden is rather simple by comparison of the normalized in vivo and phantom distribution curves. The analysis of more complicated distribution patterns, however, such as simultaneous perivascular deposits, is incomparably more difficult. The results, however, show that, even in these cases, there is a sufficient agreement between the normalized distribution curves observed in vivo and those obtained by phantom calibrations.

2. **DETERMINATION OF THE STEADY-STATE ACTIVITY RATIOS BETWEEN Th\(^{232}\) AND ITS DAUGHTERS**

2.1 Steady-state value of the activity ratio \(A(\text{Th}^{232})/A(\text{Th}^{228})\) in tissue and bone samples

A further supposition for the estimation of the internal radiation dose within the thorotrast deposits is the knowledge of the steady-state value of the activity ratio between Th\(^{232}\) and its decay products. While the daughters of Th\(^{232}\) may be detected by \(\gamma\)-ray spectrometry either directly or indirectly from their short-lived decay products, the determination of Th\(^{232}\), not in radioactive equilibrium with its daughters, is only possible by means of chemical methods or from the \(\alpha\)-radiation of Th\(^{232}\) itself, e.g. by \(\alpha\)-ray spectrometry or measurement of the total \(\alpha\)-ray activity at known Th\(^{228}\) content of the samples.

The steady-state value of the activity ratio between Th\(^{232}\) and Th\(^{228}\) in tissue and bone samples of thorotrast patients was examined by determining the total \(\alpha\)-ray activity of biopsy material and samples of tissue obtained at operation and autopsy, by means of the so-called mixing method [6, 7, 8]. By this method both the total \(\alpha\)-ray activity of ashed samples mixed with ZnS(Ag) as scintillator, and their Th\(^{228}\) content, were determined from measurements of the coincident double decay of Rn\(^{220}(\alpha)\rightarrow\text{Pb}^{216}(\alpha)\rightarrow\text{Pb}^{212}\) (half-life of Po\(^{216}\) = 0.16 s).

From the difference of the measured total \(\alpha\)-ray counting rate and the calculated counting rate of Th\(^{228}\) and its daughters, the Th\(^{232}\) activity of the samples was estimated, and the corresponding average activity ratios \(A(\text{Th}^{228})/A(\text{Th}^{232})\) for bone and soft tissue were determined. The following results were obtained:

\[
\begin{align*}
A(\text{Th}^{228})/A(\text{Th}^{232}) \text{ in soft tissue (liver, spleen)} & = 0.4 \pm 50\% \text{ (SD)}, \\
A(\text{Th}^{228})/A(\text{Th}^{232}) \text{ in bone} & = 1.67 \pm 50\% \text{ (SD)}. 
\end{align*}
\]

The results indicate that in the course of long-term ThO\(_2\) incorporation, the equilibrium value of the activity ratio between Th\(^{232}\) and Th\(^{228}\) within the organs of the RES reaches a steady state, where the ratio \(A(\text{Th}^{228})/A(\text{Th}^{232})\) is only about 40% of that at radioactive equilibrium.

For marrow-free bone the proportions are inverse. In the case of soft tissue (liver, spleen) this result may be explained by a wash-out of Ra\(^{228}\) (or Ac\(^{228}\)) as the parent of Th\(^{228}\), or of Th\(^{228}\) itself from the deposit. (See section 3.1).
In addition to determining the $^{228}$Th content by means of the mixing method, all samples were analysed by $\gamma$-ray spectrometry directly after extirpation, without any foregoing chemical treatment, or they were ashed and then assayed in a well-type crystal. The results of both the mixing method and the $\gamma$-ray spectrometry agree within $\pm 10\%$ on the average as demonstrated in Fig. 2.

![Graph showing comparison of measured $^{228}$Th activities by mixing method and both $\gamma$-ray spectrometry and histo-autoradiography.](image)

## 2.2 Histo-autoradiographic estimation of $^{232}$Th and $^{228}$Th content of tissue samples

In a series of samples the $^{232}$Th and $^{228}$Th contents were estimated autoradiographically from the number of $\alpha$-ray tracks within the photographic emulsion. Because simultaneous histological investigations were being made, the thickness of the histo-autoradiographic sections was less than in normal contact autoradiography and chosen to be 10 $\mu$m on the average. Consequently the thickness $d$ of the sections was less than the range $R$ of the $\alpha$-particles within the material. In such a case the proportion of the number of $\alpha$-particles emerging from a section of thickness $dR$ and an area $A$ to the number of $\alpha$-particles emitted within a section of thickness $d = R$ must be known. From consideration of a volume element of height $dh$ and area $dA$ at a distance $h$ from the base of the section, it can be shown that the number of $\alpha$-particles emerging from unit area per unit time is [9]

$$N_A = \frac{Nd}{2} \left(1 - \frac{d}{2R}\right) \text{ for } d \leq R,$$

(1)

where $N$ = number of $\alpha$-particles emitted by the volume element per unit
time (1/vol. \times \text{time}), \text{ and}
N_A = \frac{1}{\text{area} \times \text{time}}.

In the case where the thickness \( d \) is bigger than or equal to the range
\( R \) of the \( \alpha \)-particles in the section, 25\% of the \( \alpha \)-particles emitted within
the surface layer of thickness \( R \) emerge from an area \( A(A \gg R^2) \) per unit

\[ N_0 = \frac{N_{RA}}{4}, \quad (1a) \]

where \( N_0 = 1/\text{time} \).

The range of the \( \alpha \)-particles is itself dependent on the atomic number \( Z \)
and the density \( \xi \) of the material to be considered. After GLASSON \[10\]
there is rather a simple relation between the parameters range of the \( \alpha \)-
particles, density, and atomic number of the material, which describes
the experimental results with quite sufficient accuracy, i.e.

\[ R = 3.2 \times 10^{-4} \times R_0 Z^{2/3} (g/cm^2), \quad (2) \]

where \( R_0 = \text{range of the } \alpha \text{-particles in air (cm)} \).

The ranges of the different \( \alpha \)-particles from \( \text{Th}^{232} \) and its daughters
in air and material of atomic number \( Z \) and density \( \xi \) have been presented
by SIRI \[11\]. The resulting average mean range of the \( \alpha \)-particles of the
thorium series in radioactive equilibrium was 4.74 cm in air and
15.2 \times \left( Z^{2/3}/\xi \right) \mu \text{m in material of atomic number } Z \text{ and density } \xi.

If one takes the mean atomic number of water to be the same as that
for soft tissue, the resulting factor \( Z^{2/3} \) is 3.73, and the average mean range
of the \( \alpha \)-particles of the thorium series in radioactive equilibrium is 56.7 \mu \text{m}
in tissue of density 1 g/cm\(^3\). The actual state of the activity ratio between
\( \text{Th}^{228} \) and its parent \( \text{Th}^{232} \) in soft tissue of thorotrast patients proved to be
0.4 on the average (section 2.1), so that the resulting average mean range
is 52 \mu \text{m}.

At an average thickness of the histo-autoradiographic sections of 10 \mu \text{m}
and an average mean range of the \( \alpha \)-particles of the thorium series at a
steady state of the activity ratio considered above of about 52 \mu \text{m}, only 9\%
of the \( \alpha \)-particles emitted in a section of thickness \( d = R \) and an area \( A \) per
unit time emerge from a tissue sample of thickness \( d = 10 \mu \text{m} \) and area \( A \), i.e.

\[ N_0 = 0.087 \times N_{AR}, \quad (1b) \]

where \( N_0 = \text{number of } \alpha \text{-particles emerging from the section of thickness}
\( d(=10 \mu \text{m}) \) and area \( A \) per unit time (1/area \times \text{time}) .

The resulting number \( N \) of \( \alpha \)-particles emitted in a volume element of
radioactive tissue per unit time is

\[ N = 11.5 \times \frac{N_0}{RA}, \quad (1c) \]

and the specific radioactivity of the tissue sample
THORIUM AND ITS DAUGHTERS IN THOROTRAST PATIENTS

\[
A_s = 11.5 \times \frac{N_0}{t} \times \frac{10^2 \times 10^{12} \times 10^{-3}}{3.7 \times 10^{10} \times 3.6 \times 10^3 \times 24} \text{ (pc/mg)},
\]

where \( t \) = exposure time (d).

With Eq. (2) (Glasson’s relation between the mean range of the \( \alpha \)-particles, the mean atomic number and the density of tissue) the specific activity may be given as follows:

\[
A_s = 1.125 \times \frac{N_0}{t} \frac{10^2}{R \times A \times Z/3} \text{ (pc/mg).}
\]

At an activity ratio between \( \text{Th}^{228} \) and \( \text{Th}^{232} \) of 0.4 in soft tissue (liver, spleen) \( 1 + 5 \times 0.4 = 3.0 \) \( \alpha \)-particles per disintegrating \( \text{Th}^{232} \) atom are emitted. The resulting specific \( \text{Th}^{232} \) content of soft tissue samples at an average mean range of the \( \alpha \)-particles in air of 4.35 cm and a value of 3.73 for \( Z^{2/3} \) is

\[
A_s(\text{Th}^{232}) = 2.32 \times \frac{N_0}{t} \times 10^{-2} \text{ (pc/mg)}, \tag{4}
\]

where \( A \) = area of the examined section (mm\(^2\)).

\( N_0 \) = number of \( \alpha \)-ray tracks on the area \( A \),

\( t \) = exposure time (d).

The specific \( \text{Th}^{228} \) content of the samples may be calculated similarly under the condition that the \( \text{Th}^{228} \) activity of the tissues is taken to be 40\% of the calculated \( \text{Th}^{232} \) activity:

\[
A_s(\text{Th}^{228}) = 9.27 \times \frac{N_0}{t} \times 10^{-3} \text{ (pc/mg)}, \tag{5}
\]

In bone the activity ratio \( A(\text{Th}^{228})/A(\text{Th}^{232}) \) was found to be 1.67 on the average. The resulting average mean \( \alpha \)-particle range of \( \text{Th}^{232} \) and its decay products in soft tissue would be 58.4 \( \mu \)m. After SPIERS [12] the range of \( \alpha \)-particles in tissue is about 1.36 times the range in bone of density 2 g/cm\(^3\); so that the average mean range of the \( \alpha \)-particles in bone, at a steady-state activity ratio mentioned above, is 43 \( \mu \)m. With it the number of \( \alpha \)-particles emerging from a bone section of thickness 10 \( \mu \)m and area \( A \) per unit time is corresponding to Eq. (1b):

\[
N_0 = 0.1027 \times \text{NAR}. \tag{1d}
\]

At a disintegration rate of \( 1 + 5 \times 1.67 = 9.3 \) \( \alpha \)-particles per \( \text{Th}^{232} \) decay in bone and an average mean \( \alpha \)-particle range of 43 \( \mu \)m, the specific \( \text{Th}^{232} \) content of bone samples was calculated to be:

\[
A_s(\text{Th}^{232}) = 3.82 \times \frac{N_0}{t} \times 10^{-3} \text{ (pc/mg)}. \tag{6}
\]

Per \( \text{Th}^{228} \) disintegration \( \frac{1}{1.67} + 5 = 5.6 \) \( \alpha \)-particles of \( \text{Th}^{232} \) and its
daughters are emitted in bone, so that the resulting specific $\text{Th}^{228}$ content of bone samples is:

$$A_S(\text{Th}^{228}) = 6.35 \times \frac{N_0t}{A} \times 10^{-3} \text{ (pc/mg)}.$$ \hspace{1cm} (7)

In general, the total counted area of tissue and bone sections was 6.25 mm$^2$ divided into 100 squares at a microscopical amplification of 500 [13]. The mean exposure time amounted to 10–30 d. The actual time used was chosen according to the specific activity determined either by $\gamma$-ray spectrometry or by means of the mixing method described before. The mean $\text{Th}^{232}$ and $\text{Th}^{228}$ content of histo-autoradiographic sections calculated from the number of $\alpha$-ray tracks per unit counted area is effected with an error, which depends on the number of observed tracks per unit area and the total counted area. This error was of the same importance as the mean square error (standard deviation including biological variability) of the activity ratios $A(\text{Th}^{228})/A(\text{Th}^{232})$, that is $\pm 50\%$ on the average. In most of the cases there was good agreement ($\pm 10\%$) between the results of the histo-autoradiographic analysis and those of both $\gamma$-ray spectrometry and mixing method as can be seen in Fig. 2.

2.3 Activity ratio $A(\text{Th}^{228})/A(\text{Ra}^{228})$ by whole-body counting and analysis of autopsy and biopsy material

In a series of cases it was possible to study the question of the steady-state activity ratio between $\text{Th}^{228}$ and its parent $\text{Ra}^{228}$ by analysis of autopsy and biopsy material of thorotrast patients. The investigations were made by $\gamma$-ray spectrometry either of freshly extirpated tissue samples without any foregoing chemical treatment, or after incineration of the sample.

First the fresh samples were welded in plastic containers to obtain radioactive equilibrium between $\text{Th}^{228}$ and its daughters. They were then measured directly by $\gamma$-ray spectrometry with an 8-in X 4-in NaI(Tl) crystal. The ashed samples were sealed in test tubes and assayed in a well-type NaI(Tl) crystal of dimensions 2 in X 2.5 in [8, 14]. The results of both methods agreed to better than $\pm 10\%$. The $\text{Th}^{228}$ content of the samples was determined from the 2.62-MeV $\gamma$-rays of $\text{Tl}^{208}$, and the $\text{Ra}^{228}$ content was determined from both the 908- and 936-keV $\gamma$-rays of $\text{Ac}^{228}$ [8]. The calibration of the 8-in X 4-in NaI(Tl) spectrometer for untreated samples was done with calibrated $\text{Th}^{228}$ and $\text{ThO}_2$ solutions, the latter with known $\text{Th}^{228}$ and $\text{Ra}^{228}$ content, whereas the well-type crystal spectrometer was calibrated with $\text{Th}^{228}$ and $\text{Ra}^{228}$ labelled bone ashes. For the determination of the $\text{Ra}^{228}$ and $\text{Th}^{228}$ content of the samples the proportion of scattered quanta of energies above 1-MeV and the proportion of quanta of $\text{Th}^{228}$ daughters ($\text{Bi}^{212}$ and $\text{Tl}^{208}$) in the energy region of about 930 keV itself must be known. The proportion having to be subtracted from the integral counting rate within the chosen energy interval of 820–1020 keV of $\text{Ac}^{228}$ was determined relative to that within the energy region between 2480 and 2760 keV of $\text{Tl}^{208}$ [8].

The analysis of samples of liver, spleen and perivascular deposits led to the result that in the organs of the RES there was a 12% excess of $\text{Ra}^{228}$
over Th\(^{228}\), whereas in specimens of perivascular deposits the Ra\(^{228}\) was practically in radioactive equilibrium with its daughter Th\(^{228}\), i.e.

\[
\frac{A(\text{Th}^{228})}{A(\text{Ra}^{228})} \text{ in liver, spleen} = 0.89 \pm 10\% \text{ (SD)},
\]

\[
\frac{A(\text{Th}^{228})}{A(\text{Ra}^{228})} \text{ in perivascular deposits} = 0.96 \pm 10\% \text{ (SD)}.
\]

In compact bone the corresponding ratio proved to be 1.2, which means that Ra\(^{228}\) was in radioactive equilibrium with Th\(^{228}\) at about 80% only.

The analysis of total-body measurements led to the same results, whereby, however, the excretion of the Th\(^{228}\) decay products - as described in section 3 - had to be considered before. MILLER [15] in 1958 reported similar results as those described above concerning the activity ratio \(A(\text{Th}^{228})/A(\text{Ac}^{228})\) (0.89). Rundo [16, 17] and Muth et al. [18], however, published values of 0.65 to 0.71 and 0.79 to 0.84 respectively, related to the activity ratio \(A(\text{Th}^{228})/A(\text{Ra}^{228})\). The fact that there is no radioactive equilibrium between Th\(^{228}\) and its parent Ra\(^{228}\) may be explained by a wash-out of Th\(^{228}\) from the deposits in the liver and spleen. This wash-out seems to be different within the various organs such as liver/spleen and perivascular deposits, and it may be determined by the blood circulation within these organs. The observation of a smaller wash-out of Th\(^{228}\) in perivascular deposits, namely at about 40% of that for liver and spleen, proved true for the short-lived Th\(^{228}\) daughter Pb\(^{212}\), too. However, here the wash-out amounted to even about 80% of that for liver and spleen, as will be described in the following section.

2.4 Activity ratios \(A(\text{Ra}^{224})/A(\text{Th}^{228})\), \(A(\text{Pb}^{212})/A(\text{Th}^{228})\) and \(A(\text{Bi}^{212})/A(\text{Th}^{228})\) in autopsy and biopsy material

For the determination of the steady-state activity ratios between Th\(^{228}\) and its daughters, the tissue samples were welded in plastic containers immediately after extirpation - as described before - and were analysed by \(\gamma\)-ray spectrometry at different times after extirpation until Th\(^{228}\) and its daughters had reached radioactive equilibrium. The results showed that in all cases Ra\(^{224}\) was in radioactive equilibrium with its parent Th\(^{228}\) up to 10% corresponding to an activity ratio \(A(\text{Ra}^{224})/A(\text{Th}^{228})\) of 0.9, whereas in all but one of the spleens analysed (Fig. 3) Pb\(^{212}\) was only up to about 40% \((A(\text{Pb}^{212})/A(\text{Th}^{228}) = 0.4)\). In perivascular deposits the activity ratio \(A(\text{Pb}^{212})/A(\text{Th}^{228})\) proved to be 0.52 on the average. The 10% loss of Ra\(^{224}\) is due to the excretion of Ra\(^{224}\); the 40 - 50% loss of Pb\(^{212}\) is due to the excretion of Ra\(^{224}\), Rn\(^{220}\) and Pb\(^{212}\) itself from the deposits.

At the present time the question of the steady-state activity ratio between Pb\(^{212}\) and its decay product Bi\(^{212}\) has been answered only in one case of an extirpated spleen. Because of the short half-life of Bi\(^{212}\) of about 1 h, Pb\(^{212}\) and its daughter Bi\(^{212}\) will reach radioactive equilibrium within a few hours. In order to study the in vivo behaviour of Bi\(^{212}\) the analysis had to be started immediately after the extirpation. This was only possible by building up a mobile \(\gamma\)-ray spectrometer - consisting of a 2-in X 2.5-in NaI(Tl) crystal and a transistorized 512-channel analyser (Nuclear Data, USA) - close to the surgery. The extirpated spleen was welded in a plastic container as usual and analysed \(\gamma\)-ray spectrometrically for short counting
Activity ratio $A(\text{Pb}^{212})/A(\text{Th}^{228})$ in different extirpated organs and tissue samples

3. EXCRETION OF Th$^{232}$ DAUGHTERS IN FAECES, URINE AND EXHALATION

3.1 Excretion of Ra$^{228}$ with faeces

The analysis of samples of the liver, spleen and perivascular deposits by means of the mixing method (section 2.1) has shown that in the course of time (t ~ 20 yr) Th$^{232}$ and its decay product Th$^{228}$ reach a steady state of the activity ratio $A(\text{Th}^{228})/A(\text{Th}^{232})$ where Th$^{228}$ is in equilibrium with Th$^{232}$ at about 40% only. Furthermore, the $\gamma$-ray spectrometric analysis of the same samples led to the result that Ra$^{228}$ was in excess of Th$^{228}$ by 12% on the average (section 2.3). This means that Th$^{232}$ and its daughter Ra$^{228}$ must have reached a state of equilibrium where the Ra$^{228}$ activity of the samples was only 45% of the activity of Th$^{232}$. Even if it is assumed that at the time of incorporation of Th$\alpha_2$ no Ra$^{228}$ had been present in the deposits, the Ra$^{228}$ must have reached radioactive equilibrium during the
years (t ~ 20 yr) at about 90% with its parent Th$^{232}$. Therefore, from the actual deficiency of Ra$^{228}$ and Th$^{228}$ respectively, it seemed probable that an excretion of both nuclides from the deposits had occurred.

This assumption has been verified by the finding that Ra$^{228}$ is always present in the faeces of thorotrast patients [2, 3]. The quantitative analysis of the samples by $\gamma$-ray spectrometry proved that 0.03% of the total-body Ra$^{228}$ content are excreted with the daily faeces. Similar results had been published by HURSH [19], who had found a daily Ra$^{228}$ excretion of 0.026%.

Because of the observed daily variations in the Ra$^{228}$ content of the faeces even in the same patient (which can go up to 50%) in most of the cases excretion analyses were done over a period of at least 8-14 d. The samples were welded in plastic containers immediately after excretion and measured by $\gamma$-ray spectrometry, as described above.

The value of 0.03% Ra$^{228}$ body content excreted per day means that the body Ra$^{228}$ content increases during the years to a steady-state value equal to about 50% of the Th$^{232}$ activity, in agreement with the results by analysis of autopsy and biopsy material. In Fig. 5 the effective build-up of Ra$^{228}$ is plotted against time on the assumption that no Ra$^{228}$ was present within the deposits at the time of incorporation of ThO$_2$. The results indicate that about 10-15 yr after incorporation, Ra$^{228}$ reaches a steady-state level of about 50% (40% < $[A(\text{Ra}^{228})/A(\text{Th}^{232})]< 65\%$), in comparison with HURSH [19], who had found a value of 55% on the average.* Further results, published in literature (RUINDO, 1956/58 [16, 17]; MILLER, 1957 [15]; BASERGA/MILLER, 1960/61 [21]) generally agree within the given limits (± 50%) cited above.

In the same manner as in Fig. 5, the behaviour of Th$^{228}$ with time is demonstrated in Fig. 6, on the assumption that Th$^{228}$ was in radioactive equilibrium with Th$^{232}$ at the time of incorporation of the colloidal thorium dioxide. If there were no wash-out of Th$^{228}$ from the deposits, the Th$^{228}$ activity of the organs would decrease during the years from 100% radioactive

---

* For reasons of comparison, Hursh's values were converted for $T_{\text{phys}} = 5.84$ yr [20], instead of the former 6.7 yr.
Effective build-up of Ra\textsuperscript{228} with time in thorotrust deposits

Effective build-up of Th\textsuperscript{228} and Ra\textsuperscript{224} in thorotrust deposits
equilibrium with Th\(^{232}\) to about 50% fifteen years after the incorporation, which is the steady-state level of Ra\(^{228}\) as seen before. The actual steady-state level, however, proved to be 45% on the average as determined by in vivo whole-body counting and analysis of autopsy and biopsy material (section 2.3). This loss of Th\(^{228}\) within the deposits might be due to a translocation of Th\(^{228}\) from the deposits to the skeleton, where the activity ratios \(A(\text{Th}^{228})/A(\text{Th}^{232})\) and \(A(\text{Th}^{228})/A(\text{Ra}^{228})\) proved to be 1.67 and 1.2 respectively. In some cases, however, a measurable faecal Th\(^{228}\) excretion of 0.01% per day could be found, though no significant Th\(^{228}\) excretion should be observed \([19, 21, 22, 23]\). Nevertheless the Th\(^{228}\) activity of the deposits in the RES,liver and spleen seems to decrease at first and then to increase later on with an effective half-life of about 1.6 yr to a steady-state value equal to 45% of the Th\(^{232}\) activity on the average.

3.2 Excretion of Ra\(^{224}\) with faeces

The analysis of extirpated tissue samples by \(\gamma\)-ray spectrometry showed a steady-state value of the activity ratio \(A(\text{Ra}^{224})/A(\text{Th}^{228})\) of 0.9 on the average (section 2.4). If the 10% deficiency of Ra\(^{224}\) is assumed to be due to the excretion of this isotope from the body, an excretion of about 2% of the total-body Ra\(^{224}\) burden should be observed per day. Since 95–99% of the excreted Ra\(^{224}\) may be found in the daily faeces \([19, 24]\), the expected excretion of about 2% of the total-body Ra\(^{224}\) content must be excreted with the daily stool exclusively. This figure was verified in our series of cases as is shown in Table II. About 2% of the total body Ra\(^{224}\) content was excreted in the faeces per day with a biological variability of about 50%. A total of 80 samples from 10 patients, specified in the table, were analysed, i.e. an average of 8 daily samples per case. The results indicate an effective half-life of Ra\(^{224}\) of 3.3 d on the average, which is in good agreement with a value of 3.2 d calculated from Hursh's excretion factor for Ra\(^{224}\) \([19]\).

In Table III mean values of the effective half-lives of Ra\(^{228}\), Th\(^{228}\) and Ra\(^{224}\) are put together. These values were calculated from the steady-state values of the activity ratios between Th\(^{232}\) and its daughters, obtained by whole-body counting and analysis of autopsy and biopsy material or from the excretion factors of the radionuclides concerned. The values calculated from the different steady-state activity ratios given in the literature \([15, 16, 17, 19, 21]\) agree with our own values within the biological variability of about ±50%.

3.3 Excretion of Pb\(^{212}\) with faeces and urine

The analysis of stool samples by \(\gamma\)-ray spectrometry, immediately after excretion \((t \leq 5\) h\), showed that Pb\(^{212}\) is excreted in the faeces only up to about 80% in radioactive equilibrium with Ra\(^{224}\). Since a part of the excreted lead isotope is built up from Ra\(^{224}\) and Rn\(^{220}\) during the stay of the faeces within the intestine, an attempt was made to estimate the actual amount of Pb\(^{212}\) excreted into the intestine. It was assumed that lead is excreted into the large intestine, similar to other heavy metals, with an average stay of the faeces within the large intestine of about 10 h \([25]\). Furthermore it was
TABLE II

AVERAGE DAILY FAECAL EXCRETION OF Ra\textsuperscript{228} IN PER CENT
OF TOTAL-BODY Th\textsuperscript{228} AND Ra\textsuperscript{224} CONTENT

<table>
<thead>
<tr>
<th>Case</th>
<th>Depot</th>
<th>Total-body Th\textsuperscript{228} cont. (At)</th>
<th>Average daily Ra\textsuperscript{224} excretion (faeces) (10^{-3} c/d)</th>
<th>Average daily Ra\textsuperscript{224} excretion 10^{-3} c/d x A\textsubscript{1} (Th\textsuperscript{228})</th>
<th>Average daily Ra\textsuperscript{224} excretion 10^{-3} c/d x A\textsubscript{1} (Ra\textsuperscript{224})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bu. (1)</td>
<td>L/S P. L. (Arm)</td>
<td>0.71</td>
<td>0.30</td>
<td>1.13</td>
<td>1.26</td>
</tr>
<tr>
<td>Bu. (2)</td>
<td>L/S P. L. (Arm)</td>
<td>0.66</td>
<td>0.76</td>
<td>1.18</td>
<td>1.31</td>
</tr>
<tr>
<td>Fe.</td>
<td>L/S</td>
<td>1.64</td>
<td>1.70</td>
<td>1.04</td>
<td>1.15</td>
</tr>
<tr>
<td>A. Sch. (1)</td>
<td>L/S</td>
<td>2.90</td>
<td>2.30</td>
<td>0.79</td>
<td>0.88</td>
</tr>
<tr>
<td>A. Sch. (2)</td>
<td>L</td>
<td>1.96</td>
<td>2.90</td>
<td>1.48</td>
<td>1.55</td>
</tr>
<tr>
<td>M. Sch.</td>
<td>L/S</td>
<td>1.30</td>
<td>3.50</td>
<td>2.69</td>
<td>3.00</td>
</tr>
<tr>
<td>Sl.</td>
<td>L/S</td>
<td>1.76</td>
<td>4.70</td>
<td>2.67</td>
<td>2.97</td>
</tr>
<tr>
<td>Sz. (2)</td>
<td>L</td>
<td>4.50</td>
<td>6.95</td>
<td>1.54</td>
<td>1.71</td>
</tr>
<tr>
<td>Wa.</td>
<td>L/S P. L. (Neck)</td>
<td>2.60</td>
<td>2.10</td>
<td>0.81</td>
<td>0.90</td>
</tr>
<tr>
<td>Wil.</td>
<td>L/S</td>
<td>0.55</td>
<td>2.50</td>
<td>4.50</td>
<td>5.00</td>
</tr>
</tbody>
</table>

Average: 1.79 ± 1.17**

(1) = Before
(2) = After
exirpation of spleen or parav. infiltr.

* Calculated for A\textsubscript{1} (Ra\textsuperscript{224})/A\textsubscript{1} (Th\textsuperscript{228}) = 0.9 (biopsy and autopsy material)

** Standard deviation (including biol. variability)

L = Liver
S = Spleen
P. L = Parav. infiltr.
<table>
<thead>
<tr>
<th>Author</th>
<th>Ra²²⁶ (Tphys = 3.64 a)</th>
<th>Th²²⁸ (Tphys = 1.9 a)</th>
<th>Ra²²⁴ (Tphys = 3.54 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Autopsy biopsy</td>
<td>In vivo</td>
<td>Excretion</td>
</tr>
<tr>
<td>J. Rundo (1956)</td>
<td>3.04*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>J. B. Hursh et al. (1957)</td>
<td>-</td>
<td>-</td>
<td>3.23*</td>
</tr>
<tr>
<td>J. B. Hursh (1957)</td>
<td>2.50*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C. E. Miller (1957)</td>
<td>-</td>
<td>3.24</td>
<td>(n= 1)</td>
</tr>
<tr>
<td>R. Baserga et al., C. E. Miller (1960/61)</td>
<td>5.6</td>
<td>(n= 1)</td>
<td>-</td>
</tr>
<tr>
<td>A. Kaul (1962/63)</td>
<td>2.62±1.33**</td>
<td>(n= 10)</td>
<td>5.24±0.62**</td>
</tr>
<tr>
<td></td>
<td>2.63±0.46 ± (SD)</td>
<td>.51± 0.31 ± (SD)</td>
<td>3.05±0.34 ± (SD)</td>
</tr>
</tbody>
</table>

* Corrected for Tphys = 5.84 a
** Standard deviation (including biological variability)

- : Number of cases or samples resp.
( ): Values not well established in the author’s opinion
** : Standard deviation (including biological variability)
assumed that no resorption of lead takes place during the passage of the faeces through the intestine, and that no loss of Rn$^{220}$ by diffusion occurs. On the basis of these assumptions it may be shown that Pb$^{212}$ will be excreted into the large intestine up to about 60% ($\approx 30\% \leq 80\%$) in radioactive equilibrium with Ra$^{224}$ (Fig. 7). On the other hand, the average daily urinary Pb$^{212}$ excretion proved to be about 0.8% per total-body Th$^{228}$ content, as is demonstrated in Table IV. This means an excretion of about $8 \times 10^{-10}$ c Pb$^{212}$ with a 24-h urine sample for a total body Th$^{228}$ burden of 0.1 $\mu$C. Similar measurements were made by MUTH et al. [18], who, however, had found a 5 times lower urinary excretion of Pb$^{212}$.

3.4 Excretion of Rn$^{220}$ with exhalation.

In addition to the whole-body and excretion measurements, the Rn$^{220}$ (thoron) concentration of the expired air of a series of thorotrast patients was measured. Table V gives the results of these measurements. The equivalent total body Th$^{228}$ values calculated from the Rn$^{220}$ measurements represent the radioactivity of a Th$^{228}$ solution in radioactive equilibrium with its daughters, which gives the same thoron concentration at an emanation rate of 100% and a flow-rate corresponding to the breathing rate. By comparison of the equivalent total body Th$^{228}$ values with the actual Th$^{228}$ con-
### Table IV

**AVERAGE DAILY URINARY EXCRETION OF $\text{Pb}^{212}$ IN PER CENT OF TOTAL-BODY $\text{Th}^{228}$ CONTENT**

<table>
<thead>
<tr>
<th>Case</th>
<th>Depot</th>
<th>Total-body $\text{Th}^{228}$ cont. ($A_t$)</th>
<th>Average daily $\text{Pb}^{212}$ excretion (urine)</th>
<th>Average daily $\text{Pb}^{212}$ excretion. ($% / \text{d} \times A_t (\text{Th}^{228})$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bl.</td>
<td>L/S</td>
<td>0.89</td>
<td>7.9</td>
<td>0.89</td>
</tr>
<tr>
<td>M. Sch.</td>
<td>L/S</td>
<td>1.30</td>
<td>10.3</td>
<td>0.79</td>
</tr>
<tr>
<td>Sl.</td>
<td>L/S</td>
<td>1.76</td>
<td>13.5</td>
<td>0.77</td>
</tr>
<tr>
<td>Wil.</td>
<td>L/S</td>
<td>0.55</td>
<td>5.4</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Average</strong></td>
<td><strong>0.83 ±0.09</strong></td>
<td></td>
</tr>
</tbody>
</table>

L = Liver
S = Spleen
* = Standard deviation (including biological variability)

tent determined by whole-body counting, the rate of $\text{Rn}^{220}$ exhalation in expired air proved to be 12% on the average, in rather good agreement with RUNDO et al. [26] and MUTH et al. [18] considering the biological variability.

4. **ESTIMATION OF THE INTERNAL RADIATION DOSE IN LIVER AND SPLEEN FOR DIFFERENT AMOUNTS OF INCORPORATED THOROTRAST**

4.1 Estimation of the injected amount of thorotrast

When the different steady-state values of the activity ratios between $\text{Th}^{232}$ and its daughters, and of the corresponding excretion factors, are known, it is possible to estimate the total radiation dose delivered to the liver and spleen at different times after the incorporation of colloidal thorium dioxide. The calculations were made for injections of 10–70 ml of thorotrast as observed in a series of cases (Table VI). The estimation of the amount of $\text{ThO}_2$ which had been incorporated was accomplished on the basis of a series of assumptions which will be discussed in detail:

(a) The skeletal $\text{Th}^{232}$ content was neglected in comparison with that of the liver and spleen. This assumption is justified only within limits, as
## TABLE V

EXHALATION OF Rn$^{220}$ (THORON) IN THOROTRAST PATIENTS

<table>
<thead>
<tr>
<th>Case</th>
<th>Depot</th>
<th>Total-body Th$^{228}$ cont. ($A_t$) $(10^{-1} \text{ c})$</th>
<th>Equiv. total-body Th$^{228}$ cont. ($A_t$) from thoron measurement $(10^{-4} \text{ c})$</th>
<th>Equiv. total-body Th$^{228}$ Act. Th$^{228}$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>L/S</td>
<td>0.89</td>
<td>1.20</td>
<td>13.5</td>
</tr>
<tr>
<td>Bu. (1)</td>
<td>L/S</td>
<td>0.71</td>
<td>0.88</td>
<td>12.4</td>
</tr>
<tr>
<td>Gl.</td>
<td>L/S</td>
<td>2.60</td>
<td>5.90</td>
<td>22.7</td>
</tr>
<tr>
<td>Ha.</td>
<td>L/S</td>
<td>0.074</td>
<td>0.03</td>
<td>4.0</td>
</tr>
<tr>
<td>He.</td>
<td>L/S</td>
<td>0.60</td>
<td>0.39</td>
<td>6.5</td>
</tr>
<tr>
<td>Schr.</td>
<td>L/S</td>
<td>0.48</td>
<td>0.32</td>
<td>6.7</td>
</tr>
<tr>
<td>A. Sch. (1)</td>
<td>L/S</td>
<td>2.90</td>
<td>3.00</td>
<td>10.4</td>
</tr>
<tr>
<td>A. Sch. (2)</td>
<td>L</td>
<td>1.96</td>
<td>1.60</td>
<td>8.2</td>
</tr>
<tr>
<td>Sz. (1)</td>
<td>L/S</td>
<td>6.00</td>
<td>8.70</td>
<td>14.5</td>
</tr>
<tr>
<td>Wi.</td>
<td>L/S</td>
<td>0.17</td>
<td>0.46</td>
<td>27.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Average</td>
<td></td>
<td>12.6 ± 7.2**</td>
</tr>
</tbody>
</table>

L = Liver          S = Spleen          K = Kidney
P. L = Parav. Infiltr.
(1) Before extirpation of spleen or parav. infiltr.
(2) After extirpation

* Equivalent total-body Th$^{228}$ values from thoron measurements represent the activity of A Th$^{228}$ solution in radioactive equilibrium with its daughters, which gives the same thoron concentration at an emanation rate of 100% and a flow rate corresponding to the breathing rate.

** Standard deviation (including biological variability)
### TABLE VI

**ESTIMATED INCORPORATED AMOUNTS OF THOROTRAST BY WHOLE-BODY COUNTING**

| Case | Depot | Total-body Th$^{228}$ cont. $(10^{-7}$ c) | Th$^{228}$ cont. in Total-body Th$^{232}$ cont. Prob. amount of incorp. thorotrast (ml) |
|------|-------|------------------------------------------|-------------------------------------------------|----------------------------------------------------------------------------------|
|      |       | L.  | S.  | P. L | $(10^{-7}$ c) | (g) |                                                                                  |
| Bl.  | L/S   | 0.89(a) | 0.67(b) | 0.22(b) | 2.2(c) | 2.0(d) | ~10 |
| Bu.  | L/S/P. L | 0.71 | 0.45 | 0.15 | 0.11 | 1.8 | 1.6 | ~10 |
| Fe.  | L/S/P. L | 1.64 | 0.40 | 0.13 | 1.11 | 4.1 | 3.7 | ~20 |
| Gi.  | L/S   | 2.60 | 1.95 | 0.65 | - | 6.5 | 5.9 | ~30 |
| Ha.  | L/S/K. | 0.074 | ? | ? | ? | 0.2 | 0.18 | ~10 |
| He.  | L/S/P. L | 0.60 | 0.18 | 0.06 | 0.36 | 1.5 | 1.4 | ~10 |
| A. Sch. | L/S | 2.93 | 2.20 | 0.73 | - | 7.3 | 6.6 | ~30 |
| M. Sch. | L/S | 1.30 | 0.97 | 0.33 | - | 3.3 | 3.0 | ~15 |
| Schr. | L/S | 0.48 | 0.35 | 0.12 | - | 1.2 | 1.1 | ~10 |
| Si.  | L/S | 1.76 | 1.32 | 0.44 | - | 4.4 | 4.0 | ~20 |
| Sz.  | L/S | 6.00 | 4.50 | 1.50 | - | 15.0 | 13.5 | ~70 |
| Wa.  | L/S/P. L | 2.60 | 0.41 | 0.14 | 2.05 | 6.5 | 5.9 | ~30 |
| Wi.  | L/S | 0.17 | 0.13 | 0.04 | - | 0.4 | 0.36 | ~2(1) |
| Wil. | L/S | 0.55 | 0.41 | 0.14 | - | 1.4 | 1.3 | ~10* |

**Assumptions:**

(a) Th$^{228}$ content in bone and bone marrow neglected.

(b) Activity ratio $A$ (Th$^{228}$) (liver): $A$ (Th$^{228}$) (spleen) = 0.75:0.25.

(c) Activity ratio $A$ (Th$^{232}$)/$A$ (Th$^{228}$) = 2.5 (±50%). Th$^{232}$ content in bone and bone marrow neglected.

(d) Specific Th$^{228}$ content of thorotrast: 0.2 g/ml.

* Incorporated amount of thorotrast known to be 10 ml.
in the entire skeleton containing bone marrow, about 30% of the total injected thorium dioxide seems to be fixed, whereas only 0.6% of the total injected Th\textsuperscript{232} activity proved to be deposited in the entire skeleton free of marrow, as obtained from measurements of clean trabecular or cortical bone [27].

(b) The distribution of the total amount of Th\textsuperscript{232} and its daughters in the liver and spleen was assumed to be 3:1, according to the experimental results (see section 1).

(c) A steady-state value of 0.4 for the activity ratio between Th\textsuperscript{228} and Th\textsuperscript{232} was assumed (A(Th\textsuperscript{228})/A(Th\textsuperscript{232}) = 0.4), as was shown by analysis of autopsy and biopsy material; besides this, the excretion of Th\textsuperscript{232} was assumed to be negligible [19].

(d) The calculations of the probable amounts of incorporated colloidal thorium dioxide were made for an average specific Th\textsuperscript{232} content of 0.2 g/ml thorotrast [17].

In one case (case WIL, Table VI, last line) the amount of incorporated thorotrast was known to be 10 ml, so that a comparison between the calculated and actual amount of incorporated thorotrast became possible. By whole-body counting, and from consideration of the steady-state values of the activity ratios between Th\textsuperscript{232} and its daughters, a total-body Th\textsuperscript{232} content of about 1.3 g was determined. If a mean skeletal activity (bone + bone marrow) of 30% of injected Th\textsuperscript{232} was taken into account, the total body Th\textsuperscript{232} burden proved to be 1.8 g on the average, corresponding to 9 ml of thorotrast formerly incorporated, in comparison with the actual 10 ml injected years ago.

4.2 Self-absorption of α-particles in ThO\textsubscript{2} aggregates

As mentioned in the Introduction, in addition to the rather complicated states of equilibrium between Th\textsuperscript{232} and its daughters, an important factor (affecting the internal radiation dose) is the precise manner in which the colloidal thorium dioxide becomes distributed within the body after incorporation. Investigations by different authors have shown [28, 29, 30, 31] that the particles of the colloid form aggregates in the cells of the RES, and tend to increase in size up to even 100 \(\mu\)m in diam., resulting in a considerable self-absorption of the α-particles of Th\textsuperscript{232} and its decay products. For tissue containing aggregates of various sizes, the fraction of the energy dissipated in surrounding tissue by the emitted α-particles has been determined by ROTBLAT and WARD [30; 32] who found, by tissue analyses, a correlation between this fraction and the thorium concentration in the tissue. The corresponding formal expression has been modified by RUNDO [17] on an empirical basis to describe the formation of aggregates observed in animal experiments [31, 33].

4.3 Results of the dose calculations

Based upon the results of investigations of the redistribution of the colloid and the self-absorption of α-particles within the aggregates, the α-, β- and γ-ray dose rates as well as the corresponding cumulative doses in the liver and spleen were calculated for the observed steady-state equi-
librium values between Th$^{232}$ and its daughters. The calculations were made on the assumption that Th$^{228}$ was incorporated in radioactive equilibrium with Th$^{232}$. Besides this, it was assumed that practically no Ra$^{228}$ had been incorporated, because Ra$^{228}$ is unlikely to exist in the colloidal form at pH 7, and adsorbs on the walls of the original thorotrast ampoule [34]. The assumption that Th$^{228}$ was in equilibrium with Th$^{232}$ at the time of injection may lead to values of the dose rate and cumulative dose which are too high.

Fig. 8

Calculated α-ray dose rate in the liver and spleen at different times after incorporation of various amounts of thorotrast.

Figures 8 and 9 demonstrate the results of the dose calculations. As an example, the α-ray dose rate and cumulative dose in the liver and spleen (average mass 1700 g and 150 g respectively [35]) are plotted versus time for different amounts of incorporated thorotrast. Similar curves were obtained for both the β- and γ-ray dose rate and cumulative dose. Besides this, the calculated α-ray dose rate for a 11- and 14-yr thorium burden, as a function of the Th$^{232}$ concentration mg Th$^{232}$/g tissue of the considered organs, was compared to results of RUNDO [17], which proved to be in agreement within 10% on the average (Fig. 8). The difference is mainly due to different values of the steady-state activity ratios between the thorium daughters.

For a period of 17 yr, which seems to be the mean latent period from the injection of thorotrast to the recognition of cancer — according to published cases (average of 40 cases) summarized and studied by FABER [36] — the total internal radiation dose delivered to the liver and spleen proved to
be 370–640 rad and 970–1430 rad respectively, for an average incorporated amount of 10–20 ml of thorotrast (which is the dose of thorotrast given to about 75% of a total of 481 living patients [36]). The $\beta$-ray and $\gamma$-ray doses are about 6% and 3% respectively of the total cumulative dose.

ACKNOWLEDGEMENTS

Thanks are due to Miss B. Zimmermann for her technical assistance. Special thanks are due to Dipl. Phys. W. Stahlhofen for the analysis of tissue samples by means of the mixing method, and to Dr. F. Unnewehr for the preparations of the histo-autoradiographic tissue sections.

The author is also indebted to Drs. L. D. Marinelli and R. M. Parr of the Radiological Physics Division of the Argonne National Laboratory, United States of America, for their kind revision of the paper and discussion of the results.

REFERENCES

THORIUM AND ITS DAUGHTERS IN THOROTRAST PATIENTS

[34] RUNDO, J., Brit. J. Radiol. 28 (1955) 615.

DISCUSSION

H. WYKER: Can you tell me anything about the particle size distribution of the Thorotrast used previously?

A. KAUL: At the time of incorporation, the diameter of the colloidal ThO₂ particles was not more than 1 μm if I remember correctly.

Results of Ward, Rotblat and Rundo (United Kingdom) have shown - as mentioned in my paper - that within about 10 yr after incorporation the particles tend to form aggregates, which will increase the size up to 100 μm on the average. The result is considerable self-absorption of the α-particles
within the aggregates, so that the dose or dose rate due to the $\alpha$-particles will be reduced.

The authors I just mentioned described this self-absorption by semi-empirical equations, based upon results of tissue analyses of both Thorotrast patients and animal experiments.

J. RUNDO: Perhaps I can add that the experimental findings referred to by Dr. Kaul show that not only do the sizes of the aggregates of Thorotrast particles increase with time after deposition in liver and spleen, but at any given time the average size of the aggregates seems to increase with increasing concentration of thorium in the tissue (liver and spleen).

A. BEN HAIM (IAEA): In the IAEA Laboratory we have been trying to localize Thorotrast deposits with the aid of a collimating device, using the standard scanning geometry of our whole-body counter. The collimator consists of lead bricks with a 10-cm slit, in which a set of tungsten plates is placed. The scan was divided into 20 intervals, each of 9.4 cm in length. Although we have not done a detailed quantitative analysis of the data, Figure ID shows that we can observe the Thorotrast and its radioactive daughters to be deposited mainly in the liver and spleen. I must add that the counts plotted represent the integrated 2.6-MeV peaks, and we expect a better spatial resolution with the lower-energy gamma rays.

A. KAUL: Bearing in mind the difficulty of comparing the effects of Thorotrast and radium-226 owing to the different ways in which they are distributed after incorporation in the body, I would like to add a few words regarding the related question of the dose delivered by thorium-232 and its daughters to the marrow-free skeleton.

From measurements on clean trabecular and cortical bones we estimated that about 0.6% of the incorporated thorium-232 is deposited in the marrow-free skeleton. On the other hand, the activity ratios $A(\text{Th}^{228})/A(\text{Th}^{232})$ and $A(\text{Ra}^{228})/A(\text{Th}^{232})$ for marrow-free bones of patients with a 20 yr Thorotrast body burden proved to be 1.67 and 1.39 respectively. Assuming the translocation of radium-228 and thorium-228 to the skeleton - mainly from
the liver and spleen deposits — to be proportional to the amount of these radionuclides in the deposits, about 2% of the total radium-228 and 3% of the total thorium-228 body burden is located in the entire marrow-free skeleton 20 yr after incorporation. The α-, β- and γ-ray dose rate to 5 μm osteocytes 20 yr after the injection of, say, 20 ml of Thorotrast is thus about 13 mrad/week. The dose rate to 5 μm osteocytes corresponding to a skeletal radium-226 burden of 0.1 μc, which is the maximum permissible body burden, is about 50 mrad/week.

Consequently, even with four times as much injected Thorotrast, which is 80 ml, the dose rate to the skeleton is only comparable to that delivered by 0.1 μc radium-226. This might be the reason why practically no bone lesions have been observed in Thorotrast cases.

W. V. MAYNEORD: Perhaps I might touch on a rather different aspect of this problem. Unfortunately Thorotrast is an excellent contrast medium. Some time ago we tried to make non-radioactive media using hafnium and zirconium, the obvious choices. Using hafnium and zirconium one can, in fact, make similar media, which work fairly well. Subsequently, however, my colleagues, Lamerton, Benstead, Anderson and Crookall experimented with these non-radioactive colloids on animals, and observed histological changes similar in many respects to those produced by Thorotrast. It happens that for some years I worked in the chemical carcinogen field and it naturally occurred to me that some of these effects could in fact be due to the chemical carcinogen at work. Alternatively, I wonder if we have here an example of combined chemical and radiation effects: such additive biological effects were demonstrated by Parsons and myself some years ago. I would very much like to hear other views on this, I am afraid rather heterodox, idea.

R. A. DUDLEY (IAEA): I believe no one knows the answer to Professor Mayneord’s question. However, in conjunction with Dr. Lamerton and Dr. Faber, we are arranging some experiments which may help to provide the answer. One would like to conduct animal toxicity experiments using both radioactive and non-radioactive Thorotrast. While this is impossible, one can compare the toxicity of various Thorotrast batches having different levels of activity. Such special batches of Thorotrast are now under preparation, in which the activity level in some cases is raised above normal by the addition of thorium-230. We hope animal experiments with these special batches will help at least partially to differentiate between any possible chemical toxicity of Thorotrast and its radiation toxicity.

J. RUNDO: I can’t answer Professor Mayneord’s question from my own experience, but Dr. W. B. Looney has pointed out that the liver tumours reported in cases of Thorotrast deposits are very similar to those seen in cases of arsenical poisoning.

B. RAJEWSKY: I would like to say that in cases of Thorotrast deposit which we have observed, radiological examinations showed that the deposit was not radioactive. The radioactivity was eliminated through the organism.

R. A. DUDLEY: May I draw your attention to the fact that the Medical Section of the Agency’s Division of Isotopes has compiled a bibliography on the subject of Thorotrast. We don’t claim that it is complete, but spare copies are available should anybody be interested in having a copy.
MEASUREMENT OF THORON IN THE BREATH OF THOROTRAST PATIENTS AND EVALUATION OF THE RESULTS

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INSTITUT FÜR BIOPHYSIK DER UNIVERSITÄT DES SAARLANDES, HOMBURG (SAAR), FEDERAL REPUBLIC OF GERMANY

Abstract — Résumé — Аннотация — Resumen

MEASUREMENT OF THORON IN BREATH OF THOROTRAST PATIENTS AND EVALUATION OF THE RESULTS. Thoron is continuously measured in expired air, flowing through an ionization chamber. The ionization current is automatically recorded. A short description of method and equipment is given: (1) The patients are measured under physiological conditions; (2) The measurement of a patient is continuous. Analysis of decay curves is not necessary because the results are indicated as constant values being proportional to the thoron concentration in expired air; (3) The breathing rate is determined simultaneously.

The results with 45 Thorotrast patients are discussed. The average value of the rate of thoron being exhaled depends on the kind of the Thorotrast deposit. This value is higher if the ThO₂ is deposited only or mainly in the RES and smaller if there are bigger depositions outside the RES (Granuloms). The reason for these differences in exhalation rates is discussed. The various circulation rates of blood in the different kinds of deposition are responsible for these findings.

The rate of thoron escaping from the site of deposition into blood and the rate of thoron in blood which is excreted by breath is determined. The fraction of thoron decaying inside the lungs is estimated. The mean value of all measurements of exhaled rate of thoron is 7%.

For depositions mainly in RES the mean value is 9%, for depositions outside the RES 4%.

About 20% of thoron escapes from the site of formation. About 9% decays in blood and about 4% in the lungs.

DOSAGE DU THORON DANS L'AIR EXHALE CHEZ DES SUJETS CONTAMINES PAR LE THOROTRAST, ET EVALUATION DES RESULTATS. On dose le thoron d'une manière continue dans l'air exhalé en le faisant passer dans une chambre d'ionisation. Le courant d'ionisation est enregistré automatiquement. Le mémoire donne un bref exposé de la méthode et des appareils utilisés: 1. Les malades font l'objet des mesures dans des conditions physiologiques. 2. Le dosage se fait d'une manière continue. Il n'est pas nécessaire d'analyser les courbes de désintégration, car les résultats sont indiqués comme des valeurs constantes, étant proportionnels à la concentration du thoron dans l'air exhalé. 3. La vitesse de respiration est déterminée simultanément.

Les auteurs examinent les résultats obtenus sur 45 malades contaminés par le thorotrast. La valeur moyenne du pourcentage de thoron exhalé dépend de la nature du dépôt de thorotrast. Cette valeur est relativement plus élevée lorsque ThO₂ se dépose uniquement ou principalement dans le système réticulo-endothélial (SRE) et moins élevée lorsqu'il existe des dépôts importants en dehors du SRE (granulomes). Les auteurs cherchent à expliquer les différences relevées dans les pourcentages d'exhalation et concluent que ce phénomène est attribuable aux variations du débit sanguin selon le genre de dépôt.

Les auteurs déterminent le rythme auquel le thoron s'échappe de l'emplacement du dépôt et passe dans le sang, ainsi que le pourcentage de thoron se trouvant dans le sang qui est excrété par les poumons. Ils évaluent la fraction de thoron qui se désintègre dans les poumons. La valeur moyenne de toutes les mesures portant sur le pourcentage de thoron exhalé est de 7%.

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Lorsque le thorotrast s'est déposé principalement dans le SRE, la valeur moyenne est de 9%; lorsqu'il s'est déposé en dehors du SRE, elle est de 4%.

Environ 20% du thoron s'échappe de l'emplacement du dépôt; environ 9% se désintègrent dans le sang et environ 4% dans les poumons.
ИЗМЕРЕНИЕ ТОРОНА В ВЫДЫХАЕМОМ ВОЗДУХЕ У БОЛЬНЫХ, ПОЛУЧАВШИХ ТОРОТРАСТ, И ОЦЕНКА РЕЗУЛЬТАТОВ. Торон постоянно измерялся в выдыхаемом воздухе, проходящем через ионизационную камеру. Ионизационный ток регистрировался автоматически. Дается краткое-описание метода и оборудования: 1) измерения у больных производятся в физиологических условиях; 2) измерения производятся постоянно; анализ кривых распада не обязательно, поскольку результаты выражены в виде постоянных величин, пропорциональных концентрации торона в выдыхаемом воздухе; 3) одновременно определяется частота дыхания.

Обсуждаются результаты обследования 45 больных, получавших торотраст. Средняя величина скорости выделения торона с выдыхаемым воздухом зависит от характера депо торотраста. Эта величина повышается, если торотраст отлагается только или главным образом в ретикуло-эндотелиальной системе (РЭС), и понижается, если имеются крупные отложения вне РЭС (гранулемы). Обсуждается причина различной скорости выделения с выдыхаемым воздухом. Сделан вывод, что причиной является различная скорость циркуляции крови в различных видах отложения.

Определяли скорость выделения торона из участков отложения в кровь и долю торона в крови, выделяющуюся с дыханием. Определяли также фракцию торона, распределяющуюся в легких. Средняя величина в результате всех измерений выдыхаемого торона составляла 7%. Для отложений, главным образом в РЭС, средняя величина равняется 9%, для отложений вне РЭС 4%.

Около 20% торона удаляется из места отложения. Около 9% распадается в крови и около 4% в легких.

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MEDICIÓN DEL TORÓN EN EL ALIENTO DE PACIENTES TRATADOS CON TOROTRASTO Y EVALUACIÓN DE LOS RESULTADOS. El método descrito brevemente por los autores se basa en la determinación continua del torón en el aire expirado que se hace circular a través de una cámara de ionización. La corriente de ionización se registra automáticamente. El método se caracteriza por los siguientes factores: a) los pacientes se someten a las mediciones en condiciones fisiológicas normales; b) la determinación es continua; no es preciso analizar las curvas de desintegración porque los resultados aparecen como valores constantes que son proporcionales a la concentración del torón en el aire expirado; c) simultáneamente se determina el caudal respiratorio.

Se discuten los resultados obtenidos en 45 pacientes a los que se había administrado torotrasito. El valor medio del contenido de torón exhalado depende de la naturaleza del depósito de torotrasito. Es mayor cuando el ThO₂ se encuentra depositado principalmente en el sistema reticuloendoendotelial y menor cuando existen depósitos de mayor tamaño fuera de dicho sistema (granulomas). Los autores examinan las posibles razones de las diferencias del contenido exhalado. Atribuyen las mismas a las distintas velocidades de circulación de la sangre a través de los diferentes tipos de depósitos.

Se determinó la proporción de torón que se desprende del lugar de depósito para incorporarse a la sangre y la proporción del torón de la sangre que se excreta con el aliento. Así mismo, se calculó la fracción de torón que se desintegra dentro de los pulmones. Las determinaciones del contenido de torón exhalado arrojaron un valor medio de 7%.

El término medio de los depósitos que se encuentran principalmente en el sistema reticuloendoendotelial alcanza a 9% y en los depósitos fuera de dicho sistema a 4%.

Cerca de 20% del torón escapa del lugar de formación del depósito. Alrededor de 9% se desintegra en la sangre y un 4%, aproximadamente, en los pulmones.

One of the decay products of thorium-232 is the noble gas thoron, which partly escapes into blood from the site of formation. By the respiratory system a fraction of this thoron in blood is released into breath where it is detectable. In 1936 RAJEWSKY and co-workers [1, 2, 3, 4] pointed out the possibility of determining thorium or radium burdens in the body by measurement of thoron or radon in the breath. One year before EVANS [5] described an apparatus for the determination of minute quantities of radon and thoron in gases. In 1941 STENSTROM [6] was able to demonstrate the presence of thoron in the breath of a thorotrast patient and eleven years later AUB, EVANS, HEMPELMANN and MARTLAND [7] reported the results of
measurements of radon and thoron concentrations in expired air of persons with radium and thorium body burdens. More recently MUTH and SCHRAUB [8], TURNER, RADLEY and MAYNEORD [9], RUNDO [10] and HURSH and LOVAAS [11] published papers concerning thoron or radon measurements in breath.

EQUIPMENT

Because we laid stress on getting real values of the mean rate of exhaled thoron of each patient, we used a device enabling us to measure thoron in the breath under physiological conditions during a longer period of time and to determine the breathing rate of each patient simultaneously. Figure 1 shows the equipment schematically. The patient breathes through a CO$_2$-cooled drying column into an ionization chamber. The voltage produced by the ionization current at an ohmic resistor proportional to the thoron concentration is measured by a vibrating reed electrometer. Because of the short half-life of thoron the volume of the pipes and drying column should be as small as possible. In order to reduce the resistance for air flow, which increases with decreasing diameter, the air pressure inside the device was diminished somewhat by means of a pump and a valve-guided air container serving as buffer volume.

CALIBRATION

Calibration of the equipment was carried out by using a thorium-228 standard solution joined to the device. The graph of voltages measured at various rates of air flow is utilized as a calibration curve. There is no difference as to whether the air flow is produced by a pump (constant flow-rate) or a breathing person (interrupted flow), see Fig. 2. These voltages are produced only by the decay of thoron and polonium-216 (ThA). Because of the relatively short measuring time (not longer than 30 min) the build-up of lead-212 (ThB) is negligible. To check the calibration curve the thoron concentration within the ionization chamber was calculated. Comparison of the curve calculated by Eq. 1 with the measured curve (Fig. 3) demonstrates the accuracy of our measurements and theoretical considerations.
Fig. 2
Calibration curve of the thoron equipment

Fig. 3
Comparison of calculated and measured values of thoron concentrations

\[
\frac{N}{\lambda' n'} = 0.96 \times e^{-\frac{\lambda V_1}{\varphi}}
\]

1

N = number of thoron atoms in the ionization chamber
\(\lambda\) = decay constant of thoron
\(\lambda' n'\) = rate of disintegration of radium-224.
\(V_1\) = volume of pipes including drying column and container of the thorium-228 standard solution
\(V_2\) = volume of the ionization chamber.
The factor 0.96 represents the emanating rate of the thorium-228 solution.

The unknown concentration $C_x$ is evaluated by the following equation:

$$C_x = \frac{U(\varphi)_x}{U(\varphi)_{calib.}} \times C_{calib.} \tag{2}$$

$C_x$ = concentration of thoron in air

$U(\varphi)$ = measured voltage at breathing rate $\varphi$.

The concentration $C_{calib.}$ is

$$C_{calib.} = \frac{0.96 \times \lambda}{3.7 \times 10^{10} \times \frac{\lambda' n'}{\varphi}} \tag{3}$$

From Eqs. (2) and (3) together we get

$$C_x = \frac{U(\varphi)_x}{U(\varphi)_{calib.}} \times \frac{0.96 \lambda}{\varphi} \times A_{calib.} \left[ \frac{c \text{ Tn}}{\text{volume}} \right] \tag{4}$$

$A_{calib.}$ = activity of radium-224 or thorium-228 standard solution.

By multiplying Eq.(4) with $\varphi$ and dividing by $\lambda$ it is transformed into a term expressing the activity of a radium-224 or thorium-228 solution which could produce the same thoron concentration in air at an emanating rate of 100%. In the following this quantity is designated as radium-224 (ThX) equivalent.

The lower limit for detectable concentrations is $1.6 \times 10^{-11} \text{ c Tn/l}$ or $1.5 \times 10^{-10} \text{ c radium-224 equivalent}$ at a flow rate of 7 l/air min.

The main features of our equipment are:

(1) Measurement of patients under physiological conditions.

(2) Determination of the actual individual breathing rate at the time of thoron measurement.

(3) Measurement of thoron concentration during a longer period of breathing (10 to 15 min).

(4) No analysis of decay curves because the results are indicated as constant values being proportional to the thoron concentration.

RESULTS AND EVALUATIONS

Table I contains the results of measurements of 44 thorotrast patients including those of whole-body counting of thorium-228. Some of the patients have been measured two or three times over intervals of some months. All these patients received thorotrast as a contrast medium for arteriographic studies. From these values the following results can be deduced:
TABLE I
RESULTS OF MEASUREMENTS OF THOROTRAST PATIENTS

<table>
<thead>
<tr>
<th>No. of registration</th>
<th>Position</th>
<th>Thoron concentration (10^-4 c/1)</th>
<th>Ra228 equiv. (10^-7 c)</th>
<th>Mean Ra228 equiv. (10^-7 c)</th>
<th>Combination</th>
<th>(b) (10^-3 l/s)</th>
<th>Ra228 equiv.</th>
<th>Th228 + Ra224 equiv. (10^-7 c)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>neck</td>
<td>(a) 1.64</td>
<td>2.26</td>
<td>2.56</td>
<td>17.5</td>
<td>(ab) ident</td>
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<td>7.8</td>
</tr>
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<td></td>
<td></td>
<td>(b) 1.54</td>
<td>2.38</td>
<td>18.7</td>
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<td>neg</td>
<td>8.6</td>
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</tr>
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<td>(ab) ident</td>
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<td></td>
<td></td>
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<td>see number 40</td>
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<td>0.34</td>
<td>0.34</td>
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<td>7.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) 0.36</td>
<td>0.38</td>
<td>0.38</td>
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<td>ident</td>
<td>9.2</td>
<td>7.5</td>
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<tr>
<td></td>
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<td>0.36</td>
<td>0.36</td>
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<tr>
<td></td>
<td></td>
<td>(b) 0.34</td>
<td>0.34</td>
<td>0.34</td>
<td>12.1</td>
<td>neg</td>
<td>7.2</td>
<td>7.2</td>
</tr>
<tr>
<td>6</td>
<td>neck</td>
<td>(a) 0.36</td>
<td>0.36</td>
<td>0.36</td>
<td>10.2</td>
<td>neg</td>
<td>7.2</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) 0.34</td>
<td>0.36</td>
<td>0.36</td>
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<td></td>
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<td>3.46</td>
<td>16.7</td>
<td>neg</td>
<td>7.5</td>
<td>7.5</td>
</tr>
</tbody>
</table>

* Measured by whole-body counting.
† 1 s is equal to deposition of thoron in liver and spleen.
<table>
<thead>
<tr>
<th>No. of registration</th>
<th>Position</th>
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* Measured by whole-body counting

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* Measured by whole-body counting.

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\* Measured by whole-body counting.
\+ Is equal to deposition of thorotrast in liver and spleen.
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* Measured by whole-body counting.
† 1 s is equal to deposition of thorium in liver and spleen.
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* Measured by whole-body counting

* I s is equal to deposition of thorotrast in liver and spleen.
(1) The average thoron concentration in the breath of thorotrast patients with a thorium-228 body burden of \(1 \times 10^{-6}\) c is \(5.6 \times 10^{-9}\) c Tn/l.

(2) The fraction of exhaled thoron to the total thoron produced in the body is

(a) \(8\% \pm 3\%\) when thorotrast is deposited mainly in the reticulo-endothelial system;

(b) \(4\% \pm 1\%\) when thorotrast is deposited mainly outside the reticulo-endothelial system in paravascular infiltrates.

The value of \(5.6 \times 10^{-9}\) c Tn/l for a whole-body content of \(1 \times 10^{-6}\) c thorium-228 is nearly two times as large as values found in literature [10]. The reasons for this difference may be not only the statistical scatter but also to a certain degree the non-physiological conditions of the thoron measurement with regard to the patient's breathing. The results given under (2) above are average values of the ratios of radium-224 equivalent to the sum of thorium-228 and radium-224 equivalent, where thorium-228 value is determined by whole-body counting. It is necessary to relate to this sum because whole-body counting of thorium-228 is performed by measuring the gamma-rays of thallium-208 (ThC\(^{\text{II}}\)). The excretion of other radium-224 followers may be neglected compared to that of thoron.

The difference between the given fractions of exhaled thoron for the different kinds of deposition is probably caused by differences of the greatly hampered transport of thoron from the site of formation into blood and differences in blood circulatory rates. Compared with the conditions in the liver and spleen, the blood circulatory rate is reduced in hyalinized paravascular infiltrates, and the difficulties for the escaping thoron to reach blood may be enlarged. Because in most of the cases with paravascular infiltrates there are depositions of more or less amount in the reticulo-endothelial system, a sharp separation between these two kinds of cases is not entirely possible. The fact that the exhaled thoron fraction depends on the kind of deposition may be the reason why our average value of all cases of 6% is lower than that of 8% given in literature [10]. About half of our patients have heavy paravascular infiltrates, and some of the other ones have infiltrates in addition to their main depositions in the reticulo-endothelial system.

Before thoron is exhaled it must be released from the site of formation to the respiratory system. Because of its short half-life a good deal decays within the thorotrast deposit, and in the blood and the lungs. To get the radiation doses received by the tissues of these regions it is necessary to determine the fractions of thoron decaying within these organs. We have estimated these fractions by a calculation similar to that used by MAYS [12] in thorium-228 experiments with dogs.

ASSUMPTIONS

(1) The activity of thoron which is produced in the body at a constant rate per time unit, is \(R\), and the fraction \(f\) reaches the circulation.

(2) The mean residence time, \(t_B\), of thoron in blood is inversely proportional to the circulatory rate, \(C\).

(3) The mean residence time, \(t_L\), of thoron in the respiratory system is inversely proportional to the ventilation rate, \(\varphi\).
The circulatory rate, $C$, is directly proportional to the ventilation rate, $\varphi$.

The activity of exhaled thoron per time unit is $A$. Therefore

$$A = R \times f \times e^{-\lambda(t_b + t_l)}$$

$$t_b + t_L = \frac{k}{\lambda} \times \frac{1}{\varphi}$$

$$k = (k_1/k_2 + k_4) \times \lambda$$

To evaluate the constant $k$ we have to consider the ratio of two measurements of the same patient

$$k = \frac{\ln(A_2/A_1)/(1/\varphi_1 - 1/\varphi_2)}{(1/\varphi_1) - (1/\varphi_2)}$$

The exponential factor

$$f = \frac{A}{R \times e^{k/\varphi}}$$

$$g = e^{-k/\varphi}$$

Both of these constants are based on the constant $k$, which is tabulated in Table I. Each value of $k$ is computed by the combination of two measurements of the same person, but not each of the combination leads to a valid value of $k$. Because we avoided stimulation or diminution of the circulatory or ventilation rates, a good deal of the combinations include measurements carried out under the same physiological conditions. With these combinations (called "ident" in Table I) $k$ is undetermined. In other cases $k$ becomes negative (called "neg" in Table I), if either $A_1 > A_2$, although $\varphi_2 > \varphi_1$; or $A_1 < A_2$, although $\varphi_2 < \varphi_1$. The reasons for these facts are, that in one of the measurements the ventilation rate is increased without corresponding increase of the circulatory rate ($\varphi$ large, $A$ small), or the circulatory rate is increased without increasing the ventilation rate ($\varphi$ small, $A$ large). Obviously the assumption that the ventilation rate, $\varphi$, is directly proportional
to the circulatory rate, $C$, is not fulfilled in these cases. Therefore when calculating the average of $k$, these values were not taken into consideration.

For $\bar{k}$ and $\bar{\phi}$ we got the following mean values:

\[
\bar{k} = 0.15 \text{ l/s}, \quad \bar{\phi} = 0.14 \text{ l/s}.
\]

As shown in Table I, the scattering of $k$ is very wide. It may be that some differences of the $k$ values of different persons represent normal scatter. Another reason may be that, according to the criteria we have used, the distinction between combinations of measurements which fulfill the above assumptions (mainly point 4 above) and those which do not is not complete. Finally the errors of measurement of nearly equal values are enlarged by forming the differences of these values as has been done for calculating $k$. But since we have a large number of results, at least we can conclude from $\bar{k}$ the approximate values for $g$ and $f$.

These values are:

\[
\begin{align*}
    f &= 0.18, \\
    g &= 0.34.
\end{align*}
\]

That means that about 20% of the thoron produced within the deposits escape into blood and from this amount, $1/3$ is released from the body by breath. The remainder, about $2/3$ (13%), decays within the blood and respiratory system. From our measurements of the concentrations of thorium-232 daughters in the blood of thorotrast patients, we know that there exists about 9% of the lead-212 (ThB) equilibrium activity to radium-224 (ThX) in total blood. It is most probable that this lead-212 activity is produced by the decay of thoron within blood. If this is assumed, about 9% of thoron decays in blood. Then 3% must decay within the respiratory system. This value also may be estimated in another way by a short calculation. It is known [13] that the lungs contain about 3500 cm$^3$ of air permanently. Since the average ventilation rate is about 8 l/min, the mean time for air staying in the lungs is 26 s. After this time the thoron has decreased by decay to a fraction of 0.71. To exhale 6% of the total thoron produced in the body 8.4% has to be transported into the respiratory system. The difference of 2.4% decays inside the lungs. This value agrees with the above value of 3% within the range of error.

REFERENCES

THORON IN THE BREATH OF THOROTRAST PATIENTS


MEASUREMENTS AND CLINICAL FINDINGS ON
THOROTRAST DEPOSITS IN THE KIDNEY

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INSTITUT FÜR BIOPHYSIK DER UNIVERSITÄT DES SAARLANDES,
HOMBÜRGER (SAAR), FEDERAL REPUBLIC OF GERMANY

Abstract — Résumé — Аннотация — Resumen

MEASUREMENTS AND CLINICAL FINDINGS ON THOROTRAST DEPOSITS IN THE KIDNEY. There exists a relatively large number of publications about Thorotrast deposits in the reticulo-endothelial system and the clinical findings caused by these deposits. But only a few cases with Thorotrast deposits in the kidney have been reported. Despite this it is to be expected that there are numerous patients with Thorotrast deposits in the kidney, because Thorotrast has been used very often as a contrast medium in retrograde pyelographies. Under normal conditions all the Thorotrast should have been swept out of the kidney with the urine. But if it was applied under higher pressure or if there existed an infection of the kidney at the same time, part of the Thorotrast might have been deposited in the tissues. It is possible that a higher number of these deposits is not recognized in X-ray pictures because they look very similar to calcium deposits in the kidney and some experience is needed to distinguish calcium from Thorotrast deposits.

In co-operation with our urological clinic we have found seven cases in the last years. When there was only a deposit in one kidney, which was the case in six patients, the organ was taken out. Histological examination showed five carcinomas and in one kidney there were already enormous degenerative changes. According to our observations the time necessary for the development of carcinoma is between 20 and 25 yr. In two cases we have been able to measure the patient in the whole-body counter and to measure the radioactive substances in the urine and the thoron in the breath. All these measurements have been done before and after nephrectomy. The gamma-rays of the isolated organ itself have also been measured. From these measurements an evaluation of radiation dose is possible.

MESURES ET OBSERVATIONS CLINIQUES FAITES SUR DES DÉPÔTS DE THOROTRAST DANS LE REN.
Il existe un nombre relativement grand de publications sur les dépôts de thorotrast dans le système réticulo-endothélial et les phénomènes cliniques provoqués par ces dépôts. Par contre, on n'a signalé que peu de cas de dépôts de thorotrast dans le rein. Il n'en faut pas moins s'attarder à trouver de nombreux malades dont les reins contiennent des dépôts de thorotrast, car le thorotrast a été utilisé très souvent comme substance opaque dans les pyélographies rétrogrades. Dans les conditions normales, tout le thorotrast aurait dû être emporté par l'urine. Cependant, si l'application a été faite sous forte pression ou qu'il y eût à l'époque une infection rénale, il se peut qu'une partie du thorotrast se soit déposée dans les tissus. Il est possible qu'un nombre important de ces dépôts ne puisse être identifié sur les radiographies, car ils ressemblent beaucoup à des dépôts de calcium dans le rein et il faut une certaine expérience pour distinguer les dépôts de calcium des dépôts de thorotrast.

Au cours des dernières années, les auteurs, en collaboration avec des urologistes, ont pu repérer sept cas de ce genre. Lorsqu'il n'y avait pas de dépôt que dans un seul rein, ce qui était le cas chez six patients, on a procédé à l'ablation de l'organe. L'examen histologique a révélé cinq carcinomes ainsi qu'une dégénérescence très poussée d'un rein. Dans les observations des auteurs, il faut entre 20 et 25 années pour qu'un carcinome se développe. Dans deux cas, il a été possible d'examiner le sujet dans l'anthropogamamètre et de doser les radionucléides contenus dans l'urine et le thoron contenu dans l'air exhalé. Ces dosages ont été effectués avant et après la néphrectomie. On a également mesuré les rayons gamma émis par l'organe isolé. Ces diverses mesures ont permis de procéder à une évaluation de la dose de rayonnements.

ИЗМЕРЕНИЯ И КЛИНИЧЕСКИЕ ИССЛЕДОВАНИЯ ПРИ ОТЛОЖЕНИИ ТОРОТРАСТА
В ПОЧКАХ. Существует относительно большое количество публикаций об отложении торотраста в ретикуло-эндотелиальной системе и о клинических изменениях, вызываемых этими отложениями. В последние годы у авторов в сотрудничестве со специалистами-урологами было установлено семь случаев. Примем, что только в одном случае развивалось заболевание в одном почечном органе. Особое значение приобретает изучение клинической картины при ОТЛОЖЕНИИ ТОРОТРАСТА В ПОЧКАХ.

* Work performed under the auspices of the Bundesminister für Wissenschaftliche Forschung of the Federal Republic of Germany.
отложениями. Однако имеется лишь несколько сообщений о депо торотрasta в почках. Не­смотря на это, полагают, что существует большое количество пациентов с отложениями торо­трasta в почках, который очень часто использовался в качестве контрастного вещества для ретроградной пилографии. В норме весь торотраст должен удаляться из почек с мочой. Но если торотраст вводился под большим давлением или в то время имело место инфициро­вание почек, то часть его могла осесть в тканях. Возможно, что часто эти отложения не распознаются на рентгенограммах, так как они очень похожи на отложения кальция в поч­ках и требуется некоторый опыт, чтобы научиться отличать кальциевые отложения от торо­трasta.

В сотрудничестве с урологической клиникой авторы выявили семь случаев за послед­ние годы. В тех случаях, когда отложения имелись лишь в одной почке, как это было у шести пациентов, произведен удаление органа. При гистологическом исследовании в 5 слу­чаях обнаружена карцинома и в одном—очень большие дегенеративные изменения. Согласно наблюдениям необходимый для развития карциномы срок составляет 20—25 лет. В двух слу­чаях удалось обследовать больного с помощью счетчика для измерения активности всего организма и измерить радиоактивные вещества в моче, торон в выдыхаемом воздухе. Все эти исследования производились до и после нефрэктомии. Определяли также гамма-излучение изолированного органа. На основе этих измерений может быть определена доза облучения.

DETERMINACIONES Y DATOS CLÍNICOS RELATIVOS A LOS DEPÓSITOS RENALES DE TOROTRASTO.

Los trabajos publicados acerca de los depósitos de torotrasto en el sistema reticuloendotelial y de los datos clínicos obtenidos son bastante abundantes. En cambio, son contados los casos de depósitos renales de toro­trasto descritos en la bibliografía. Sin embargo, es de suponer que hay muchos pacientes con estos últimos depósitos, ya que el torotrasto se utilizó con mucha frecuencia como medio de contraste en la pielografía ascendente. En condiciones normales, todo el torotrasto debería haber sido expulsado del riñón con la orina. Pero al aplicarlo a gran presión o si en el momento de la inyección el riñón estaba infectado, parte del torotrasto puede haberse depositado en los tejidos. Es posible que no se identifique por medios radiográficos un número mayor de estos depósitos porque se asemejan mucho a los depósitos de calcio en el riñón y hace falta cierta experiencia para diferenciar unos de otros.

Los autores, en colaboración con la clínica de urología de la Universidad del Sarre han descubierto siete casos en estos últimos años. Cuando el depósito se encontró exclusivamente en un riñón, cosa que ocurrió con seis pacientes, se extirpó el órgano. El examen histológico reveló cinco carcinomas y en un riñón se observaron alteraciones degenerativas muy pronunciadas. Según las observaciones de los autores, el tiempo necesario para el desarrollo de tales carcinomas es de 20 a 25 años. En dos casos pudieron examinar al paciente con el antropogammámetro y medir las sustancias radiactivas presentes en la orina y el torón en el aliento. Hicieron todas estas determinaciones antes y después de la nefrectomía. Asimismo, midieron los rayos gamma emitidos por el órgano aislado. Partiendo de estas mediciones, es posible evaluar la dosis de radiación.

In the period from 1930 to 1948 thorotrast was used as a contrast medium in roentgen diagnosis, not only for angiography, but also for pyelography. Since after injection into the circulatory system, as in the case of pyelography, thorotrast is not excreted by the kidneys, it is necessary to fill the outflow tract in a retrograde fashion. It is known from arteriography that thorotrast is deposited in the reticuloendothelial system if it is administered intravenously, and at the site of injection and in the regional lymph nodes if it is injected paravascularly. In retrograde pyelography thorotrast normally should be excreted with the urine from the calyceal system of the kidney, thus in such cases deposits in the kidney should not normally exist. Only if pyelography was used in cases of inflammation of the pelvis of the kidney or if the pressure was too high at the time of retrograde filling, thorotrast may have penetrated into the tissues of the pelvis of the kidney. According to our findings, it seems that this occurred more often than would be indicated by the few cases with deposits of thorotrast in the kidney reported in literature [1]. The probable reason is the difficulty in recognizing these deposits.
Figure 1 shows the roentgenography of a kidney with a deposit of thorotrast. In many cases such a picture would have been diagnosed as a calcification which frequently occurs as a result of tuberculosis in the kidney. In co-operation with the Urological Hospital of the University of the Saarland, five cases with deposits of thorotrast in the kidney have been observed in the period since 1958*. The first two cases with autoradiographic measurements have already been reported in a former paper [2, 3]. In addition to these five cases, we know of two other cases where nephrectomy had been done in other hospitals in the close vicinity without recognizing the deposit of thorotrast which was found later by histological examinations and measurements of radioactivity. These seven cases come from a total population of about 5 $\times$ 10^6 persons. If we try to extrapolate this to the total population of the Federal Republic of Germany — though the number is relatively small — we may estimate 140 clinical cases for the same period. Probably most of them have not been recognized as cases of thorotrast retention.

* We thank Dr. K Hubmann for letting us use the clinical findings. They will be published in detail elsewhere together with the histological findings.
Below are described the clinical findings of three of our patients in order to illustrate their physical conditions due to the deposits of thorotrast in the kidney.

Case 1

Patient K. P., 55 yr-old female. In 1932 roentgen diagnosis was performed because of pain in the region of the right kidney. The patient only remembered the diagnosis of one double kidney on each side. Eight weeks prior to the hospital admission in 1962, she first suffered from pain in the right kidney region and repeated episodes of severe haematuria. In the clinical examination tenderness was elicited with pressuring and percussion over the right flank region. Blood pressure was 100/80, erythrocyte sedimentation rate 105/120. The urine sediment contained more than 50 leucocytes and up to 5 erythrocytes per field of vision. The albumin excretion was 1%, measured with Esbach's method. In the urogram, given in Fig. 2, double kidneys are seen on each side. Only the lower pole of the right kidney is sharply defined. The upper pole is enlarged, and the striped and sharply limited polymorphic shadows due to the thorotrast deposit are striking. In addition there are in the region of the twelfth dorsal and the first lumbar...

Fig. 2.

Urogram of patient K. P. showing thorotrast in the right kidney
vertebrae several dense shadows due to thorotrast deposits in the para­vertebral lymph nodes. The measurement of the patient in the whole-body counter gave a total amount of $3.1 \times 10^{-8}$ c mesothorium (radium-228) and $2.6 \times 10^{-8}$ c of the gamma-ray emitting 'daughter products of thorium-228. Because of the haematuria and the measured thorotrast deposit a malignant degeneration of the right kidney was expected. Therefore a nephrectomy was done. There were found accretions of connective tissue of very hard consistency in the cranial part of the kidney. The malignant process already had invaded the suprarenal gland and attached to the diaphragm. During dissection about the upper pole of this kidney, a perforation of the inferior vena cava occurred. The venous perforation was closed immediately, but the patient died 12 h later of hypotensive shock.

Figure 3 shows the sectioned pathological specimen. On the sectional plane the tissue of the kidney is completely interspersed with marrow-like tissue in the entire region of the upper pole. Intact tissue is not seen. The epithelium of the pelvis of the kidney is replaced completely by tumour tissue, and the outflow tract can only be imagined. On the upper pole of the kidney is a nodular swelling. In this region no tissue of the suprarenal gland is recognized.

Case 2

Patient E. M., 48 yr-old female. In 1935 a retrograde pyelography on the right side was done because of minor pains. In 1959 an increased whole-body burden of radioactivity was found inadvertently by routine measurement in the whole-body counter. Further examination revealed the deposit of thorotrast in the kidney. In 1960 the patient was informed that an operation was necessary, but she refused. At this time she suffered only from slight drawing pains in the right flank area. In July 1963 the pain greatly increased, and in October 1963 haematuria began which led to hospitalization.
The erythrocyte sedimentation rate was rapid with 65/83. The urine sediment contained numerous erythrocytes and 30-40 leucocytes per field of vision. An X-ray picture of the abdomen demonstrated a wide striped ring-shaped shadow in the region of the right kidney. Also on the right side in the paravertebral region at the level of the second and third lumbar vertebrae small dense shadows were seen. Nephrectomy showed that the tumour, originated in the kidney, invaded the surrounding tissue. It was not possible to remove the tumour tissue completely. Therefore after healing of the wound without complications, the patient was additionally treated with therapeutic X-radiation. Figure 4 shows the sectioned pathological specimen. The pelvis of the kidney is completely filled with tumour tissue, growing exuberantly in broad strains to the cortex and forming greyish-white marrow-like regions. The calyces are dilated markedly. In the region of the lower pole of the kidney the collecting tubules are filled with coagulated blood. Often nodular swellings of tumour penetrate the mucous membrane of the renal pelvis.

Case 3

Patient M.H., 62 yr-old female. The retrograde pyelography which led to the deposit of thorotrust was done in 1937. Four months before she came to the hospital, the patient first noticed bloody urine. Since that time haematuria without pain occurred two or three times a week. The day before she came to the hospital, small blood-clots were passed with severe rightsided renal colic. During clinical examination tenderness was elicited with pressing and percussion over the right flank region. The erythrocyte sedimentation rate was 7/31. In the urine sediment 40-50 erythrocytes were found per field of vision. The pyelogram given in Fig. 5, shows dense striped circular shadows in the region of the calyceal system. Covered by the right
transverse processes of the first and second lumbar vertebrae, dense shadows are seen due to the thorotrast in the local lymph nodes. By urogram no function of excretion could be recognized for the right kidney within the first two hours. The right kidney was extirpated by operation. Healing took place without complication. The X-ray picture made after extirpation (Fig. 6) still shows the dense paravertebral shadows. Figure 7 shows the sectioned pathological specimen. The cortex is sharply defined. In the pelvis of the kidney are large regions of haemorrhagic, thickened tissue, interspersed by grayish-white striped parts. These red and gray regions encroach on the peaks of the papillae and raise into the angles of the calyces.

It was possible to carry out extended measurements of the thorotrast deposits of the last two patients. The total amounts of radium-228 and thorium-228 were determined before and after the nephrectomy. Additionally the decay products of thorium-228 were measured in 24-h samples of urine and faeces. Gamma spectroscopic measurements of the extirpated kidneys were carried out during a period immediately after the extirpation of each to determine whether thorium-228 was in radioactive equilibrium with its daughter products or not [4]. This is possible by determining the increase of the gamma radiation emitted by ThC¹¹ (thallium-208). In one case this
Fig. 7
Sectioned pathological specimen of the kidney of patient M. H.

Fig. 6
X-ray picture after extirpation of the right kidney (patient M. H.)
was done at the energy of 560 keV (Fig. 8, kidney of patient E. M.) and in the other case at the energy of 2.6 MeV (Fig. 9, patient M. H.). During the first 150 h after extirpation a distinct increase of the activity of ThC" was measured; hence we may conclude that the decay products of thorium-228 have not been in radioactive equilibrium with thorium-228 in the deposits in the kidney. By subtracting the activity measured at a definite time from the value of equilibrium, it can be determined which of the decay products from radiothorium to ThC" (polonium-212) were enriched during the time of measurement. The equilibrium activity was found by measuring the gamma-ray activity during a period of three months. In both cases this operation clearly leads to the half-lives of ThB (lead-212) and ThX (radium-224). This means that ThX and ThB have not been in radioactive equilibrium in the kidney at the time of extirpation.

The following survey gives all results of the measurements with the analysis of the curve of increasing activity.

**Patient E. M.**

I. Measurements before extirpation of the kidney:

1. Whole-body counter: Mesothorium (Ra228) = 8.2 \times 10^{-9} \text{ c}  
   Radiothorium (Th228) = 7.5 \times 10^{-9} \text{ c}

2. Expired air: Thoron concentration = 9.2 \times 10^{-11} \text{ c/l}
   This concentration is due to the emanation rate of 8.4 \times 10^{-10} \text{ c Th228}.

This means that 10% of the built-up thoron is eliminated by the respiratory system.

II. Measurements of the isolated kidney:

   Mesothorium (Ra228) = 3.9 \times 10^{-9} \text{ c}  
   Radiothorium (Th228) = 3.9 \times 10^{-9} \text{ c}

Relations of equilibrium activity of the decay products:

   ThX = 80\% of Th228  
   ThB = 38\% of Th228.

III. Measurements after extirpation of the kidney:

   Whole-body counter: Radiothorium (Th228) = 3.9 \times 10^{-9} \text{ c}.

**Patient M. H.**

I. Measurements before extirpation of the kidney:

1. Whole-body counter: Mesothorium (Ra228) = 5.0 \times 10^{-9} \text{ c}  
   Daughter products of radiothorium (Th228) = 4.4 \times 10^{-9} \text{ c}
Fig. 8
Increasing $^{208}\text{TI}^{+}$ activity in the isolated kidney of patient E. M.

Fig. 9
Increasing $^{208}\text{TI}^{+}$ activity in the isolated kidney of patient M. H.

2. Expired air: Thoron concentration $= 7.0 \times 10^{-11}$ c/l.
   This concentration is due to the emanation rate of $6.4 \times 10^{-10}$ c $^{228}\text{Th}$.

   This means that 13% of the built-up thoron is eliminated by the respiratory system.

3. Blood: Total amount of ThB $= 5.9 \times 10^{-10}$ c
4. Excretion with urine:
THOROTRAST DEPOSITS IN THE KIDNEY

5. Excretion with faeces:

\[ \text{ThX} = 2.1 \times 10^{-10} \text{ c/daily excretion.} \]

II. Measurements of the isolated kidney:

Mesothorium (Ra\textsuperscript{228}) = 2.4 \times 10^{-9} \text{ c} \\
Radiothorium (Th\textsuperscript{228}) = 2.3 \times 10^{-9} \text{ c}

Relations of equilibrium activity of the decay products:

\[ \text{ThX} = 81\% \text{ of } \text{Th}\textsuperscript{228} \] \\
\[ \text{ThB} = 40\% \text{ of } \text{Th}\textsuperscript{228}. \]

III. Measurements after extirpation of the kidney:

1. Whole-body counter: Radiothorium (Th\textsuperscript{228}) = 2.5 \times 10^{-9} \text{ c.}
2. Excretion with urine:

\[ \text{ThX} = 2.1 \times 10^{-12} \text{ c/daily excretion} \] \\
\[ \text{ThB} = 1.4 \times 10^{-11} \text{ c/daily excretion.} \]

3. Excretion with faeces:

\[ \text{ThX} = 1.8 \times 10^{-11} \text{ c/daily excretion.} \]

The comparison of the values measured in the whole-body counter to those of the extirpated kidneys show that only about half the activity was located in the kidney. One reason may be that part of the thorotrast was deposited in the local lymph nodes as already shown by X-rays. Another factor that must be taken into account is the elimination of mesothorium from the deposits in the kidney and the resulting deposition of this radium isotope in bone [4, 7]. The measurements of the isolated kidneys significantly show a deficit of ThX (Ra\textsuperscript{228}), which means that an elimination of radium isotopes from the deposits took place. The excretion of radium-224 with faeces is 50 times that in the urine. This is the same ratio found for the excretion of radium-226 by patients with radium burdens [5] and of ThX by patients with deposits in the reticulo-endothelial system [8]. Thus we may conclude that also in cases of thorotrast deposits in the kidney the excretion of the decay products does not take place by urine directly. As in the case of radium-226 and ThX in the reticulo-endothelial system they are excreted via blood and lymph. This is confirmed by measurements of the concentrations of thoron in breath and of ThB in blood. Summarizing, we may conclude that the conditions of equilibrium of the decay products are almost the same in the case of thorotrast deposits in the kidney as in the case of deposits in the reticulo-endothelial system, or paravascular deposits [6, 8].
The most striking result is the relatively small amount of thorotrast in the kidneys with regard to the fact that six of our seven patients had developed carcinoma. This may be due to the special kind of deposition in the spaces between the tissue formations in the pelvis of the kidney. Because of this distribution thorotrast in very high concentration is deposited in a relatively small space which leads to very high radiation doses in the local environment [9]. The time between the deposition of thorotrast and the appearance of clinical symptoms caused by the carcinoma was more than 20 years in all cases.

REFERENCES


DISCUSSION

J. RUNDO: I would like to ask Dr. Oberhausen if he has confirmed his previously reported values (in 2 cases) of about 0.1 for the Th228/Th232 ratio in kidney, which is much lower than usually found in liver and spleen.

E. OBERHAUSEN: Autoradiographic examinations on the cases reported in the present paper are not yet finished, so I cannot tell you the Th228/Th232 ratio for these cases.

H. WYKER: In the ICRP calculations for the kidney as critical organ the mass of the kidney of the standard man is taken. As you found that the thorium is concentrated mainly in a small part of the kidney, what percentage of this mass would you suggest taking for these calculations?

E. OBERHAUSEN: About 10%.

R. I. MOORE: What type of carcinoma appeared in the kidney?
E. OBERHAUSEN: Epithelium carcinoma in all cases.

E. POCHIN: Is it possible to give any estimate of the number of retrograde Thorotrast pyelographies in the same region, to which these six renal carcinomas would correspond?

E. OBERHAUSEN: Not at the moment, I'm afraid.

E. POCHIN: Secondly, is it known for what clinical conditions the pyelographies were originally done in the six patients developing carcinoma much later? Were they for conditions such as renal stone which might themselves be followed by carcinoma, or for conditions such as local renal infection which might favour the entry of Thorotrast into the renal substance?

E. OBERHAUSEN: In four cases we had the opportunity to see the old records of the hospitals in which the pyelographies had been done. There was no evidence of renal stones or local renal infection. One thing I might add, however, is that all the patients told us that, during the retrograde filling, they had much pain so my opinion is that in all these cases too high a pressure caused the Thorotrast to go into the kidney tissues.

A. BEN HAIM (IAEA): I should like to mention in this connection that in our Agency laboratory in Vienna we are studying a population of Thorotrast cases. So far, we have measured two pyelographies and one of them had developed a carcinoma.
MEASUREMENT OF THE NATURAL CONTENT OF Th$^{228}$, Ra$^{226}$ AND THEIR DAUGHTERS
IN THE HUMAN BODY

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Abstract — Résumé — Аннотация — Resumen

MEASUREMENT OF THE NATURAL CONTENT OF THORIUM-228, RADIUM-226 AND THEIR DAUGHTERS
IN THE HUMAN BODY. The purpose of these investigations was the determination of both the content and the
distribution of the alpha emitters radium-226, thorium-228 and polonium-210 in the human body.
The content of radium-226 in human bones and soft tissues was determined by the emanation method,
the content of polonium-210 by chemical enrichment followed by measuring the activity in a methane flow
counter. The thorium-228 content as well as the total alpha activity was measured by means of a specially-
developed scintillation method, the so-called mixing method.
The content of radium-226 in human bones and organs related to the patient's age is performed in order
to get information on the incorporation of this nuclide at continuous administration of extremely low amounts.
As to bones and soft tissues the specific activity of radium-226 in man showed to be constant from the fourth
month of pregnancy up to an age as high as 80 yr.
The content of polonium-210 and lead-210 in femur and tibia bones was measured in order to determine
the ratio of polonium-210 and lead-210 in the human skeleton of the living organism. This ratio is 0.8 on
the average.
The content of thorium-228 and radium-226 in human bone ashes is about 0.4. The age of the examined
persons ranged from 5 to 70 yr. As a result of these investigations the human radiation burden caused by the
radium-226, thorium-228 and polonium-210 content was estimated.

TENEUR NATURELLE DU CORPS HUMAIN EN THORIUM 228 ET EN RADIUM 226 ET SES PRODUITS
DE FILIATION. Les travaux de recherche avaient pour objet de déterminer à la fois la charge corporelle de
radium 226, thorium 228 et polonium 210, qui émettent des rayons alpha, et leur répartition dans l'organisme.
Les auteurs ont déterminé la teneur du squelette et des tissus mous en radium 226 par la méthode de
l'émanation, et la teneur en polonium 210 au moyen d'un compteur à méthane, après enrichissement chimique.
Pour mesurer la teneur en thorium 228 ainsi que l'activité alpha globale, ils ont utilisé une méthode par scin­
tillations spécialement mise au point, dite « méthode de mélange »
Ils ont étudié la teneur en radium 226 des tissus osseux et des organes selon l'âge du patient, en vue
d'obtenir des renseignements sur la rétention de ce radionucléide lorsqu'il est administré de façon continue
en quantités très faible. Pour ce qui est du squelette et des tissus mous, ils ont constaté que chez l'homme
l'activité spécifique du radium 226 est constante depuis le début de la vie fœtale jusqu'à un âge très avancé
pouvant atteindre 80 a.
Ils ont mesuré la teneur du fémur et du tibia en polonium 210 et plomb 210 pour déterminer le rapport
polonium 210/plomb 210 dans le squelette de l'homme vivant. Ce rapport est de 0,8 en moyenne.
Dans les cendres d'os humains, le rapport thorium 228/radium 226 est d'environ 0,4. Les sujets examinés
étaient âgés de 5 à 70 a. Ces études ont permis d'évaluer la dose interne due à la charge corporelle
de radium 226, thorium 228 et polonium 210.

ИЗМЕРЕНИЕ ЕСТЕСТВЕННОГО СОДЕРЖАНИЯ ТОРИЯ-228, РАДИЯ-226 И ИХ ПРО­
ДУКТОВ РАСПАДА В ЧЕЛОВЕЧЕСКОМ ОРГАНИЗМЕ. Целью исследования являлось опре­
дление содержания и распределения альфа-излучателей ради-226, тория-228 и полония-210
в организме человека.
Содержание ради-226 в костях и мягких тканях человека определяли с помощью мето­
da эманации, содержание полония-210 путем химического обогащения с последующим изме­
ренiem активности в метановом проточном счетчике. Содержание тория-228 и общий уро­
вень альфа-активности измеряли с помощью специально разработанного метода, так называемого метода смешивания.

Содержание радия-226 в костях и органах человека в зависимости от возраста определяли для получения информации об инкорпорации крайне малых количеств этого изотопа при постоянном его поступлении. Специфическая активность радия-226 в костях и мягких тканях у человека оказалась постоянной, начиная с четвертого месяца беременности вплоть до 80 лет.

Содержание полония-210 и свинца-210 в бедренной и большеберцовой костях измерялось для определения отношения этих элементов в костях скелета при жизни человека. Это отношение составляло в среднем 0,8.

Отношение тория-228 и радия-226 в костях человека в зависимости от возраста определяли для получения информации о радиоактивном заражении, вызванном радием-226, торием-228 и полонием-210 у человека.

1. INTRODUCTION

The estimation of any toxic concentration of radioactive nuclides is based on the "natural burden caused by radiation" which, in its turn, is composed of the burden caused by the total external radiation and the burden caused by the radiation of the incorporated naturally-occurring radioactive nuclides. The investigations which are given in detail in this paper were performed in order to obtain information on the presence of all naturally-occurring alpha emitters, and the burden caused by these radionuclides. The mechanism of the enrichment of the naturally-occurring radioelements and their distribution pattern are studied in detail.

2. RELATION TO AGE OF Ra²²⁶ CONTENT IN HUMAN BODY

To obtain information on the incorporation of the permanent deposit of radium-226 in the human and animal organism, RAJEWSKY, MUTH and HANTKE [1, 2, 3] performed animal experiments and carried out investigations with human bones in 1958. The relation of the radium-226 content to the age of chicken bones revealed that the radium-226 content per gram
of bone ash decreased within the first days of the chicken's life. After a period of about 100 d, however, the specific activity reached a constant level \[2, 3\]. The radium-226 content per gram of ash for this level is about three times lower than the specific radium-226 content for a chicken aged 1 d. The specific radium-226 content in the human skeleton proved to be on a constant level, as shown by RAJEWSKY, MUTH et al. \[2, 3\], HALLDEN et al. \[4\], LUCAS \[5\], HURSH et al. \[6, 7\], WALTON et al. \[8\] and TURNER et al. \[9\]. The individuals tested covered the period from those still-born to 80 yr of age. The results were confirmed by our own measurements with the bones of 70 persons of various ages within the same age interval. The radium content was determined by the emanation method \[3\]. No correlation between the radium-226 content and age could be observed.

In addition to these measurements RAJEWSKY, BELLOCH, LOHR and STAHLHOFEN \[10\] investigated the content of radium-226 in human foetal bones correlated to the stage of foetal development. The measurements revealed the content of radium-226 in human foetal bones to remain constant from mens IV to mens X within the different stages of foetal development (1 mens = 28 d). This constant level is identical with the specific activity of radium-226 in the bones of adults (Fig. 1). The specific activity of radium-226 in different stages of development is related to one gram of bone ash, fresh weight or calcium (Table I).

The natural Ra\(^{226}\) content of foetal bones and its relation to the stage of development (average values)

The standard deviations of the average specific radium-226 activities are also shown in Table I. The total standard deviation is composed of instrumental error and the deviation of the radium-226 content of the individual bones caused by biological variability.

As can be seen in Table I, the average specific radium-226 content is \(1.3 \times 10^{-14}\) c/g of bone ash, respectively \(4 \times 10^{-14}\) c/g calcium. The amount of calcium in the bone ash within the different stages of foetal development was constant and was almost identical with the amount of calcium in the bones of adults (370 mg/g of bone ash). The amount of calcium was determined by precipitation as oxalate followed by a volumetric determination with potassium permanganate.

The specific activity of radium-226 in foetal soft tissue, such as muscles, intestine, liver and spleen was approximately \(1 \times 10^{-16}\) c/g of fresh weight.
### TABLE I

**THE NATURAL Ra^{226} CONTENT OF HUMAN FOETAL BONES**

<table>
<thead>
<tr>
<th>Stage of development (mens)</th>
<th>Ra^{226} content/g wet bone (10^{-15}) c/g (average values)</th>
<th>Mean-square variance</th>
<th>Ra^{226} content/g ash (10^{-15}) c/g (average values)</th>
<th>Mean-square variance</th>
<th>Ra^{226} content/g calcium (10^{-15}) c/g (average values)</th>
<th>Mean-square variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>12.0</td>
<td>-</td>
<td>17.0</td>
<td>-</td>
<td>0.52</td>
<td>-</td>
</tr>
<tr>
<td>V</td>
<td>11.3</td>
<td>-</td>
<td>12.6</td>
<td>-</td>
<td>0.36</td>
<td>-</td>
</tr>
<tr>
<td>VI</td>
<td>13.6</td>
<td>± 0.6</td>
<td>13.5</td>
<td>± 0.7</td>
<td>0.47</td>
<td>± 0.20</td>
</tr>
<tr>
<td>VII</td>
<td>13.2</td>
<td>± 4.7</td>
<td>13.1</td>
<td>± 6.2</td>
<td>0.37</td>
<td>± 0.20</td>
</tr>
<tr>
<td>VIII</td>
<td>13.2</td>
<td>± 7.6</td>
<td>12.8</td>
<td>± 6.8</td>
<td>0.33</td>
<td>± 0.17</td>
</tr>
<tr>
<td>IX</td>
<td>11.2</td>
<td>± 6.7</td>
<td>11.3</td>
<td>± 4.5</td>
<td>0.38</td>
<td>± 0.14</td>
</tr>
<tr>
<td>X</td>
<td>17.5</td>
<td>± 12.7</td>
<td>12.6</td>
<td>± 6.0</td>
<td>0.35</td>
<td>± 0.22</td>
</tr>
<tr>
<td><strong>Total average values</strong></td>
<td>13.0</td>
<td>± 8.0</td>
<td>13.0</td>
<td>± 6.0</td>
<td>0.40</td>
<td>± 0.20</td>
</tr>
</tbody>
</table>
which is identical to the activity determined in the tissues of adults [5,6,8,11].
The specific activity is constant in all investigated stages of foetal development (mens IV to mens X). The specific activity of radium-226 of samples obtained by ashing the whole foetus is of the same order of magnitude as the corresponding values of foetal bones as summarized in Table I. These findings are explained by the small amount of radium-226 in the soft tissue. The specific activity of radium-226 per gram of ash obtained by cremating the total foetus is constant within all stages of foetal development. This means that the total amount of radium-226 in the foetus increases during the foetal development (as shown in Fig. 2) i.e., corresponding to calcium—the chemical homologue of radium-226—there is a linear correlation of the total amount of radium-226 and the development of the foetus. The calcium content increases linearly with the time of development, as already found by others [12, 13, 14].

In the adult, the content of radium-226 reaches a constant value of about $0.4 \times 10^{-10}$ c [11, 15]; 85% of the total body radium-226 content is distributed in the skeleton, whereas about 15 to 20% is deposited in the soft tissue [6,11].

3. THE RADIIUM-226 CONTENT OF THE HUMAN PLACENTA

Investigations on the content of radium-226 in the placenta were performed in order to obtain information on the eventual placental transfer of this element at natural activity level [10]. Measurements of placental tissue revealed a specific radium-226 activity of $1.6 \times 10^{-15}$ c/g of fresh weight or $1.4 \times 10^{-14}$ c/g of ash. These specific activities are identical within the biological variability with the specific activity of radium-226 in the foetal soft tissue and the average radium-226 activities of the different organs of adults. On the other hand, as the specific radium-226 activities of the foetal bones are equal to those of adults, preferential discrimination of radium-226 by the placental barrier may not be assumed in these cases of natural activity level. Similar results for strontium-90 were found by KRIEGEL [16] who injected carrier-free strontium-90 into the tail vein of albino rats 21 d prior to and shortly after conception, as well as on the tenth and seventeenth day after the gestation period. These experiences revealed the placenta not to be a barrier for the used strontium isotope which is a chemical homologue of radium-226.

4. DISTRIBUTION OF Po$^{210}$ IN THE HUMAN ORGANISM

The next problem to be investigated was the ratio of Pb$^{210}$/Po$^{210}$ and the distribution pattern of polonium-210 in the human organism. Ashes of human femur and tibia bones which were stored for two years, were dry-ashed at 500°C, brought into solution, and the lead-210 activity was estimated by the alpha ray activity of its daughter polonium-210 which was chemically separated by silver-plating. The specific activity of lead-210 was $3.7 \times 10^{-15}$ c/g of wet bones [11]. The specific activity of polonium-210 was determined by wet ashing immediately after section and proved to be
3 × 10^{-14} \text{c/g} \text{ of wet bones on the average} [17]. From these values the ratio of Po^{210}/Pb^{210} is calculated to be 0.8. Comparable results were found by OSBORNE [18], HOLTZMAN [19], and OBERHAUSEN [20].

The distribution of the total polonium-210 in the human body was studied by measuring the polonium-210 activity of different organs using the chemical procedure of wet ashing and chemical separation by silver-plating [17]. As can be seen in Table II, the skeleton contains about 60% of the total polonium-210. The activities determined in the different organs are identical with the measurements performed by HILL [21], OSBORNE [18], and HOLTZMAN [19]. From these measurements the content of polonium-210 in the total body of the standard man (70 kg total weight) proved to be 490 pc. To this calculation the average specific activity of polonium-210 is assumed to be 0.3 × 10^{-14} \text{c/g} \text{ of fresh soft tissue (Table II).}

5. ESTIMATION OF THE TOTAL ALPHA-RAY ACTIVITY AND DETERMINATION OF THE CONTENT OF Th^{228} IN HUMAN BONES BY MEANS OF THE MIXING METHOD

5.1. Brief review on the mixing method

The activities of thorium-228 or the total alpha-ray activity respectively in human bone ashes were measured by the so-called mixing method suggested by ROSHOLT, MUTH and OBERHAUSEN [22, 23]. Here, the ash is mixed homogeneously with a scintillator (ZnS(Ag)), the light pulses of which are measured by a photomultiplier [11, 22, 23, 24]. By mixing the ashes with the scintillator a significant increase in efficiency could be obtained in comparison with the ZnS(Ag) screen method of MAYNEORD et al. [25]. The activity of thorium-228 was determined by the coincidences of the transitions radon-220 to polonium-216 to lead-212, which follow one another very quickly and which indicate the thorium-228 content directly (half-life of polonium-216 = 0.158 s). The counting yield of this method is determined by the following parameters:
1. the mixing proportion of the scintillator ZnS(Ag) and ash;
2. the thickness of the layer of the sample;
3. the size of particles of ZnS(Ag) and ash;
4. the absorption coefficient of the mixture for the luminescence light of ZnS(Ag);
TABLE II

THE DISTRIBUTION OF Po$^{210}$ IN THE HUMAN BODY

<table>
<thead>
<tr>
<th>Organ</th>
<th>Ratio: Organ weight to body weight (%)</th>
<th>Po$^{210}$ content/g wet tissue ($10^{-14}$ c/g)</th>
<th>Po$^{210}$ content/g wet tissue average values ($10^{-14}$ c/g)</th>
<th>Fraction of total activity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>2.40</td>
<td>0.5</td>
<td>1.3</td>
<td>5.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>0.21</td>
<td>0.1</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>43.00</td>
<td>0.05</td>
<td>0.2</td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>0.43</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>10.00</td>
<td></td>
<td>3.2</td>
<td>60.5</td>
</tr>
<tr>
<td>Other tissues</td>
<td>44.00</td>
<td></td>
<td>0.2</td>
<td>16.6</td>
</tr>
<tr>
<td></td>
<td>(assumed to have same concentrations as muscle)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. the chemical consistency of the sample.
Investigation of the influence of these different parameters on the counting yield led to the following results:
1. the optimal mixing ratio of bone ash and ZnS(Ag) is 1:2;
2. the saturation thickness of the mixture was 5.4 g (with a sample container of 4.5 cm diam.);
3. there was no correlation between the counting rate and the size of particles of bone ash if their diameter was smaller than 3 μm;
4. the optical remission is a measure for the absorption of the luminescence light in the mixture.

An empirical correlation of the optical remission and the counting yield of the sample was found for the total alpha-ray activity of radium-226 and its daughters, thorium-228 and its decay products and polonium-210. Besides this, the counting yield as a function of the optical remission of the sample was determined for the coincidences of the transitions radon-220 to polonium-216 and polonium-216 to lead-212.

In the measurement of the total alpha-ray activity by this method we obtain a counting rate which is on the average 15 times higher than by measuring the same specific activity by the ZnS(Ag) screen method. Con-
cerning the coincidences radon-220 to polonium-216 to lead-212 this factor is about 20.

Time could thus be saved in measurements of the lowest natural alpha activities at the same standard deviation as the counting rate.

5.2. Determination of the radon-226 and thorium-228 content in human bones

This mixing method was used in order to determine the total alpha-ray activity and the thorium-228 content in human bone ashes. The radium-226 content of the same samples was calculated as described below. The sealed bone ash samples were stored for three weeks in order to equilibrate radium-226 and thorium-228 with its daughters. Measurements of the equilibrated samples were repeated two or three times.

The portion of the activity of thorium-228 in human bone ashes was determined by measuring the coincidences. The content of polonium-210 in the bones was separately determined, as described in Chapter 4. The portion of the counting rate caused by polonium-210 was subtracted from the counting rate due to the total alpha-ray activity; the counting rate is due to the alpha-ray activity of radium-226, thorium-228 and their short-lived decay products. The subtraction of the portion of the counting rate due to the activity of thorium-228 and its daughters, calculated with the corresponding thorium-228 counting efficiencies, results finally in the counting rate due to the activity of radium-226 and its short-lived decay products. The radium-226 content of the samples is determined by means of the corresponding counting efficiencies.

The radium-226 content obtained by this method was controlled by the emanation method. Here the radon was measured in an electrometer arrangement with two ionization chambers in compensation. The results of both methods are identical within the limits of error, which were ±30% at the emanation method and ±35% for the mixing method. The naturally-occurring thorium-228 is brought into human bones by radium-228 [25]. Therefore, there were good reasons to correlate the measured activity of thorium-228 to the content of radium-226 in human bones [25]. Presuming radium-228 and thorium-228 to be in radioactive equilibrium, the ratio $\text{Th}^{228}/\text{Ra}^{226}$ is representative for the ratio of two radium isotopes, radium-228 and radium-226 in human bones [26]. The observed thorium-228 to radium-226 ratio was 0.34 if the three values marked with an asterisk in Table III were not taken for the calculation of the average value.

The average content of radium-226 was calculated to be $(1.4 \pm 0.5) \times 10^{-14} \text{c/g}$ of bone ash. This value is identical with the specific radium-226 activity obtained by means of the emanation method. The average thorium-288 activity is $(4 \pm 1) \times 10^{-15} \text{c/g}$ of bone ash as shown in Tables III and IV. If all the values scheduled in Table III are taken for the calculation of the average, the ratio $\text{Th}^{228}/\text{Ra}^{226}$ is 0.4. Since the elevated activities of thorium-228 were found in such bones which contained an elevated amount of radium-226, it might be concluded that there are persons concerned with a high level of naturally-occurring activity in their food. These results are identical within the instrumental errors with values published by SOMMERMEYER et al. and LUCAS et al., who used a chemical enrichment method [26, 27, 28].
TABLE III
THE NATURAL Ra\(^{226}\) AND Th\(^{228}\) CONTENT IN HUMAN BONES (FEMUR) MEASURED WITH THE "MIXING METHOD"

<table>
<thead>
<tr>
<th>Ra(^{226}) content/g ash ((10^{-14} \text{ c/g}))</th>
<th>Ra(^{226}) content/g wet tissue ((10^{-15} \text{ c/g}))</th>
<th>Th(^{228}) content/g ash ((10^{-14} \text{ c/g}))</th>
<th>Th(^{228}) content/g wet tissue ((10^{-15} \text{ c/g}))</th>
<th>(\frac{\text{Th}^{228}}{\text{Ra}^{226}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>6.3</td>
<td>0.6</td>
<td>1.8</td>
<td>0.28</td>
</tr>
<tr>
<td>2.2</td>
<td>6.1</td>
<td>0.6</td>
<td>1.7</td>
<td>0.27</td>
</tr>
<tr>
<td>1.3</td>
<td>4.3</td>
<td>0.7</td>
<td>2.3</td>
<td>0.54</td>
</tr>
<tr>
<td>1.4</td>
<td>4.2</td>
<td>0.1</td>
<td>0.3</td>
<td>0.07</td>
</tr>
<tr>
<td>1.1</td>
<td>3.7</td>
<td>0.5</td>
<td>1.7</td>
<td>0.45</td>
</tr>
<tr>
<td>0.7</td>
<td>1.8</td>
<td>0.4</td>
<td>1.1</td>
<td>0.67</td>
</tr>
<tr>
<td>2.5</td>
<td>6.5</td>
<td>0.7</td>
<td>1.8</td>
<td>0.28</td>
</tr>
<tr>
<td>0.9</td>
<td>2.4</td>
<td>0.4</td>
<td>1.0</td>
<td>0.45</td>
</tr>
<tr>
<td>0.9</td>
<td>2.7</td>
<td>0.1</td>
<td>0.3</td>
<td>0.10</td>
</tr>
<tr>
<td>1.3</td>
<td>3.7</td>
<td>0.4</td>
<td>1.1</td>
<td>0.31</td>
</tr>
<tr>
<td>2.9</td>
<td>7.8</td>
<td>2.9 +</td>
<td>7.8 +</td>
<td>1.00 +</td>
</tr>
<tr>
<td>2.4</td>
<td>6.1</td>
<td>0.4</td>
<td>1.0</td>
<td>0.17</td>
</tr>
<tr>
<td>0.7</td>
<td>1.8</td>
<td>0.1</td>
<td>0.3</td>
<td>0.14</td>
</tr>
<tr>
<td>0.8</td>
<td>2.4</td>
<td>0.3</td>
<td>0.9</td>
<td>0.38</td>
</tr>
<tr>
<td>2.2</td>
<td>5.5</td>
<td>2.2 +</td>
<td>5.5 +</td>
<td>1.00 +</td>
</tr>
<tr>
<td>1.3</td>
<td>3.3</td>
<td>0.5</td>
<td>1.3</td>
<td>0.38</td>
</tr>
<tr>
<td>1.2</td>
<td>3.6</td>
<td>0.2</td>
<td>0.6</td>
<td>0.17</td>
</tr>
<tr>
<td>1.0</td>
<td>2.6</td>
<td>0.5</td>
<td>1.3</td>
<td>0.50</td>
</tr>
<tr>
<td>1.3</td>
<td>3.3</td>
<td>0.8</td>
<td>2.1</td>
<td>0.62</td>
</tr>
<tr>
<td>1.6</td>
<td>3.3</td>
<td>1.6 +</td>
<td>3.3</td>
<td>1.00 +</td>
</tr>
<tr>
<td>1.1</td>
<td>2.0</td>
<td>0.5</td>
<td>0.9</td>
<td>0.45</td>
</tr>
<tr>
<td>1.2</td>
<td>2.9</td>
<td>0.3</td>
<td>0.7</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Values noted (+) are not considered at the average values.

| Average values of all samples |
|---|---|---|---|---|
| 1.46 | 3.9 | 0.4 | 1.2 | 0.34 |
| 1.46 | 3.9 | 0.7 | 1.8 | 0.42 |

The values published by MUTH and OBERHAUSEN and by MAYNEORD et al. are also comparable [20, 25, 29].
### TABLE IV

AVERAGE VALUES OF THE NATURAL $^{226}$Ra AND $^{228}$Th CONTENT IN HUMAN BONES

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean $^{226}$Ra content $/g$ ash $(10^{-14}c/g)$</th>
<th>Mean $^{228}$Ra content $/g$ wet bone $(10^{-14}c/g)$</th>
<th>Mean $^{226}$Th content $/g$ ash $(10^{-14}c/g)$</th>
<th>Mean $^{228}$Th content $/g$ wet bone $(10^{-14}c/g)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emanations method</td>
<td>$1.37$</td>
<td>$3.7$</td>
<td>$1.46$</td>
<td>$5.9$</td>
</tr>
<tr>
<td>The mixing method</td>
<td>$1.2$</td>
<td>$3.9$</td>
<td>$0.4$</td>
<td>$1.2$</td>
</tr>
</tbody>
</table>

### Average Values

- Average $^{226}$Ra content: $1.37$ $10^{-14}c/g$
- Average $^{228}$Ra content: $3.7$ $10^{-14}c/g$
- Average $^{226}$Th content: $1.46$ $10^{-14}c/g$
- Average $^{228}$Th content: $5.9$ $10^{-14}c/g$

### Mean Square Error of the Measurement

- $^{226}$Ra: $0.4$ $10^{-14}c/g$
- $^{228}$Ra: $1.5$ $10^{-14}c/g$
- $^{226}$Th: $0.4$ $10^{-14}c/g$
- $^{228}$Th: $1.4$ $10^{-14}c/g$

### Mean Square Variance of the Biological Variability

- $^{226}$Ra: $0.4$ $10^{-14}c/g$
- $^{228}$Ra: $1.5$ $10^{-14}c/g$
- $^{226}$Th: $0.4$ $10^{-14}c/g$
- $^{228}$Th: $1.4$ $10^{-14}c/g$
6. ESTIMATION OF THE DOSE-RATE IN HUMAN TISSUES BY THE ALPHA-RAY ACTIVITY OF THE NATURALLY-OCCURRING RADIOELEMENTS

6.1. Estimations for human bones

The activities found by these investigations were used for an estimation of the internal radiation dose-rate caused by radium-226, thorium-228 and polonium-210. The dose-rate in the soft tissues within the cavities of bones is estimated below. This body-burden is caused by the alpha-ray activity deposited in the mineral zones of the bone. Estimation of the absorbed dose-rate is performed for the different diameters of the cavities, since it is necessary to distinguish the Haversian systems, the osteocytes and the still smaller canaliculi.

Distribution pattern of the alpha-rays in the mineral zones of the bone presumed to be homogeneous, the dose $D_b/T$ at point $P$ of the soft tissue within the cavity may be calculated according to SPIERS [30, 31, 32] by means of the following formula

$$D_b/T = \frac{(NE/\rho')F}{(1.36)} \quad (1)$$

where $\rho'$ is the ratio of ranges of the alpha particles in soft tissue and bone which is equal to 1.36, $E$ is the energy of the alpha particles, $N$ the number of alpha-decays per second and cm$^2$ and $F$ a geometrical factor which is dependent on the diameter, the shape of the considered cavity and the range of the alpha particles [30, 31]. It is called the mean factor of geometry and converges to unity for very small diameters of the cavity. In this paper we use for the $F$ factors of radium-226 the values published by CHARLTON and CORMACK [33]. Also by this method we calculated the $F$ factors of thorium-228 and its daughters and polonium-210. With these $F$ values the dose-rates absorbed by soft tissues were calculated as shown in Eq.(2)

$$D_b/T = \frac{51.15 \times 1.85}{1.36} c \sum n_p E_p F = 69.6 c \sum n_p E_p F \text{ rad/d} \quad (2)$$

where $\sum n_p E_p$ is 10.56 for radium-226 and 30% of its short-lived decay products, 32 for thorium-228 equilibrated with its daughters and 5.3 for polonium-210; $c$ is the specific activity of the radionuclide in microcuries per gram of compact bone. The density of the bone is assumed to be 1.85 g/cm$^3$ according to SPIERS [30]. These calculations were performed with an average content of radium-226 of $4 \times 10^{-15}$ c/g of compact bone a content of thorium-228 of $1.2 \times 10^{-15}$ c/g and a content of polonium-210 of $3.1 \times 10^{-16}$ c/g respectively.

It became evident that the absorbed dose-rate of polonium-210 in bone was four times the calculated value of radium-226 and 30% of its daughters. The absorbed dose calculated for thorium-228 equilibrated with its daughters is likewise approximately equal to the dose of radium-226 and its daughters, as shown in Table V where the doses are given in millirems. The quality factor of 10 is used in order to convert the doses absorbed from alpha particles from millirads into millirems.
6.2. The absorbed dose-rate by alpha rays emitted by the naturally-occurring radioelements within the human soft tissue

The average absorbed dose-rate caused by the alpha-ray activity emitted from radium-226, thorium-228 and their daughter products, and polonium-210 in human soft tissue, was also calculated. A homogeneous distribution pattern of the radionuclides in soft tissue was presumed.

A representative average of the specific activity of $0.3 \times 10^{-14}$ c polonium-210 per gram of fresh tissue was assumed. The resulting body burden was 3 mrem/yr. The specific activity of thorium-228 in soft tissue was calculated, and it was assumed in analogy to radium-226, that the content of thorium-228 is similarly only about 20% of the activity of thorium-228 of the total body [34]. In other words, the specific activity of thorium-228 is assumed to be $0.4 \times 10^{-16}$ c/g of fresh tissue. With this assumption the annual dose-rate absorbed by the soft tissue from thorium-228 and its daughters is 0.3 mrem.

The activity of thorium-228 in the total body of the standard man (70 kg) proved to be 14 pc at a specific thorium-228 content per gram of bone ash of $0.4 \times 10^{-14}$ c and a skeleton ash weight of 2.8 kg.

Estimating the absorbed dose-rate by radium-226, this radioelement is assumed to be equilibrated with not more than 35% of its short-lived daughters. With this assumption the annual dose-rate is 0.2 mrem. If we presume, however, the amount of radon escaping from soft tissue to be compensated by the content of radon inhaled through the respiratory tract, the annual dose-rate is 0.5 mrem.

The distribution pattern of the descendants of radon borne in soft tissue is not known exactly [3,34]. Consequently, estimation of the absorbed dose-rate by the alpha rays of radium-226 and its daughters, as given above, is certainly not without error. It is possible that the content of radon in the soft tissue of some well-circulated organs is higher, due to the content of radium-226 as the blood is supplied with radon by inhaled air [3,34]. JACOBI estimated the average body burden caused by a parameter inhalation of specific activity of radon-222 to be as high as $10^{-13}$ c/l. Estimation was done by consideration of the short-lived daughters polonium-218 to polonium-214 which arise from radon-222 in soft tissue. In the state of saturation radon is in equilibrium in the tissue with its daughters polonium-218 through polonium-214 [35]. Presumed the solubility of radon to be 0.3 in the soft tissue and 5 in the fat deposit, the annual absorbed dose-rate is 0.1 mrem, or 2 mrem, respectively.

The burden of the lung caused by the respiration of radon-222, radon-220 (thoron) and their daughters has to be discussed separately. JACOBI, SCHRAUB and co-workers calculated the annual dose-rate in the lung. Concentration of radon-222 in the respiratory air presumed to be $1 \times 10^{-13}$ c/l the radiation burden within the lower and upper respiratory tract proves to be 50 to 250 mrem [35,36] respectively, whereas the annual lung burden caused by an equivalent concentration of radon-220 and its daughters is approximately 10 mrem, according to JACOBI [25].

Estimations of the absorbed dose-rate discussed so far cover only the alpha-ray radiation emitted by the radioelements of the radium and thorium series. Estimation of the additional body burden caused by the radiation
### Table V

**DOSE-RATE OF THE NATURAL ALPHA-EMITTING RADIOACTIVE NUCLIDES IN THE HUMAN BODY IN COMPARISON TO THE DOSE-RATE OF THE FISSION PRODUCT Sr\(^{90}\)**

<table>
<thead>
<tr>
<th>Natural radioactive nuclide</th>
<th>Dose-rate in mrem/yr</th>
<th>Gonad</th>
<th>Bone (Haversian systems)</th>
<th>Lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ra(^{226}) (and one-third of the short-lived products)</td>
<td>0.2</td>
<td>10.7 Canaliculi 0 μ</td>
<td>10.3 Osteocytes 5 μ</td>
<td>5.3 Haversian canals 50 μ</td>
</tr>
<tr>
<td>Th(^{228}) (in radioactive equilibrium)</td>
<td>0.3</td>
<td>9.8 Canaliculi 0 μ</td>
<td>9.4 Osteocytes 5 μ</td>
<td>5.7 Haversian canals 50 μ</td>
</tr>
<tr>
<td>Po(^{210})</td>
<td>3</td>
<td>42.0 Canaliculi 0 μ</td>
<td>39.5 Osteocytes 5 μ</td>
<td>20.0 Haversian canals 50 μ</td>
</tr>
<tr>
<td>Rn(^{222}) (and short-lived products)</td>
<td>∼0.1</td>
<td>∼0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ra(^{220}) (and short-lived products)</td>
<td>---</td>
<td>---</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Sr(^{90}) + Y(^{90})</td>
<td>---</td>
<td>2.7</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

of beta- and gamma-rays emitted by radionuclides of the radium- and thorium series was undertaken and revealed the portion of the dose emitted by the beta- and gamma-ray radiation of radium-226, thorium-228 and lead-210, including their daughters, to be low in comparison with the body burden caused by the alpha-ray radiation emitted by these radionuclides. For the purpose of comparison, the radiation burden caused by the fission-product strontium-90, presuming a specific activity of \(1 \times 10^{-12} \text{ c/g}\) of calcium, is 2.7 mrem/yr in the compact bones, as shown in Table V. The internal radiation dose to the skeleton caused by the alpha-ray radiation emitted by plutonium-239, the alpha-emitting isotopes of uranium, and the radionuclides of the actinium series is low in comparison to the radiation dose caused by the alpha-ray emitting radionuclides of the radium- and thorium-series [28,37,38,39]. Besides this, the identical radium activities obtained from measurements made according to the mixing and emanation method show the alpha-ray radiation of uranium-235, uranium-238, thorium-232, thorium-230 and
plutonium-239, and the radioelements of the actinium series, to be without any significant importance. Consequently they may be discounted in the estimation of the absorbed dose-rate. In fact, these nuclides are not measured by the radium-emanation method, but contribute to the measuring effect of the mixing method and would cause a radium-226 activity being apparently higher than that measured by the emanation method.

**REFERENCES**

C. R. HILL: Table V of your paper gives the dose rate to gonad due to polonium-210. Is this based on measurement or estimated from the general level found in other soft tissues?

In this connection it is interesting to recall that autoradiographs were published by Lacassagne as early as 1924* showing strong uptake of polonium in several soft tissues including testes.

W. STAHLHOFEN: The calculation of the dose rate of polonium-210 in testes is based on an assumed average specific activity of polonium-210 in the soft tissue equal to $0.3 \times 10^{-14}$ c/g wet tissue.

W. V. MAYNEORD: I find myself in almost embarrassing agreement with Dr. Stahlhofen's results. Leaving aside the general problem, I think some of the most interesting results are certainly those relating to the foetus and the invariance, as it were, of the radium concentration in relation to age. In 1958 we measured 11 stillborn children and, I must confess to my great surprise, found concentrations agreeing very well with the adult cases. We have since made measurements on a number of foetal samples of varying age and again we found - in exact agreement with Dr. Stahlhofen - that the concentration seems to be independent of age, though of course, at the early ages, the measurements are in fact very difficult and error is likely to be high.

URANIUM
(Session 15)
DETECTION AND EVALUATION OF URANIUM EXPOSURES

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OAK RIDGE, TENN., UNITED STATES OF AMERICA

Abstract — Résumé — Аннотация — Resumen

DETECTION AND EVALUATION OF URANIUM EXPOSURES. Approximately 1800 personnel of the Union Carbide Corporation-operated United States Atomic Energy Commission Y-12 Plant are involved in the routine industrial-scale processing of uranium. Personnel monitoring is accomplished by means of urinalysis and \textit{in vivo} gamma-spectrum analysis programmes. The interpretation of data from the two programmes and the relationship thereof are presented.

Personnel-monitoring results from the two programmes are divided into four classes:

1. low urinalysis and low \textit{in vivo} results;
2. high urinalysis and low \textit{in vivo} results;
3. low urinalysis and high \textit{in vivo} results; and
4. high urinalysis and high \textit{in vivo} results.

The majority of the persons monitored fall into the first class; however, from the exposure standpoint the last three classes are of prime interest. Examples of cases falling into these classes are presented. Cases exhibiting biological half-life in the lung, ranging from less than 100 d to approximately 800 d, are presented and discussed.

Correlation coefficients for results of the two programmes, grouping data by type work, are also presented. Correlations ranged from 0 to +0.32.

DÉTECTION ET ÉVALUATION DE LA CONTAMINATION PAR L'URANIUM. Détection et évaluation de la contamination par l'uranium. Quelque 1800 membres du personnel de l'usine Y 12 de la Commission de l'énergie atomique des États-Unis, exploitée par la Union Carbide Corporation, s'occupent de façon régulière de la préparation industrielle de l'uranium. Le contrôle dosimétrique du personnel se fait selon un programme d'analyses des urines et un programme d'analyses \textit{in vivo} du spectre gamma. Les auteurs interprètent les données obtenues au moyen des deux programmes et en dégagent les relations.

Les résultats du contrôle dosimétrique du personnel, donnés par les deux programmes, sont répartis en quatre catégories:

1. faibles pour l'analyse des urines et faibles pour l'analyse \textit{in vivo};
2. élevés pour l'analyse des urines et faibles pour l'analyse \textit{in vivo};
3. faibles pour l'analyse des urines et élevés pour l'analyse \textit{in vivo};
4. élevés pour l'analyse des urines et élevés pour l'analyse \textit{in vivo}.

La majorité des résultats se classent dans la première catégorie; toutefois, du point de vue de la contamination, ce sont les trois dernières catégories qui présentent le plus grand intérêt. Les auteurs citent des exemples de résultats se classant dans ces catégories. Ils présentent et discutent des cas où la période biologique dans les poumons allait de moins de 100 j à environ 800 j.

Les auteurs présentent également les coefficients de corrélation pour les résultats obtenus au moyen des deux programmes, les données étant groupées par type d'activité. Les coefficients varient entre 0 et +0.32.

ОБНАРУЖЕНИЕ И ОЦЕНКА ОБЛУЧЕНИЯ УРАНОМ. Почти 1800 служащих "Юнион карбид корпорейшн", работающих на заводе Y-12 Комиссии по атомной энергии США, связаны с обычной промышленной обработкой урана. Дозиметрия персонала проводится по программам проведения анализов мочи и анализов гамма-спектра \textit{in vivo}. Представлена интерпретация данных, полученных при выполнении этих двух программ и взаимосвязь между ними.

Результаты дозиметрии персонала, проводимой на основании этих двух программ, делятся на четыре категории: 1) результаты анализов мочи низкой активности и результаты измерений низкой активности; 2) результаты анализов мочи высокой активности и результаты измерений высокой активности; 3) результаты анализов мочи низкой активности
and C. M. WEST

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INTRODUCTION

Background

The origin of the detection and evaluation of uranium exposures can be traced back to the University of Rochester during the early days of the Manhattan Project. The guidelines derived from the work of HODGE et al., [1] are still in wide use today. Since the 1940's, when the original research was undertaken, the quantities, isotopic enrichments, and chemical and physical forms of uranium have greatly increased. It is logical to assume that this increase in the variety of forms of uranium has been accompanied by a like increase in body reactions when such materials are assimilated in the body.

The Y-12 Plant which is operated by the Nuclear Division of Union Carbide Corporation for the United States Atomic Energy Commission (USAEC) does uranium chemical and metallurgical processing on a large scale. Uranium enriched in the uranium-235 isotope is received as UF₆ converted to UF₄, and reduced to metal. This enriched metal, as well as normal or depleted uranium metal, is cast, rolled, formed, and machined into many configurations to fill the needs of the USAEC. In addition, scrap from many stages of these operations is treated for the recovery of uranium.

Personnel exposure control and monitoring

Approximately 1800 persons routinely work with uranium in the forms and under the conditions previously mentioned. It is established practice to
limit internal exposure to acceptable levels by appropriate environmental controls. Environmental air sampling is conducted on a routine basis in all processing areas to evaluate internal exposure potential via inhalation. In general, environmental air levels are within the limits prescribed by the National Committee on Radiation Protection (NCRP) [2] and the International Committee on Radiological Protection (ICRP) [3]. In order to evaluate the effectiveness of such controls and to estimate the degree of internal exposure, routine personnel monitoring programmes have been established. Due to the number of persons involved, these programmes must be such that a large number of persons can be adequately monitored with a minimum of attention to individual cases. Consequently, the personnel monitoring programmes are designed and administered to highlight the potential elevated exposure cases and at the same time provide an adequate monitoring history regardless of the level of exposure.

Purpose

The purpose of this paper is to: (1) discuss the Y-12 internal personnel monitoring techniques and how each contributes to the task of exposure evaluation; and (2) present experience as to the mode and rates of elimination of uranium from the body. Since the lung is considered to be the critical organ for inhaled uranium under the conditions encountered in the Y-12 Plant, the discussion herein is restricted to lung burden considerations.

CHARACTERISTICS OF EXPOSURE MATERIAL

To accomplish production objectives, uranium is handled in many chemical forms. Examples are: UF₅, UF₄, UO₂(NO₃)₂, U₃O₈, UO₂, U metal, and U alloys. In these operations, enrichments in the uranium-235 isotope range from near zero to approximately 90%. In the uranium-235 enrichment process, the percentage of uranium-234 is also increased. Due to the high alpha specific activity of uranium-234 this isotope is the chief source of potential internal hazard from enriched uranium.

It has been determined that uranium particles in environmental air range in size from submicron to greater than 10 μm, the upper limit for internal deposition by inhalation.

The solubility of the uranium compound ranges from the highly soluble UO₂(NO₃)₂ to the highly insoluble high-fired oxides, ceramics, and alloys.

PERSONNEL MONITORING PROGRAMMES

Routine monitoring of all personnel who work in uranium areas is accomplished by uranium urinalysis and in vivo gamma spectrum analysis. If either method points up potential exposure cases, more frequent urinalyses and in vivo gamma spectra analyses are used to evaluate better the degree of exposure.
Urine samples are submitted after at least a two-day work break. The two-day work break allows time for the highly soluble uranium to be eliminated. The uranium voiding rate of the sample, together with the time between voidings as listed by the employee voiding the sample are used to calculate the urinalysis results in units of disintegrations per minute per 24-h voiding. Frequency of participation ranges from weekly to quarterly as determined statistically to assure, with 95% confidence, that 95% of the persons average below a pre-set limit if in reality they do. WEST and REAVIS have discussed in detail the determination of participation frequency in a previous paper [4]. The analytical technique employed consists of electroplating the uranium from duplicate 20-ml aliquants of raw urine onto silver discs. Each disc received duplicate 30-min alpha counts. Details of the method have been previously described by PATTERSON [5] and HAMRICK [6].

In vivo spectrum analyses

In vivo spectrum analyses are made by utilizing two 9 by 4-in NaI detectors, one against the chest and the other against the back, positioned to detect the 186-keV gamma from the uranium-235 located in the lung region. Prior to a routine 20-min measurement, the subject takes a shower to remove surface contamination. In order to determine the total burden of uranium, the isotopic distribution of the exposure material must be known. COFIELD's paper [7] presents a comprehensive description of the general techniques of uranium detection by an in vivo gamma spectrum analysis. A description of the presently used facility can be found in the Y-12 Radiation Safety Manual [8]. Personnel are monitored by in vivo analysis once a month if they participate each week in the urinalysis programme and once every 12 months if they participate less frequently than weekly. More frequent monitoring is initiated on an individual or group basis as merited by elevated urine and/or in vivo results, or when it is known that special exposure conditions exist.

Method used to minimize exposure

Personnel who have monitoring data above the Plant Action Limit (PAL) are re-assigned to areas that do not process uranium in any form until their personnel monitoring results return to levels less than 25% of the Radiation Protection Guide (RPG) limits. The PAL for urinalysis results is set at approximately 35% of the uranium excretion rate that will indicate a lung burden that is equivalent to a maximum dose of 0.3 rem/week. The PAL is set at this level to increase the assurance of protection by allowing for such variables as; (1) longer biological half-lives than the assumed 120 d; (2) other biological variations; and (3) laboratory imprecision, any of which can result in large sample-to-sample variations. These variations are shown in the data that are presented later. The PAL for in vivo analyses is set at that level of uranium lung burden which results in a dose of 0.3 rem/week.
DATA

Evaluation of personnel monitoring data

The personnel monitoring data obtained from uranium urinalysis and in vivo spectrum analysis can be categorized into four general classes: (1) low urinalysis, low in vivo spectrum analysis; (2) high urinalysis, low in vivo spectrum analysis; (3) low urinalysis, high in vivo spectrum analysis; and (4) high urinalysis, high in vivo spectrum analysis.

Class 1

Ninety-eight per cent of the personnel monitoring data falls into Class 1 and creates no problem in evaluating exposures. However, the other classes present some unique exposure evaluation problems.

Class 2

The personnel monitoring data for Employee Y2A, shown in Fig. 1, is an example of Class 2 exposure data – high urinalysis and low in vivo
spectrum analysis. This employee worked on jobs involving soluble uranium, such as dissolving, leaching, and evaporation operations. Note that the urine excretion level is well above the PAL, but the in vivo spectrum analyses indicate levels of approximately 50% of the PAL. Utilizing the excretion rate, assuming a biological half-life of 120 d, an estimated lung burden of 56% of the PAL is derived. Figure 2 shows the uranium urine excretion rate of another Class 2 case. This employee (Y2g) was exposed to a release of gaseous uranium hexafluoride. The drop in the urine excretion rate is indicative of a biological half-life of approximately 20 h. An in vivo spectrum analysis made four days after the exposure revealed no uranium lung burden. This case is typical of so-called soluble uranium compounds. Soluble uranium is considered to be material which is readily removed from the lungs in a matter of days.

Class 3:

Figure 3 is the personnel monitoring data for Employee Y3 whose results fell into Class 3 (low urinalysis and high in vivo spectrum analysis). This employee worked in a salvage operation where exposure materials include such highly insoluble uranium as high-fired uranium oxides, uranium ceramics, and certain uranium metal alloys. Special attention was focused on this employee by a series of five elevated urine samples over the PAL. As shown in Fig. 3, with the exception of the five original elevated samples,
Internal monitoring data (case Y₃)

only one subsequent urine sample has been above the PAL. Notice, however, that in vivo analysis of Employee Y₃ revealed a level of approximately 140% of the PAL.

If one assumes a lung burden of 140% of the PAL and primary elimination via the urine with a 120-d biological half-life, the urine excretion rate should be approximately 430% of the PAL rather than the observed 40%. Thus, doubt was cast on the validity of the 120-d biological half-life assumption and/or the mode of elimination. In order to evaluate further the mode of elimination, faecal samples from this employee have been analysed for the past several months. The data shows that faecal excretion is approximately equivalent to that of the urine. Comparison in this case between the observed decrease in lung burden as evidenced by in vivo spectrum analysis and the total estimated amount excreted agree within 5%. Two other similar cases show a like relationship of urine and faecal excretion. As seen in Fig. 3, this employee is exhibiting a biological half-life of approximately 800 d which is almost seven times the normally assumed 120 d.

Class 4

The monitoring results from Employee Y₄ with both elevated urine and in vivo spectrum analysis (Class 4 monitoring data) are shown in Fig. 4. This employee worked in an area where the most probable exposure material was uranium oxide or metal. Notice that for an extended period of time both the urinalysis data and in vivo spectrum analysis data were above
the PAL. Such elevated urinalysis results are reassuring when in vivo analyses indicate a lung burden because they offer assurance that the burden is being eliminated at a reasonable rate. However, the urine excretion for this case accounts for only about half of the drop in the lung burden shown by in vivo spectrum analyses. This case exhibits a biological half-life of approximately 130 d and is an example of a typically insoluble uranium biological half-life (insoluble uranium is considered to be any material which is eliminated from the lung over a period of months). However, there is a flattening of the lung burden curve which increases the biological half-life.

DISCUSSION

Class differences

As shown previously, the overall experience at Y-12 has been that 98% of personnel have low results from both monitoring programmes (Class 1). Of the personnel who have to be reassigned to non-uranium activities due to elevated personnel monitoring results, the majority have been those of Class 4 (elevated results from both programmes). Exposure where high urinalysis results are not substantiated by in vivo spectrum analysis (Class 2) can, in general, be disregarded as far as the lung is concerned. The material will be clearing the lung at such a rate that no significant lung exposure will result. Those cases which show low urinalysis and high
in vivo spectrum results (Class 3) present the most tenacious problem. As monitoring data from Employee Y3 showed, it is possible for a person to have a significant amount of lung-stored uranium without the expected elevated urinalysis results.

Statistical correlation of personnel monitoring data

The individual examples of the types of personnel monitoring data presented show that the degree of relationship between urinalysis and in vivo spectrum analysis can vary greatly. Additional evidence of this comes from the correlation coefficients compiled for 200 persons whose exposures ranged from minimal to the levels shown by Case Y2A, Y2B, Y3, and Y4. As was expected, the correlation coefficients ranged from -1.0 to +1.0. These results re-emphasize the possibility of the four classes of personnel monitoring data. Table I lists correlation coefficients by job and exposure potential. Notice, that in the type of job where exposure potential is low and where Class 1 monitoring results are most frequent, the correlation coefficient is larger. Also note that as the potential for exposure increases, the degree of correlation decreases because cases belonging to Classes 2 and 3 begin to occur.

Metabolic model for uranium elimination

Through the evaluation of the data from the cases presented it has been possible to evolve a crude metabolic model for the elimination of uranium from the lung. In any uranium exposure there is a soluble component which is readily moved from the lung into the blood stream and excreted in the urine. The size of the soluble component is governed by the ultimate solubility of the exposure material. Figure 2 is an example where, for all practical purposes, the soluble component constituted all of the material. After the initial excretion of soluble material, the remaining deposit is eliminated via both the urine and the faeces. Not enough faecal data have been accumulated to establish its relative importance as a mode of elimi-
nation, but the preliminary data indicate that faecal excretion is approximately equivalent to urine excretion.

**Biological half-life**

The contrast in the type of personnel monitoring results can be partially explained by the evaluation of the rate of elimination from the body. Biological half-lives have been found to range from hours to several hundred days. Examples of short, medium, and long biological half-lives have been presented. An evaluation of potential exposure material can give insight into the type of monitoring results to be expected. However, there are many biological differences which may cause different individuals to eliminate similar exposure material at varying rates. The data for Case Y indicate an increase in biological half-life with time for insoluble uranium. This phenomenon has been observed in several cases and it appears that uranium does not follow a set biological half-life, but increases with time. Thus, the elimination of insoluble uranium from the lung follows a series of exponential functions or a power function. A previous uranium urine excretion data study also showed this pattern [9].

**Lung-deposited uranium guidelines**

As evidenced by the data, it is not possible to generalize about the detection and evaluation of uranium exposures. However, experience at Y-12 has shown that certain guidelines are applicable to lung-deposited uranium. If only soluble uranium compounds are involved, there is no problem as far as lung burden is concerned. For insoluble uranium, controls based on a 120-d biological half-life are adequate in the large majority of the exposure cases. Urinalyses are usually adequate to highlight potential exposure cases. However, when dose evaluations are to be made, considerations should be given to the possibilities of faecal excretion and moderate extents of the biological half-life beyond 120 d. In cases with biological half-lives of several hundred days (low urinalysis and high in vivo spectrum analysis results), in vivo spectrum analyses may be essential to estimate lung burdens adequately. Urine and faecal analyses in these cases are helpful in assessing the material balance between observed excretion and reduced lung burden as evidenced from in vivo spectrum analyses.

**SUMMARY**

All personnel monitoring data can be put into one of four classes: (1) low urinalysis and low in vivo spectrum analysis; (2) high urinalysis and low in vivo spectrum analysis; (3) low urinalysis and high in vivo spectrum analysis; and (4) high urinalysis and high in vivo spectrum analysis. Class 1 covers 98% of the personnel monitored at the Y-12 Plant. Of those who do show elevated results, the majority are Class 4. Class 2, which constitutes no significant lung exposure problem, and Class 3, which generally shows a biological half-life of several hundred days, can and do appear.
The cases illustrate that the elimination of uranium from the lung varies both in mode and rate of elimination depending, in part, on the exposure material. Insoluble uranium is excreted by both urine and faeces. Urinalyses are usually adequate to highlight potential exposure cases. However, when dose evaluations are to be made, considerations should be given to the possibilities of faecal excretion and moderate extenstions of a biological half-life beyond 120 d. To evaluate a uranium exposure thoroughly, urinalyses, faecal analyses, and in-vivo spectrum analyses are desirable.

REFERENCES


DISCUSSION

S. JACKSON: I should like to ask Mr. Scott two questions. Is it his experience that a half-life of about 120 d for uranium in the lung is associated with a single intake, whereas a longer half-life is observed in the case of multiple or chronic intake? And how many cases has he measured with a half-life in the lung of about 120 d?

L. M. SCOTT: We have several cases which show half-lives of approximately 120 d. However, we cannot determine whether they resulted from a single exposure or from a chronic exposure.
A CASE OF INHALATION OF ENRICHED URANIUM DUST

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Abstract — Résumé — Аннотация — Resumen

A CASE OF INHALATION OF ENRICHED URANIUM DUST. This paper presents the results obtained in the study of a case of inhalation of insoluble enriched uranium dust. The operational background to the case is explained. The results of urine and faecal sampling, and of body radioactivity measurements are presented and discussed. The authors' tentative conclusions include an assessment that the apparent half-life of insoluble uranium dust in the chest was about 1 yr and a note on the fact that the excretion data do not apparently account for all the material leaving the chest, the fact that the faecal excretion rate was higher than the urinary excretion rate for about 1½ yr after inhalation, and the suggestion that at times between 30 and 60 d a factor of 500 may be used to convert daily urinary uranium excretion levels to the level retained in the lung.

CAS D'INHALATION DE POUSSIÈRES D'URANİUM ENRICHİ. Les auteurs présentent les résultats qu'ils ont obtenus en étudiant un cas d'inhalation de poussières insolubles d'uranium enrichi. Ils indiquent les activités qui sont à l'origine de cette contamination. Ils exposent et discutent les résultats d'un échantillonnage d'urines et des matières fécales, et ceux de mesures de la radioactivité du corps. Dans leurs conclusions provisoires, les auteurs donnent une évaluation de la période apparente des poussières d'uranium insolubles déposées dans les poumons qu'ils estiment à un an environ; ils notent en outre que, d'après les données relatives à l'excrétion, les matières éliminées par les poumons ne se retrouvent apparemment pas toutes dans les excréta et que le taux d'excrétion fécale reste supérieur au taux d'excrétion urinaire pendant un an et demi environ après inhalation; enfin ils proposent qu'entre le trentième et le soixantième jour qui suit l'inhalation, on applique le coefficient 500 pour déterminer l'activité retenue dans les poumons à partir des quantités d'uranium excrétées chaque jour dans les urines.

СЛУЧАЙ ВДЫХАНИЯ ПЫЛИ ОБОГАЩЕННОГО УРАНА. Представлены результаты, полученные при изучении случая вдыхания нерастворимой пыли обогащенного урана. Дается описание рабочих условий, при которых произошло облучение. Представлены и обсуждаются результаты взятия проб мочи и экскрементов и измерения радиоактивности организма. Предварительные выводы авторов включают предположение, что предполагаемый период полураспада нерастворимой урановой пыли, находящейся в грудной клетке, равен примерно 1 году, отмечается, что данные выделения, очевидно, не соответствуют всему количеству материала, удаляемому из грудной клетки, и что скорость выделения изотопов с экскрементами выше, чем с мочой в течение 15 лет после вдыхания. Предполагается, что в период между 30 и 60 днями для пересчета величины суточного выделения урана с мочой на величины задержки в легких следует использовать фактор равный 500.

UN CASO DE INHALACIÒN DE POLVO DE URANIO ENRIQUECIDO. La memoria expone los resultados obtenidos en el estudio de un caso de inhalación de polvo insoluble de uranio enfriecido. Se explican las condiciones laborales en que se produjo la contaminación. Se indican y discuten los resultados del análisis de muestras de orina y de heces, así como los datos obtenidos en las mediciones de la radioactividad corporal. Las conclusiones provisionales de los autores comprenden un cálculo del período aparente del polvo insoluble de uranio en el tórax, que fue del orden de 1 año, y observaciones sobre el hecho de que los datos relativos a la excreción no parecen explicar todas las sustancias que elimina el tórax, y el hecho de que la velocidad de excreción por vía fecal fue superior a la velocidad de excreción por vía urinaria durante 1½ año, aproximadamente, después de la inhalación. Por último, sugieren que para intervalos comprendidos entre 30 y 60 d cabe
1. INTRODUCTION

When an insoluble compound of uranium is inhaled a proportion of the material is retained in the lung where it may give prolonged irradiation to the alveolar tissue and possibly to the tracheo-bronchial lymph nodes. In the absence of sufficient knowledge of the effects of radiation on lymphatic tissue, the lung is the organ potentially most at hazard following the inhalation of insoluble radioactive material. The criterion for determining the critical organ is here a radiological one, whereas with most soluble uranium compounds the limiting criterion is one of chemical toxicity in the kidney.

There is a considerable body of data relating to the exposure of people to soluble uranium compounds but, with the notable exception of a paper by FISH [1] and another by SCOTT [10] presented at this symposium, little has so far been published on exposure to insoluble uranium compounds.

At first sight this situation may appear surprising since very large quantities of uranium are handled in the metallurgical plants operated by the atomic industries, but when the low specific activities of natural and depleted uranium are taken into account, it is evident that relatively large masses of such materials need to be inhaled to produce a potentially hazardous condition. It is a simple matter to control the dust and fumes produced when processing unenriched uranium and the processes can be operated very safely. As the uranium is enriched in U\(^{235}\), and also in U\(^{234}\), the relative hazard, which is mainly associated with the U\(^{234}\) content, increases rapidly and when, for example, the U\(^{235}\) content is 93\% by weight the mass of enriched uranium required to produce a specified dose of radiation is one hundredth of the mass of natural uranium required to produce the same dose. The handling precautions and the efforts given to containment are correspondingly greater for enriched uranium than for natural uranium and of course the risk of a significant exposure may be greater if the precautions are not completely followed.

The case described in this paper was one of inhalation of enriched uranium dust, probably in the form of the insoluble oxide U\(_3\)O\(_8\). Urinary and faecal excretion samples were obtained at intervals over a period of nearly two years and in vivo measurements of the uranium in the region of the lungs were also carried out over the same period using the low background equipment at the Atomic Energy Research Establishment (AERE), Harwell.

2. OPERATIONAL BACKGROUND

A preliminary series of experiments was being undertaken with the object of comparing the performances of personal air samplers with those of permanently installed and other conventional air sampling systems. A workshop and foundry used for the fabrication of enriched uranium were chosen as the site for the experiments.
INHALATION OF ENRICHED URANIUM DUST

Three different processes were selected which could be expected to give widely different exposure conditions in the environmental air. For each process a team of two was chosen from those normally employed in that particular job. Each team member wore a personal air sampler, and kept a record of his work. In addition each member was asked to provide daily urine samples for radioassay.

As might be expected the levels of uranium in the urine increased as the radioactivity found on the personal air samplers increased, and also the activities in the samplers increased as the possibility of the release of airborne uranium dust increased.

Two workers (UR-1 and UR-2), both engaged in fettling moulds used for casting uranium ingots, were found to have considerably higher activities in their air samplers than the other teams and their urinary excretion of uranium was also substantially higher than in the other team. In this team both men did essentially the same work and their personal air samplers had remarkably similar quantities of radioactivity deposited in them. However at the beginning of the experiment the daily uranium excreted by UR-2 was about six times that of UR-1. Furthermore UR-2's daily excretion rate was falling fairly rapidly whereas that of UR-1 was remaining reasonably constant. These differences suggested that UR-2 had received at least one recent large acute exposure, whereas UR-1 might be excreting uranium at a level governed by the environment in which he had worked for many years and roughly in equilibrium with his intake from that environment.

Investigation showed UR-1 to be a hard-working man who had been engaged in this type of task for many years. UR-2 was a younger man with about eighteen months' experience in the plant; he was also a hard-working individual but with a number of idiosyncrasies which probably led to his exposure to high concentrations of uranium dust in a fume cupboard while breaking up graphite casting moulds.

Both individuals were working in an environment containing significant quantities of airborne uranium dust during the first week of sampling and the two previous weeks. UR-1 had been engaged in similar operations on numerous occasions during his many years of employment in the building concerned. UR-2 had also had similar experience on a few occasions during the previous eighteen months. Both continued to work in a similar but less radioactive environment until just before the body radioactivity measurements. The case of UR-1 is of no further relevance in this report.

It is likely that a proportion of the intake of UR-2 resulted from chronic exposure or from a number of small sporadic acute exposures during the previous eighteen months, but the major part was probably received as an additional large intake of enriched uranium dust either during the first week of sampling, or, more probably, a few days before during a period of intensive work breaking up graphite casting moulds.

3. RESULTS

3.1. The data obtained from UR-2 over a period of nearly two years from excretion sampling are summarized in Tables I and II and those from the body radioactivity measurements at AERE in Table III. All activity levels
are quoted in picacuries (pc). The curie is here defined as \(3.7 \times 10^{10}\) dps arising from all the radionuclides \(^{238}\text{U}, ^{235}\text{U}\), and \(^{234}\text{U}\) in the material.

The time datum \((t = 0)\) is in the middle of a period of intensive work with the mould fettling process when the exposure potential was high. Subject UR-2 did not work with radioactive materials after \(t = 63\) d.

### TABLE I

**DAILY URINARY EXCRETION OF URANIUM — CASE UR-2**

<table>
<thead>
<tr>
<th>Day (d)</th>
<th>6</th>
<th>15</th>
<th>22</th>
<th>30</th>
<th>66</th>
<th>79</th>
<th>90</th>
<th>125</th>
<th>148</th>
<th>225</th>
<th>317</th>
<th>593</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean activity excreted per day (pc/d)</td>
<td>195</td>
<td>149</td>
<td>103</td>
<td>52</td>
<td>11</td>
<td>45</td>
<td>24</td>
<td>21</td>
<td>17</td>
<td>3.9</td>
<td>10.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Number of samples averaged</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

3.2. Urine sampling. Table I shows the data from the urine sampling programme. The data have been presented as the means of groups of samples because of the wide variations in levels between samples taken on successive days. In any sampling group there was a factor of up to 4 or 5 between the radioactivity levels in samples on successive days and of up to about 8 between the highest and the lowest sample in a particular group. In our experience this type of variation occurs commonly in the results of urine analyses following inhalation of insoluble material, and in this case it was most marked at early times.

The samples varied from single voidings at early times, through samples collected during the eight-hour working day to samples collected over 24 h in the later groups. Some of the scatter at earlier times could be attributed to the short sampling periods represented by single voiding samples.

The data are presented graphically in Fig. 1.

3.3. Faecal sampling. The faecal sampling data are shown in Table II. The data presented are again the means of groups of samples. In this case the samples were normally taken over about four days, and there were usually four samples per group. The variation between the radioactivity levels in each group of samples was not so large as in the urine analysis data and the maximum variation within a group was covered by a factor of about four between the highest and lowest results.

The sampling periods were chosen to coincide with measurements of body radioactivity whenever practicable.

The data are presented graphically in Fig. 1.

3.4. In vivo measurements. Subject UR-2 was sent to the Atomic Energy Research Establishment, Harwell for estimation of his burden of \(^{235}\text{U}\), by detection of the 186 keV gamma-ray emitted in 55% of the disintegrations. The use of thallium activated sodium iodide scintillation counters in the measurement of chest activated sodium iodide scintillation counters in the measurement of chest
Fig. 1

Lung retention, urinary and faecal excretion of uranium (probably insoluble U₃C₇) in Case UR-2.
burdens of enriched uranium has been described by others [2, 3]. The tech­
nique used in the present case was similar; the gamma-ray spectrum was
determined with a 23 cm × 15 cm crystal placed about 2 cm below the thorax
of the supine subject [4]. On one occasion the crystal was placed below the
sacrum, but no radiation attributable to U\(^{235}\) was detectable. The spectra
from the thorax were analysed by a computer method of least squares, using
standard spectra of K\(^{40}\) and Cs\(^{137}\) in humans and of U\(^{235}\) in a lung phantom
[4, 5]. The statistical standard error on the computed contents ranged from
±1100 pc to ±2100 pc (±3% to 15%), but there may have been a systematic
error as a result of the method of calibration. It was not possible to assess
this directly nor was it possible to show that the U\(^{235}\) was specifically in
the lungs. These limitations should be borne in mind when considering all
the data. The results of seven measurements are set out in Table III.

TABLE III.

IN VIVO MEASUREMENTS - CHEST BURDEN - CASE UR-2

<table>
<thead>
<tr>
<th>Day</th>
<th>69</th>
<th>73</th>
<th>91</th>
<th>149</th>
<th>226</th>
<th>304</th>
<th>594</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest activity measured (pc)</td>
<td>33 600</td>
<td>35 900</td>
<td>33 400</td>
<td>26 600</td>
<td>23 000</td>
<td>-23 800</td>
<td>13 800</td>
</tr>
</tbody>
</table>

The data are also presented graphically in Fig. 1.

3.5. In Fig. 2 the chest burden in picacuries and the total excretion rates
in picacuries per day are shown separately on a logarithmic scale against
time in days on a logarithmic scale.

4. DISCUSSION

4.1. The urinary excretion data of Table I can be described approximately
by a two-component exponential function of time:

\[
U_t = 290 e^{-0.06t} + 73 e^{-0.01t} \text{ pc/d},
\]

where \(U_t\) is the daily urinary excretion at time \(t\) days after assumed intake
date.
The two components of this expression have half-lives of about 11 d and about 70 d respectively. The urinary excretion at early times is strongly influenced by the exponential component with the 11-d half-life. FISH [1] noted that similar short-lived components \( (t_1 = 20 \text{ d}) \) were present in his two cases of inhaled uranium oxides.

4.2. The faecal excretion data of Table II between 70 and 600 d can be described approximately by the expression:
where $F_t$ is the daily faecal excretion on day $t$.

This expression has a half period of about 70 d. For times earlier than about $t = 70$ d there are no data, but the excretion pattern would probably have been similar to that in the urine, and the broken curve in Fig. 1 indicates the possible faecal excretion pattern at times prior to $t = 70$ d, but ignoring any additional faecal excretion arising from a very rapid initial lung clearance during the first few days after inhalation.

4.3. The total quantity of uranium excreted daily during the period from 69 to 600 d is described approximately by the expression:

$$E_t = 320 \ e^{-0.01t} \ pc/d,$$

where $E_t$ is the total daily excretion on day $t$.

Integration of this expression between the limits $t = 69$ d and $t = 594$ d shows that about 16 000 pc were excreted.

4.4. The chest burden data for the period from 69 to 594 d can be described approximately by the expression:

$$C_t = 40 000 \ e^{-0.0018t} \ pc,$$

where $C_t$ is the chest burden on day $t$.

This expression has a half period of about 380 d. During the period of measurement about 20 000 pc were lost from the chest region. This compares well with the total quantity excreted (16 000 pc) in the same period and implies that there were no large systematic errors in the body radioactivity measurement.

In Fig. 2, added since the main report was written, the calculated line of best fit for the chest burden data is shown. This line is that described by the expression $C_t = 1.9 \times 10^5 t^{-0.4} pc$. The line representing the first derivative of this function is also shown, i.e.

$$\frac{dC_t}{dt} = 7.8 \times 10^4 t^{-1.4} E_t \ pc/d.$$

As can be seen this provides a remarkably good description of most of the total excretion data, only the point at $t = 590$ d being poorly described.

The remaining two lines in Fig. 2 ($F_t$ and $U_t$) have been drawn assuming that the ratio $F_t/U_t$ is approximately 3.3. It should be noted that the initial date used when assembling this data for the logarithmic presentation is 7 d earlier than that given in the text and used in Fig. 1, and also that Fig. 2 includes data at $t = 720$ d, not used either in the text or in Fig. 1 (see 4.9 below).

4.5. According to the ICRP [6] the effective half-life of retained insoluble uranium dust in the lung is to be taken conventionally as 120 d, whereas for plutonium the figure is 1 yr and for thorium 4 yr. Our data suggest that the apparent half-life in the chest during the period 60 to 600 d following in-
halation is about one year and if, in the absence of a specific identification of the site of the location of the material, it is assumed that all the uranium in the chest is in the lung, then the half-life in the lung also appears to be about 1 yr. A change in the effective half-life by a factor of 3 or more would not affect calculations of derived permissible lung burdens but would affect the derived MPC₃ for insoluble uranium which would need to be reduced by a factor of about 3.

4.6. The daily excretion rate found changed rapidly with time and at the end of the sampling period the daily rate was small (about 0.7 pc/d). On the other hand the chest burden appeared to be falling exponentially with a rate of loss at 600 d of about 25 pc/d which was considerably greater than could be accounted for by urinary and faecal excretion. A tentative explanation might be that a substantial proportion of the material retained in the lung was in some way being transferred to another compartment where it was retained for a very long time but was not separately detectable; this, for example, might be in bone. If such were the case the uranium in the bones of the chest would contribute to the measured radiation and this would lengthen the apparent half-life in the chest compared with the true half-life in the lung.

An alternative and more likely explanation is that part of the chest content was essentially "fixed" (possibly in lymph nodes). To take account of this, Eq. (3) should then be re-formulated with two components; one with a very long half-life (the "fixed" component) and one with a shorter half-life (perhaps only 70 d as observed in the excretion data). This would account for the fact that between 70 and 200 d the excretion rate exceeded the apparent rate of decrease of the chest content. This hypothesis can be tested by continued measurements of the chest content over a protracted period; we hope to be able to carry out a long-term study. It should be noted that at 600 d the slopes of the lines through the points for the chest burden, urinary and faecal excretion rely mainly on single values, obtained after an interval of 290 d (see 4.9 below).

The adoption of such a model would not substantially alter the value of the apparent half-life which, over a period of about two years, would be about 1 yr, although it would of course be shorter during the first few months following exposure to an insoluble aerosol.

4.7. Over a period of nearly two years the daily faecal excretion rate was consistently greater than the daily urinary excretion rate by a factor of about three. A similar pattern was observed in a case of inhaled insoluble, or slightly soluble, plutonium [7]. It is known that, following the inhalation of an insoluble aerosol, the faecal excretion is largely determined by material moved up the bronchial tree and subsequently swallowed; it is suggested that this may continue for several years for materials with long effective half-lives in the lung. The faecal elimination in this case is attributed to this mechanism since the data obtained following injection [8, 9] indicate that endogenous faecal excretion can only be a small fraction of the urinary excretion. In FISH's case [1] it appeared however that the whole of the decrease in the uranium determined by in vivo measurement could be accounted for by urinary excretion. A possible explanation of some of the difference
between his case and the case in this paper might be sought in differences in particle size and effective solubility.

4.8. Workers expected to be exposed to potential intake of radioactive material are subject to urine sampling at regular intervals of one to two months. The present data indicate that where exposure to insoluble uranium is suspected, and sampling for uranium is carried out at intervals of 30–60 d, a factor of about 500 should be used to convert the quantity of uranium excreted per day in the urine to the quantity of uranium retained in the lung. Fish suggested a smaller factor of between 80 and 180, but in his cases no faecal excretion was observed and his factor is comparable with that needed to convert the total daily excreted uranium of this case to that in the lung. The use of a factor of 500 to convert daily urinary excreted uranium to that retained in the lung, when calculating uptake for staff who are regularly sampled and working in a well-designed facility, should not seriously underestimate the potential hazard and at the same time should not give an unreasonably large number of indications of falsely high exposures to insoluble uranium dusts; experience in the United Kingdom Atomic Energy Authority's Aldermaston plant in recent months indicates that this is so. The differences in the various cases emphasize the need to obtain both faecal and urinary data whenever a significant intake of radioactive material is suspected.

4.9. Additional data. Since this report was written data has been obtained at t = 722 d. These data are as follows:
- Daily urinary excretion rate at t = 722 d: 2.21 pc/d from four samples.
- Daily faecal excretion rate at t = 722 d: 4.85 pc/d from three samples.
- Total daily excretion rate at t = 722 d: 7.16 pc/d.
- Chest burden from in vivo counting at t = 717 d: 13600 pc ± 15%.

The data are shown graphically in Fig. 2 only. Although these data will have the effect of lengthening the apparent half-life in the chest, and of lengthening the half periods of the excretion functions, they do not seriously affect the discussion above, but serve to emphasize that transfer from the chest is a complex mechanism with some portion of the material either retained permanently or at least being transferred with a very long half period.

5. CONCLUSIONS

An experiment to investigate the use of personal air samplers revealed that an individual had readily measurable quantities of enriched uranium in his chest and was excreting substantial quantities in his urine and faeces. Urine and faeces were sampled intermittently for a period of nearly two years and chest measurements were made over the same period. The data are still being collected and the following tentative conclusions have been put forward.

The data from the body radioactivity measurements suggested that the apparent half-life of insoluble uranium dust retained in the lung was at least 1 yr, the same as that adopted by the ICRP [6] for insoluble plutonium, and this might lead to a reduction in the MPC for insoluble uranium by a factor
of 3. There was evidence that at early times the excretion rate was signifi­
cantly affected by a component with a half-life of about eleven days; such a
component is consistent with the findings of FISH [1].

At about one year after the inhalation of insoluble uranium there appeared
to be a larger rate of loss from the chest than could be explained by daily
excretion losses, and this might indicate either transfer to an organ having
a long residence time, or retention in the chest area with a long half-life.
The excretion of uranium following the inhalation of insoluble material
was in this case mainly by the faecal route for $1\frac{1}{2}$ yr at least.

In an operational urine analysis programme for uranium workers the
daily urinary excretion level at about a month after exposure should be
multiplied by a factor of 500 to give a first approximation to the chest burden
if inhalation of insoluble uranium is suspected. Where a significant intake
is suspected both urinary and faecal sampling should be instituted and body
radioactivity measurements made if possible.

ACKNOWLEDGEMENTS

We wish to thank the Director of the Atomic Weapons Research Estab­
lishment, Aldermaston, for permission to publish this paper, and to record
our thanks to subject UR-2 for his patient and good-humoured acceptance
of the experimental, sampling and counting procedures.

REFERENCES


DISCUSSION

G. W. DOLPHIN: By way of comment I should like to make a plea for
careful interpretation of data obtained by counting over the chest region.
Activity in the chest region may be in the lungs, bronchial lymph nodes,
liver, or bones of the upper parts of the body. Unless there is other evi­
dence for its being located there it must be understood that to assign arbi­
trarily all this activity to the lungs is an assumption.

W. N. SAXBY: I agree entirely with Dr. Dolphin. In the written text
of our paper we were careful to generalize much more than perhaps I did
when actually presenting the paper.
J. RUNDO: May I add a comment to what Dr. Saxby has just said? We did in fact have some indirect evidence as to the likely location within the chest of at least some of the enriched uranium in the case reported by Dr. Saxby. The in vivo measurements were interpreted on the assumption that the uranium-235 was distributed throughout the lung. During the first 200 days, the total amount of uranium excreted was in altogether respectable agreement with the observed reduction in chest content. If the uranium had in fact been in the tracheo-bronchial lymph nodes, we estimate that our calibration factor would have been in error by a factor of perhaps 2.

H. WYKER: I understand Dr. Saxby wishes to replace his power function by a set of exponentials. Although, from a theoretical point of view, exponentials can give much more information, I think we should not introduce too many parameters. I have not had very much experience with this mathematical procedure, but I had the impression that small changes in the experimental points to be fitted can give great variations in the values of the parameters, so that we must be careful in drawing theoretical conclusions from these parameters.

W. N. SAXBY: I think I may have been misunderstood. In my view a series or mixture of exponential functions must be the fundamental way of describing retention or excretion functions. A power function is a convenient way of describing such functions over the limited period of time represented by the observations. It may be very helpful to us, but as Dr. Pochin has said, we cannot extrapolate beyond the limits of the information. Of course, a set of exponential functions suffers from the same limitations but it has in my opinion a more fundamental basis.

N. A. TAYLOR: I would like to give some preliminary information on a procedure which I and my colleagues of the U.K.A.E.A., Mr. Coleman and Mr. Brookes, have recently developed for the determination of uranium in urine and faeces. The procedure is an adaptation from a method for the determination of uranium in minerals. It is particularly useful when exposure to enriched uranium occurs.

The basis of the method consists of counting the delayed neutron emission from the fission of uranium-235. The sample of urine is irradiated in a polyethylene container for one minute close to the core of a nuclear reactor by the use of a pneumatic transfer facility (the "rabbit" tube). The sample is then transferred to a counter with six BF$_3$ tubes surrounded by 15 cm of paraffin wax. Counting is commenced 25 s after the termination of irradiation to permit the decay of nitrogen-18, produced from the oxygen in the sample. The total count in one minute is then obtained.

The procedure is practically specific for uranium-235 and no separations are required. If the isotopic composition of the uranium is known the determination of the uranium $\alpha$-activity within a few per cent is possible; if it is not known, the value is obtained within 20%. For a neutron flux of about $5 \times 10^{12}$ n/cm$^2$/s about $7 \times 10^4$ counts in one minute are obtained from 1 mg of uranium-235. Or about 1000 counts per pc of uranium $\alpha$-activity. The blank is about 80 counts if the sample is counted without transfer from the irradiation container. The sensitivity for a 20-ml aliquot of urine is about 2 pc/24 h; if 100 ml of urine is evaporated to about 15 ml before irradiation the sensitivity is about 0.4 pc/24 h.
The method gives the rapid determination Mr. Harley calls for, about 4 min per sample when no concentration is carried out, a little longer when preliminary evaporation is used. It also has good precision and adequate sensitivity for routine surveillance. On the other hand, precautions have to be taken to protect the operator from the β-γ radiation from the induced activities of the urine constituents, and there is the disadvantage that suitable irradiation facilities are required.
THE ESTIMATION OF INTERNAL CONTAMINATION WITH URANIUM FROM URINE ANALYSIS RESULTS

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Abstract — Résumé — Аннотация — Resumen

THE ESTIMATION OF INTERNAL CONTAMINATION WITH URANIUM FROM URINE ANALYSIS RESULTS.

The most common cause of internal contamination with uranium is inhalation of uranium dust. Soluble uranium compounds are rapidly absorbed from the lungs, and most of the uranium entering the circulation is rapidly excreted in the urine. The intake of soluble uranium at work can be estimated from the uranium content of urine samples taken immediately afterwards.

It is a special feature of soluble compounds of natural uranium that the primary consideration is not radiological but toxicological due to chemical effects of uranium deposited in the kidneys. Some uranium is also deposited in the skeleton, but the irradiation of bone is less critical, in the case of natural uranium, than the toxicity to kidney.

For soluble compounds of highly-enriched uranium with its high specific activity, the primary concern is radiological; the chemical effects on the kidneys are less limiting than the irradiation of bone, which thus becomes the critical organ.

In this case, it is better to attempt to assess the retained body burden rather than the intake of uranium. This may be done by analysing urine samples taken not immediately after exposure but when some time has elapsed. Samples taken after a holiday are probably the best material available in practice, but it may be necessary to accept samples after only a week-end of removal from uranium work.

ÉVALUATION DE LA CONTAMINATION INTERNE PAR L'URANIUM À PARTIR DES RÉSULTATS DE L'ANALYSE D'URINES. Evaluation de la contamination interne par l'uranium à partir des résultats de l'analyse d'urines. La cause la plus fréquente de contamination interne par l'uranium est l'inhalation de poussières d'uranium. Les composés solubles de l'uranium sont rapidement absorbés au niveau des poumons et la plus grande partie de l'uranium qui passe dans le sang est rapidement rejetée avec l'urine. La quantité d'uranium soluble actif qui est absorbée peut être déterminée à partir de la teneur en uranium d'échantillons prélevés immédiatement après.

Les composés solubles de l'uranium naturel ont une particularité, en ce sens que la considération principale dont il faut tenir compte est d'ordre non pas radiologique mais toxicologique, en raison des effets chimiques que produit l'uranium déposé dans les reins. Une certaine quantité d'uranium se dépose également dans le squelette mais, dans le cas de l'uranium naturel, la radioexposition du squelette est moins critique que des effets toxiques sur les reins.

Dans le cas de composés solubles de l'uranium fortement enrichi ayant une activité spécifique élevée, la considération principale est d'ordre radiologique; les effets chimiques sur les reins sont moins limitatifs que la radioexposition du squelette, qui devient ainsi l'organe critique.

Dans ce cas, il vaut mieux essayer d'évaluer la charge corporelle retenue et non la quantité d'uranium absorbée. On peut y parvenir en analysant des échantillons d'urines prélevées, non pas immédiatement après la contamination, mais après un certain délai. Les échantillons prélevés après une période de vacances sont probablement les meilleurs que l'on puisse obtenir en pratique, mais on peut avoir à se contenter d'échantillons prélevés après le repos hebdomadaire qui suit une semaine de travail dans une atmosphère chargée de poussières d'uranium.

ОЦЕНКА СОДЕРЖАНИЯ УРАНА В ОРГАНИЗМЕ С ПОМОЩЬЮ АНАЛИЗА МОЧИ. Наиболее частой причиной попадания урана в организм является вдыхание урановой пыли. Расторвимые урановые соединения быстро всасываются из легких, и большая часть урана, по-
In the case of inhalation of insoluble uranium compounds, irradiation of the lungs is critical. Estimation of the lung burden of insoluble uranium from urine analysis results may be feasible in a case of acute intake, but supplementary information is required if the lung burden is due to chronic intake.

1. INTRODUCTION

1.1. Intake of uranium compounds

Internal contamination with uranium compounds usually occurs by inhalation. Ingestion of uranium compounds is not an important route of entry to the body, because the fractional absorption of uranium from the gastrointestinal tract is only about 1% [1, 2].
1.2. Uranium in urine [3]

Intake of uranium at work is minimized by careful control of the environment, which can be surveyed by measuring uranium in air and in surface contamination. Routine urine samples can be analysed for uranium to provide confirmation that environmental control is satisfactory [4, 5]. If it is believed that an individual has received a significant intake in a recognized accident, his body burden may be estimated from, inter alia, the amount of uranium found in a planned series of urine samples taken after the accident [5].

Soluble compounds of uranium deposited in the lungs are rapidly and completely absorbed [6]. A large proportion is excreted rapidly in the urine (only a negligible amount in the faeces), but significant fractions are deposited in the kidneys and the skeleton [6, 7]. In the case of soluble compounds of natural uranium, the critical factor is non-radiological toxicity of uranium to the kidney [8, 9]. If, however, the uranium has been enriched in uranium-235 (by the diffusion process) to a concentration greater than 8.5% (12 times the level present in natural uranium) the critical consideration is irradiation of the bone, due to the enhanced concentration of the shorter-lived isotope uranium-234 [3].

When insoluble uranium compounds are inhaled, a proportion is retained in the lungs for long enough to make irradiation of lung the critical factor; this applies to all isotopes of uranium. Absorption into the bloodstream is sufficient to lead to a significant level of urinary excretion, especially in the early stages after an intake.

2. THE RELATIONSHIP BETWEEN URANIUM CONCENTRATION IN AIR AND URANIUM CONCENTRATION IN URINE

2.1. General surveys in uranium factories

Several attempts have been made to discover a correlation between uranium concentration in air and urine by analysing the records accumulated at uranium factories:

SCHULTZ and BECHER [10] found (for monthly averages) that the concentration of uranium in urine samples taken during work with soluble and insoluble uranium was correlated with the level of surface contamination, but could find no correlation with the concentration of uranium in air. (The monthly average air concentrations were largely distributed into two groups, one at about 50 μg/m³, the other at less than 10 μg/m³; the mean concentration ratio Urine/Air was about $1.2 \times 10^3$).

However, while recognizing the wide scatter of individual results, HEATHERTON and HUESING [11] and FISCHOFF [12] have found correlations between the concentrations of uranium in urine and in air, for air concentrations distributed fairly evenly over the range 10 to 80 μg/m³. For the relationship between Monday morning urine samples and air inhaled during the previous week, HEATHERTON and HUESING [11] found a mean concentration ratio Urine/Air of about 600. For each operation, all individual concentration measurements were averaged, and the ratio Urine/Air
then calculated. Various operations with soluble and insoluble uranium were involved. In FISCHOFF's study [12], mid-week urine samples were collected throughout the time between work-shifts with insoluble uranium compounds. The mean concentration ratio Urine/Air, calculated from monthly averages of all the results, was about 500. Statistical analysis of the individual results revealed a correlation between urine and air concentrations which was significant at a level of greater than 95% confidence.

2.2. Comparison of different operations in a uranium factory

A very valuable study has been reported by LIPPMANN [13]. For each of four different operations, separate comparisons were made of the concentration ratio Urine/Air. The urine sampling programme comprised sampling both immediately before the week-end (i.e. immediately after inhalation of uranium dust during the last work-shift of a week of such shifts) and immediately after the week-end (when there had been no inhalation of uranium for 48 h). Measurements were made throughout a period of two years, and the results for each month were averaged. A summary of the published data is presented in Table I; the data for two different operations with uranium hexafluoride (soluble) have been combined. The serial concentrations of uranium were similar for both operations, and the coefficient of variation of the mean of the concentration ratios Urine/Air was reduced when the data were combined. In the air UF₆ is rapidly hydrolysed by water vapour to UO₂F₂ which is also soluble.

The concentration of uranium in urine was markedly higher before the week-end than afterwards. This actually held for every pair of monthly values; it is in accord with the rapid decline in urinary excretion rate of uranium observed after cases of acute intake of either soluble compounds [1, 14, 15] or insoluble compounds [15, 16]. The decline in excretion rate over the week-end was relatively greater for soluble than for insoluble uranium.

There was a marked difference in the uranium concentration ratio Urine/Air between the two different operations with insoluble uranium compounds, but no conclusions can be drawn from this because respirators were sometimes worn; according to LIPPMANN [13] they could not have reduced average exposure by more than 75%.

2.3. Deposition and retention of uranium in the lungs in relation to inhalation and urinary excretion

There is good evidence that absorption of soluble uranium dust from the lungs is rapid and complete [6, 17]; the excretion of this absorbed uranium may reasonably be assumed to resemble that of intravenously-injected uranium (see section 3.1).

The International Commission on Radiological Protection (ICRP), Committee II (1959) has proposed standard values for the volume of air breathed during a work-shift, the fraction of inhaled particulates deposited in the lungs and the volume of urine excreted daily [8].
<table>
<thead>
<tr>
<th>Operation</th>
<th>1. Fluorination of UF₄ to UF₆</th>
<th>2. Re-distillation of UF₆</th>
<th>3. Loading UO₂ for fluorination</th>
<th>4. Fluorination of UO₂ to UF₆</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uranium compounds in air</td>
<td>UF₆, UO₂F₄ (both soluble)</td>
<td>UO₂₉, UF₄ (both insoluble)</td>
<td>UF₄, UO₂ (both insoluble)</td>
<td>UF₆, UF₄ (both insoluble)</td>
</tr>
<tr>
<td>Concentration range of uranium in air</td>
<td>61–940</td>
<td>1300–9700</td>
<td>88–626</td>
<td></td>
</tr>
<tr>
<td>Concentration range of uranium in urine before week-end (µg/l)</td>
<td>150–5000</td>
<td>40–210</td>
<td>10–130</td>
<td></td>
</tr>
<tr>
<td>Concentration range of uranium in urine after week-end (µg/l)</td>
<td>26–860</td>
<td>15–70</td>
<td>6–35</td>
<td></td>
</tr>
<tr>
<td>Mean of uranium concentration ratios: urine before week-end/air</td>
<td>2.3 × 10³ (0.11)</td>
<td>2.1 (0.14)</td>
<td>230 (0.21)</td>
<td></td>
</tr>
<tr>
<td>Mean of uranium concentration ratios: urine after week-end/air</td>
<td>390 (0.14)</td>
<td>10 (0.13)</td>
<td>110 (0.19)</td>
<td></td>
</tr>
<tr>
<td>Mean of uranium concentration ratios: urine before week-end/urine after week-end</td>
<td>8.3 (0.079)</td>
<td>2.7 (0.10)</td>
<td>4.4 (0.23)</td>
<td></td>
</tr>
</tbody>
</table>

After each value for a mean concentration ratio, the coefficient of variation is given in parentheses.

* Monthly averages. (Taken from the data of LIPPMANN [13]).
Combining all the figures:
Concentration of uranium in air = \( C/l \).
Volume of air breathed during a work-shift = \( V = 10^4 \) l
Fraction of inhaled particulates deposited in lungs = \( R \)
(lower respiratory passages) = 0.25
Time taken for soluble uranium to be absorbed = 0
Fraction of absorbed uranium excreted in urine during first 24 h = \( E = 0.67 \) [7, 20]
Volume of urine excreted daily = \( U' = 1.4 \) l
Concentration of uranium in urine during first 24 h after inhalation = \( D_1/1 \)

\[
D_1 = \frac{C \cdot V \cdot R \cdot E}{U} = \frac{C \times 10^4 \times 0.25 \times 0.67}{1.4} = 1.2 \times 10^3 \ C.
\]

Hence, concentration ratio Urine/Air = \( D/\ C = 1.2 \times 10^3 \).
This assessment gives a ratio which lies within a factor of two of that found for factory conditions from Lippmann's data (see section 2.2). Such a degree of compatibility suggests that the ICRP parameters used are fairly satisfactory for soluble uranium.

For insoluble particulates, ICRP Committee II (1959) has postulated that half of the 25% of inhaled material which is deposited in the lungs is eliminated from the lungs and swallowed in the first 24 h — in effect, \( R = 0.125 \); the 12.5% is retained in the lungs with a half-life of 120 d, it being assumed that this portion is taken up into body fluids [8]. Hence:
Daily retention of particulates = \( C \cdot V \cdot R \)

\[
= C \times 10^4 \times 0.125 = 1.25 \times 10^3 \ C.
\]

Concentration of uranium in lung = \( L/kg \)
Mass of lungs = 1 kg [8]. Hence:
Daily absorption of retained uranium = \( L \times \log \frac{2}{120} = L \times 0.693 \frac{120}{120} = 5.7 \times 10^{-3} \ L \)
At equilibrium, Daily retention = Daily absorption

\[
1.25 \times 10^3 \ C = 5.7 \times 10^{-3} \ L
\]

\[
\frac{L}{C} = \frac{1.25 \times 10^3}{5.7 \times 10^{-3}} = 2.2 \times 10^5
\]

This ratio is very close to the experimental value of \( 1.4 \times 10^5 \) for dog experiments on chronic inhalation of insoluble uranium [6].

However, EISENBUD and QUIGLEY [16] have reported results of a very different order, from post-mortem examination of two men who died (from unrelated causes) after chronic inhalation of insoluble uranium dust at work. One man died 10 months after a 2-yr spell of work in a mean air concentration of 17 000 g of insoluble uranium per cubic metre; the concentration of uranium found in his lungs was \( 1.2 \times 10^3 \) times less than was predicted from the dog results [6]; the other man died 15 months after a 1-yr spell of work in a mean air concentration of 5000 g of insoluble uranium per cubic metre; his lung concentration of uranium was 200 times less than that predicted by extrapolation from the dog data [6].
EISENBUD [18] has suggested that the high relative density of uranium dust may have resulted in poor penetration to the lower respiratory passages, but Lippmann's results for the concentration ratio Urine/Air in the case of soluble uranium dust make it clear that deposition of this dust, similar in density, exceeded 25% of the amount inhaled (see section 2.2). Neither is the lack of agreement with the dog results attributable to a difference in dust concentration or particle size - both were very similar in the dog experiments [6] and the human cases [16]. (For data relating to particle size see [6, 12, 14]).

It appears that the difference in long term retention must be due to a higher rate of removal from the lungs in man. This could be due to a higher rate of absorption, a higher rate of ciliary clearance or a higher rate of transfer to lymph nodes. Although Lippmann's results (section 2.2) imply a higher rate of absorption than that corresponding to a lung half-life of 120 d, individual case histories show that the excretion rate after an acute intake of insoluble uranium falls off rapidly [14, 16], and the data of Fish and Saxby et al. show that the rate of absorption of a chronic lung burden may be much slower (see section 3.2).

On the other hand, Saxby et al. showed that in their case faecal exceeded urinary excretion throughout one and a half years, making it clear that ciliary action may be much more prolonged than is postulated in the ICRP model.

There appears to be no real prospect of being able to estimate the concentration of insoluble uranium in air from the urinary excretion rate of uranium. The obscurity surrounding the rate of removal of uranium from the lungs by absorption, and by other processes, completely confuses the situation, which is so comparatively simple in the case of soluble uranium.

3. THE RELATIONSHIP BETWEEN URANIUM CONCENTRATION IN URINE AND THE BODY BURDEN OF URANIUM

3.1. Human excretion and body burden of uranium after intravenous injection of soluble uranium compounds

The best available evidence for the pattern of distribution and excretion of soluble uranium compounds in man comes from the work of BERNARD and STRUXNESS [7]. They describe experiments in which uranyl nitrate (5 to 15 mg of uranium) was injected intravenously into six terminal brain cancer patients, and a complete analytical study of the urinary and faecal excretion was made. When death occurred (due to the original incurable disease), uranium analyses were carried out on the tissues (this was done with five of the six patients).

Ratios of Body Burden/Urinary Excretion Rate calculated from the equations fitted to these data (see [7, 19]) are presented in Table II [3]. Comparable results were obtained in another human study by BASSETT et al. [20].

The post-mortem data collected by Bernard and Struxness suggest that the total-body burden after 7 d is about 1/4th of the amount injected, and after 30 d about 1/10th. The principal sites of retention are the bone and the kidneys.
<table>
<thead>
<tr>
<th>Time from injection until urine sampling (d)</th>
<th>Ratio I/D = Original deposit Urinary excretion per day</th>
<th>Ratio I/D × 1.4 = Original deposit Urinary excretion per litre</th>
<th>Ratio B/D = Present body burden Urinary excretion per day</th>
<th>Ratio B/D × 1.4 = Present body burden Urinary excretion per litre</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (same day)</td>
<td>~2</td>
<td>~2</td>
<td>~2</td>
<td>~2</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>34</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>83</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>93</td>
<td>130</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>7</td>
<td>230</td>
<td>330</td>
<td>38</td>
<td>53</td>
</tr>
<tr>
<td>10</td>
<td>420</td>
<td>590</td>
<td>60</td>
<td>84</td>
</tr>
<tr>
<td>14</td>
<td>710</td>
<td>990</td>
<td>93</td>
<td>130</td>
</tr>
<tr>
<td>21</td>
<td>1300</td>
<td>1900</td>
<td>160</td>
<td>220</td>
</tr>
<tr>
<td>30</td>
<td>2300</td>
<td>3200</td>
<td>250</td>
<td>350</td>
</tr>
</tbody>
</table>

* (Calculated from the data of BERNARD and STRUXNESS, [7]).
Bernard and Struxness also describe two patients injected intravenously with uranium tetrachloride. The rate of urinary excretion was less than in the case of uranyl nitrate, and the post-mortem evidence (on one case only) showed considerable deposits of uranium in the liver and spleen. These differences in metabolism between uranyl nitrate and uranium tetrachloride have also been observed in animals [6] and must be borne in mind if consideration of uranium tetrachloride or other soluble tetravalent uranium compounds is necessary.

3.2 Human excretion and lung burden of uranium after inhalation of insoluble uranium

In view of the great uncertainties about the deposition and retention of insoluble uranium dust in the lungs (see section 2.3) it is necessary to have a direct measurement of the magnitude of the lung burden to establish its relationship to the rate of excretion.

Measurements of the chest burden have been made in a few human cases involving enriched uranium, by making use of the 186-keV X-radiation emitted in 55% of the disintegrations of uranium-235.

One case, apparently arising from acute intake, has been reported from Oak Ridge. Measurements of the chest burden were made over a period of about a year, and comparisons were made with the results of urine analysis [21, 22]. It appears that the rate of departure of uranium from the region of the man’s chest was matched by the rate of urinary excretion, but the margin of error is uncertain.

Ratios of Lung Burden/Urinary Excretion Rate calculated from the equations fitted to these data by FISH [19, 22] are presented in Table III [3]. For a half-life of 120 d the ratio would be 170.

The earliest report of this case [21] implies that the follow-up programme of urine analysis was not begun until several days after the accidental intake; the rate of urinary excretion during this period may have been considerably higher than the estimated values (compare [14, 16]).

The ratio of lung burden to urinary excretion may be very different if the uranium has accumulated as a result of chronic exposure. For such a case, FISH [22] interpreted the results by assuming that about one-quarter of the chest burden was completely immobile, and made no contribution to the urinary excretion. This portion of the chest burden was presumed to be located in the pulmonary lymph nodes, where high concentrations of uranium have been found in animals which had chronically inhaled insoluble uranium [23].

Saxby et al. [24] have found in another human case that the half-life of insoluble uranium dust in the lungs was about 380 d. In this case, faecal excretion was measured in addition to the measurements of urinary excretion and direct measurement of the chest burden. Throughout one and a half years, the excretion rate in faeces exceeded that in urine. The ratio of excretion rate to chest burden showed a consistently downward trend. The initial and final figures for faecal excretion were 1/165 and 1/30,000; for urinary excretion 1/680 and 1/64,000 respectively. In the later stages, there was considerable movement of uranium from the chest, in marked excess of the amount excreted.
**TABLE III**

**URINARY EXCRETION AFTER ACUTE INHALATION OF INSOLUBLE URANIUM COMPOUNDS**

<table>
<thead>
<tr>
<th>Time from inhalation until urine sampling (d)</th>
<th>Ratio I/D =</th>
<th>Ratio I/D x 1.4 =</th>
<th>Ratio B/D =</th>
<th>Ratio B/D x 1.4 =</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original deposit + urinary excretion per day</td>
<td>Original deposit + urinary excretion per litre</td>
<td>Present body burden + urinary excretion per day</td>
<td>Present body burden + urinary excretion per litre</td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>90(a)</td>
<td>130(a)</td>
<td>90(a)</td>
<td>130(a)</td>
</tr>
<tr>
<td>7</td>
<td>100</td>
<td>140</td>
<td>90</td>
<td>130</td>
</tr>
<tr>
<td>10</td>
<td>110</td>
<td>150</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>14</td>
<td>120</td>
<td>170</td>
<td>93</td>
<td>140</td>
</tr>
<tr>
<td>21</td>
<td>150</td>
<td>210</td>
<td>97</td>
<td>150</td>
</tr>
<tr>
<td>30</td>
<td>190</td>
<td>270</td>
<td>110</td>
<td>160</td>
</tr>
</tbody>
</table>

* (Calculated from the equations fitted by FISH [22, 19] for the case reported in [21]).

(a) Calculated from the ratios derived by FISH [19] which may underestimate the rate of excretion immediately after intake, as discussed in section 3.2.
4. PRACTICAL ASSESSMENT OF INTERNAL CONTAMINATION WITH URANIUM FROM THE RESULTS OF URINE ANALYSIS

In this section, evaluations are made of the urinary excretion rate of uranium corresponding to the presence of one-tenth of the relevant maximum permissible level of uranium.

4.1. Soluble compounds of natural uranium

The maximum permissible levels for this case are understood to be based on animal experiments reported by VOEGTLIN and HODGE. After intermittently inhaling soluble uranium dust at controlled and measured aerial concentration, some for a month, some for a year, animals were examined for the incidence of kidney damage. It is therefore appropriate to interpret the results of urine analysis as an index of the concentration of soluble natural uranium in the air which has been breathed. Since inhaled soluble uranium is rapidly excreted, it is desirable to take urine samples immediately after a work-shift. The following assessment can then be made:

Concentration ratio Urine/Air = 1.2 X 10^3 (section 2.3)

Occupational 40-h (MPC)_a for soluble natural uranium = 7 X 10^{-11} \mu c per cm^3 = 0.21 \mu g/l.

Concentration of natural uranium in urine after working in one-tenth (MPC)_a = 24 \mu g/l.

(If the concentration ratio is well established for a particular operation, it seems reasonable to use this rather than the model ratio. Thus, for Lippmann's operations 1 and 2 (Table I) the measured value 2.3 X 10^3 would give a result of 48 \mu g/l of urine corresponding to one-tenth (MPC)_a).

4.2. Soluble compounds of enriched uranium

Here, the important consideration is irradiation of bone, which is more critical than irradiation of other tissues, and also than the non-radiological toxicity to kidney; this conclusion is based on the results of dosimetry calculations which take cognizance of the distribution of uranium in the body after entry of soluble compounds. To estimate the body burden of uranium from the amount of uranium in urine at known intervals after acute intake, the ratios listed in Table II can be used.

In cases of bone burden acquired by chronic intake, a different approach must be made. The value of 300 d has been adopted for the biological half-life of uranium in bone; this implies a ratio of 430 for Bone Burden/Daily Excretion and of 600 for Bone Burden/Urine Concentrations. The maximum permissible bone burden recommended by ICRP (1959) is 0.05 \mu c, hence the urinary excretion rate arising from one-tenth of the maximum permissible bone burden is 12 pc/d of 8 pc/l of urine. The urinary excretion rate is unlikely to fall to the level truly representative of the bone burden until a considerable time has elapsed since the last intake. For application of these standards to assess the significance of internal contamination due to soluble enriched uranium, routine urine samples should be
taken after the week-end, to minimize the contribution from any recent intake at work to the urinary excretion rate. (Even samples taken after the week-end are likely to give an exaggerated impression of the bone burden; samples taken on return from holiday would give a better indication).

It is conceivable that a uranium worker, while keeping within the urinary excretion rate set by reference to (MPC)$_a$ for kidney (see section 4.1) may eventually accumulate a radiologically significant bone burden. His urinary excretion of natural uranium should satisfy the same radiological standard as in the case of enriched uranium. The limits defined earlier in this section are equivalent to 17 µg/d, i.e. 12 µg/l, corresponding to one-tenth of the maximum permissible bone burden of natural uranium (1/10 × 90 000 µg).

4.3. Insoluble uranium compounds

The difficulties of predicting deposition and retention of insoluble uranium dust in the lungs have been described (section 2.3), but it is clear nevertheless that the lung is the critical organ in this case. By calculations of dosimetry made according to the procedure of ICRP Committee II (1959) [8] the maximum permissible lung burden is estimated to be 0.02 µc of any of the isotopes uranium-238, 235 or 234, equivalent to 30 000 µg of natural uranium.

To estimate the magnitude of a lung burden from the uranium content of urine samples taken during the period after an acute intake which occurred on a known date, the ratios listed in Table III may be used; after a longer period, the ratio of Lung Burden/Daily Urinary Excretion may be taken as 170 (corresponding to a lung half-life of 120 d). These ratios are based on the evidence from only one case (Section 3.2) [21].

This proposal is made very tentatively, because if there is any possibility that the lung burden has been acquired by chronic inhalation, the only approach offering any reasonable degree of reliability is direct measurement of radiation from the chest. About one-third to one-half of the maximum permissible lung burden of uranium-235 can be measured by making use of the 186 keV X-radiation, and a similar fraction of the maximum permissible lung burden of natural uranium should be measured by means of the 90 keV radiation from decay products of uranium [25]. It is not practicable to suggest any ratios relating chronic lung burden to urinary excretion rate.

The possible presence of a chronic lung burden must be judged from the records of a man's working history – especially the measurements of environmental conditions and urinary excretion; an estimate of the significance of his current urinary excretion rate of uranium must be based on the case histories outlined in section 3.2. In view of the findings of SAXBY et al. [24] it is clear that the investigation of cases of inhalation of insoluble uranium compounds should include the analysis of faeces as well as urine.

ACKNOWLEDGEMENT

The author is most grateful to Dr. G.W. Dolphin, Dr. K.P. Duncan and Dr. I.S. Eve for their very helpful advice on all matters connected with this paper.
REFERENCES

PLUTONIUM AND RARE EARTH ELEMENTS
(Session 16)
PHYSIOLOGICAL PROPERTIES OF PLUTONIUM AND ASSESSMENT OF BODY BURDEN IN MAN

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Abstract — Résumé — Аннотация — Resumen

PHYSIOLOGICAL PROPERTIES OF PLUTONIUM AND ASSESSMENT OF BODY BURDEN IN MAN. Twenty
years have elapsed since enough plutonium became available to create a potential industrial health problem.
Subsequent human experience and animal experimentation show that, of the three principal modes of exposure
(inhalation, ingestion and skin absorption), inhalation is the most important. Deposition, elimination, ab-
sorption and tissue distribution of inspired plutonium are strongly dependent on chemical form, particle size,
exposure procedure and animal species, resulting in quantitative exceptions to any generalized model as to
disposition and fate of inhaled plutonium. Exposure via ingestion is of little importance; gut absorption is
about 0.002% of the ingested dose. Absorption through unbroken skin is less than 0.0002%/h of contact. Con-
taminated wounds (second only to inhalation as a potential industrial medical problem) result in slow absorption
into the circulation, contributing to a systemic burden and producing chronic radiation changes at the site of
implant. Tissue distribution of plutonium is dependent on mode of exposure, chemical form, particle size and
colloidal aggregation.

Presently the only routine method of assessing plutonium body burden is to relate urinary excretion to
body burden through the expression \( D = 435 Ut^{-0.76} \), where \( D \) is body burden, \( U \) is daily output in urine, both
in the same units, and \( t \) is time (in days) following exposure. This empirical relationship was established in
a limited number of terminal human subjects following a single intravenous injection of a small amount of
Pu\(^{4+}\)-citrato.

Two computer methods have been developed to relate excretion rate under chronic exposure conditions
to body burden on the basis of the above expression. Validity of these methods has not been proven. Although
improved methods of urine analysis have been developed, no improvement in the basic expression or its ap-
plicability to exposure conditions more closely approaching those encountered in practice has been produced.
No procedure exists for diagnosis of plutonium in the lungs and lymph nodes. Application of whole-body
counting procedures based on measuring soft X-rays from plutonium has met with limited success. Existing
critical problem areas in industrial medical control of plutonium are discussed.

CARACTÉRISTIQUES PHYSIOLOGIQUES DU PLUTONIUM ET ÉVALUATION DE LA CHARGE CORPORELLE
CHEZ L'HOMME. Depuis vingt ans, la production de plutonium est assez importante pour créer un problème
d'hygiène industrielle. Il ressort de l'expérience acquise directement par l'homme, comme de travaux faits
sur des animaux, que des trois principaux modes de contamination - inhalation, ingestion et absorption trans-
cutanée - le plus important est l'inhalation. Le dépôt, l'élimination et l'absorption du plutonium absorbé
par inhalation, ainsi que sa répartition dans les tissus, varient beaucoup selon la forme chimique, la dimension
des particules, les conditions de l'exposition et l'espèce animale; il en résulte qu'à tout modèle visant à re-
présenter la répartition et le sort du plutonium absorbé par inhalation, il y a de nombreuses exceptions.
La contamination par ingestion est peu importante et la quantité de plutonium absorbée par la paroi intestinale
représente environ 0.002% de la dose ingérée. En l'absence de lésions, la quantité de plutonium absorbée
par voie transcutanée est de moins de 0.0002% de la dose absorbée totale par heure de contact. Les plaies
contaminées qui, après l'absorption par inhalation constituent le plus grave problème d'hygiène, provoquent
une lente absorption du plutonium dans l'appareil circulatoire, ce qui contribue à créer une charge dite
<systémique> et produit des affections chroniques à l'endroit où le plutonium se fixe. La répartition du plu-
tonium dans les tissus varie selon le mode de contamination, la forme chimique, la dimension des particules,
et l'agglomération colloïdale.

À l'heure actuelle, la seule méthode courante pour évaluer la charge corporelle de plutonium est d'utiliser
la relation entre la charge corporelle et l'élimination urinaire exprimée par la formule \( D = 435 Ut^{-0.76} \)
da laquelle \( D \) représente la charge corporelle, \( U \) la quantité de plutonium évacuée quotidiennement dans l'urine,
ces deux quantités étant exprimées dans les mêmes unités, et \( t \) le temps - en jours - qui a suivi la contamination.
Cette relation empirique a été établie chez un nombre restreint de sujets humains se trouvant à la dernière extrémité, à la suite d'une seule injection intraveineuse d'une petite quantité de citrate de Pu⁺⁴.

A partir de la formule ci-dessus, l'auteur a mis au point deux méthodes pour calculatrices afin d'établir un rapport entre le taux d'élimination du plutonium et la charge corporelle, en cas de contamination interrompue. La validité de ces méthodes n'a pas été démontrée. Malgré les perfectionnements apportés aux méthodes d'analyse des urines, on n'est pas parvenu à améliorer la formule de base ni son applicabilité à des conditions de contamination plus proches de celles qu'on rencontrent dans la pratique. Il n'existe pas de procédés pour diagnostiquer la présence de plutonium dans les poumons ou les ganglions lymphatiques, l'application de méthodes anthropogammamétriques fondées sur la mesure des rayons X mous émis par le plutonium n'a eu qu'un succès limité. L'auteur discute les aspects les plus urgents du problème que pose le contrôle médical du personnel qui manipule du plutonium.

PROPRIEDADES FISIOLÓGICAS DEL PLUTONIO Y EVALUACIÓN DE LA CARGA CORPORAL EN EL HOMBRE.

Han transcurrido veinte años desde que las existencias de plutonio alcanzaron un volumen suficiente como para crear un problema de higiene industrial. La ulterior experiencia recogida en los seres humanos y los resultados de los ensayos con animales indican que, de los tres principales modos de exposición (a saber, la inhalación, la ingestión y la absorción cutánea) el primero es el más importante. La forma química, el tamaño de las partículas, el procedimiento de exposición y la especie animal influyen apreciablemente sobre el depósito, la eliminación, la absorción y la distribución en los tejidos del plutonio inhalado, y esto hace que cualquier modelo general que se pretenda establecer para representar la eliminación y el destino final del plutonio inhalado deba admitir excepciones cuantitativas, La exposición por ingestión reviste escasa importancia; la absorción por el intestino representa alrededor del 0,002% de la dosis ingerida. La absorción a través de la piel ilesa es inferior al 0,0002% por hora de contacto. Las heridas contaminadas (que como problema de higiene industrial sólo ceden en orden de importancia a la inhalación) originan una lenta absorción por el caudal circulatorio, contribuyen a la carga general y producen alteraciones radiológicas crónicas.
1. INTRODUCTION

Historically, plutonium still may be considered a material of very recent vintage, having been discovered only 24 yrs ago by SEABORG, McMILLAN, KENNEDY and WAHL [1]. Within a few months after discovery, the fissionable properties of the Pu$^{239}$ isotope were established by the same group using an amount of material (0.5 μg) equal to what is now considered to be approximately one maximum permissible body burden. In late 1942, HAMILTON and co-workers [2] began studying the assimilation, distribution, and excretion of fission products and the heavy elements. Shortly thereafter, they observed that plutonium deposited in the bones of rats and postulated its similarity to radium in the production of bone sarcoma. From that time on, plutonium has been considered one of the most toxic substances known. Because of this early recognition of the potentially hazardous nature of plutonium, not one person is known to have been harmed by it other than under conditions resulting in criticality. Only 20 yr have elapsed, however, since enough plutonium became available to create a potential industrial health problem. During this period, less than 50 people are suspected of having accumulated body burdens equal to or greater than the maximum permissible level and, as was observed from the radium poisoning cases, a delay of from 12 to 30 yr may be expected between time of exposure and appearance of symptoms of chronic radiation damage. In view of the above circumstances, it is not surprising that a case of plutonium poisoning has never been observed.

2. PHYSIOLOGICAL PROPERTIES OF PLUTONIUM

2.1. Absorption and modes of exposure
(a) Ingestion and gastro-intestinal absorption

Absorption of plutonium from the gastro-intestinal tract has been studied in rats under a variety of conditions [3-5], including chronic administration
in drinking water. Under the more usually anticipated conditions of exposure, absorption of \( \text{Pu}^{4+} \) is only about 0.003% of the ingested dose. Hexavalent plutonium is absorbed at a somewhat higher rate than \( \text{Pu}^{3+} \) or \( \text{Pu}^{4+} \). Absorption of the lower valence states is increased by strong acidity and the presence of complexing agents such as citrate. There appears to be no mass effect when the amount of plutonium ingested is varied over a wide range. Very young animals absorb more than older ones by factors of 10 to 100. Gastro-intestinal absorption has not been determined in man, but the pig with an anatomically similar digestive tract showed an absorption of only 0.002% when administered \( \text{Pu(NO}_3\text{)}_4 \) solutions at pH 2 [4]. Ingestion, therefore, is not considered to be a particularly significant mode of exposure.

(b) Absorption through the unbroken skin

Only one experimental attempt (involving a single individual) to measure plutonium absorption through the intact human skin has been reported [6]. In this case, \( \text{Pu(NO}_3\text{)}_4 \) in 0.4 N HNO\(_3\) was placed on the palmar surface and allowed to remain for several hours. Assay of urine samples during and for several days after the experiment showed no absorption within the limits of detection. All that could be said was that if absorption occurred, it was less than 0.0002% of the amount applied per hour of contact. WILSON [7] reported an accidental exposure involving complete immersion for several minutes of the hand and wrist in a carbon-tetrachloride-tributyl phosphate solution containing 2 to 3 mc Pu/ml. Prior to decontamination, total deposition on the hand was estimated as about 5 mc and after one week was still 10 \( \mu \text{c} \). Urine analysis suggested that total absorption through the skin was about 0.00002% of the initial amount present on the skin surface. The Hanford group has reported a number of experiments on absorption of plutonium through the intact skin of rats [8-12]. These observations show that absorption is to some degree affected by the chemical form of the plutonium, nature of the solution, area exposed, and mass of plutonium applied. Acidity and nature of the solvent through irritation or other effects on the skin surface and complexing of the plutonium in soluble form tend to increase absorption. Because of the difference in physiological and anatomical properties of the rat and human skin, these results probably have little quantitative significance. Qualitatively, however, they may be significant in that conditions enhancing absorption through rat skin might enhance to some degree absorption through human skin also. As with gastrointestinal absorption, plutonium absorption through the intact skin under the more usually anticipated conditions appears not to be a particularly significant mode of exposure.

(c) Absorption from contaminated wounds

Contaminated wounds have constituted a much more troublesome problem than either gastro-intestinal absorption or absorption through the unbroken skin. There are two aspects to the contaminated wound problem. If the plutonium is allowed to remain in the wound, it may (a) elicit a chronic local response, and (b) it will be slowly translocated to other tissues and
organs, thereby contributing to local exposure of adjacent tissues and to an increased systemic burden.

Studies of absorption from contaminated wounds inflicted in experimental animals show great variations. These variations are not surprising. It is virtually impossible to reproduce or to standardize the characteristics of a wound, and if standardization of a wound could be accomplished the probability that one sustained in an accident would have the same characteristics would be slight indeed. Many of these observations, however, are of considerable qualitative significance. Plutonium applied as the oxide to abrasion-type lesions is absorbed very little, if at all. The material is trapped in tissue exudate, is thereby mobilized in the eschar, and lost when the eschar is detached [13]. Contamination of more substantial wounds, however, results in local deposition in the tissues and slow absorption into the systemic circulation. Qualitatively at least, it seems that PuO$_2^{++}$ is absorbed most rapidly from sites of intramuscular injection, Pu$^{+3}$ next, and Pu$^{+4}$ least rapidly [14]. The presence of complexing agents such as citrate enhances the absorption rate. The absorption rate might be expected to depend also on depth of the wound and vascular and lymphatic circulation in the immediate area. OAKLEY and THOMPSON [11] studied the relative absorption of Pu(NO$_3$)$_4$ in 0.1 N HNO$_3$ through intact skin, through dermal cuts (1.5 cm long), through comparable subcutaneous cuts, and from subcutaneous injection in rats and found the amount of systemic absorption at 24 h to be 0.33, 0.55, 0.85, and 2.7%, respectively. Variations in the nature, location or depth of the wound, difference in chemical nature of the solution and form of the plutonium, or use of a different species probably would have produced quantitatively different results. Practically speaking, the most important feature of such observations is that they show a relatively slow rate of translocation regardless of chemical form of the plutonium, nature of the solution, and character of the wound. Under the more usually anticipated conditions of exposure, from about 70 to 95% of the plutonium may be confined to the locality of the wound 4 to 10 d after infliction. This affords an opportunity to assess the seriousness of contamination and to judge the feasibility and value of surgical intervention.

(d) Inhalation and pulmonary absorption

The ultimate fate and biological effects of inhaled plutonium are dependent on the kinetics of deposition, retention, distribution, and absorption of the inspired material. The kinetic parameters of these factors are dependent on a large number of interrelated physical, chemical and biological variables, all of which are difficult to control and to evaluate experimentally. Among the most troublesome variables are particle size, particle density, aerosol concentration, chemical form and solubility of the plutonium, respiratory rate, tidal volume, and the animal species. BAIR and associates of the Hanford laboratory are making a concerted effort to study effects of some of these variables on the kinetics of inhaled plutonium in beagles [15-20]. Their studies to date have involved primarily effect of particle size and chemical form of the plutonium. Although these experiments have been nobly and carefully pursued, they are difficult and time-consuming and results to date do not seem adequate to provide a basis
for any quantitative refinement of the lung retention model adopted by the International Commission on Radiological Protection (ICRP) [21]. The ICRP model assumes that 25% of the inhaled material is exhaled immediately, 50% is deposited in the upper respiratory passages and subsequently swallowed, and 25% is deposited in the lower respiratory passages. If the material is soluble, the 25% deposited in the lower recesses of the lung is absorbed into the systemic circulation. If the material is insoluble, half of the amount deposited (12.5% of that originally inhaled) is rapidly eliminated via the bronchial tree and the other half is retained in the lungs with a half time of 120 d, being eliminated via absorption into the body fluids.

The observations of the Hanford group and others definitely indicate, however, that absorption from the lung into the systemic circulation (with subsequent deposition in the bone, liver, kidneys, spleen, and other tissues) is only one facet of a much more complicated problem. The persistently high concentrations and long retention times in the lungs and pulmonary lymph nodes following inhalation may result in greater potential risk to these tissues than to the bone, etc., from systemic absorption.

2.2: Plutonium deposition and distribution

Early work on deposition and distribution of plutonium was predicated on the assumption that the potential hazard was a systemic one, that clearance and absorption from the gastro-intestinal tract and pulmonary tissues would be relatively rapid, and once plutonium was absorbed into the circulation its distribution would be relatively independent of chemical or physical form and the route of entry. Intramuscular [14] and intravenous [5] injections were used, therefore, to establish tissue distribution patterns, and the results led to the conclusion that bone (which showed the highest concentrations under these conditions) was the critical tissue. Collection of data from a number of subsequent papers [4, 13, 17, 22-25] shows that deposition and distribution are highly variable and dependent on a variety of factors, including route of administration, chemical or physical form of the plutonium, and animal species. Several generalizations are possible from the collected data. Following intravenous injection, bone and liver are the primary organs of deposition. The ratio between bone and liver, however, is dependent on chemical composition of the solution, valence state of the plutonium, and its colloidal state. The rate and degree of hydrolysis and polymerization of plutonium upon contacting the body fluids are largely responsible for variations in distribution observed for different valence states, different solution compositions, and different routes of administration. Those factors favouring colloid formation result in higher concentrations in liver and spleen and lower deposition in bone. Plutonium absorbed from the gastro-intestinal tract and from intramuscular injection is deposited predominantly in the skeleton; as is highly complexed material administered intravenously. Plutonium absorbed from the lungs is deposited both in the liver and bone, with the relative distribution showing dependence on chemical form, solubility, and particle size of the inhaled material. The tissues with the maximum concentrations, however, are the lungs and pulmonary lymph nodes. Fragmentary autopsy data from workers who may have been
chronically exposed to low-level plutonium inhalation [13] tend to support the high accumulation in lungs and lymph nodes observed in experimentally-exposed animals.

2.3. Plutonium elimination

(a) Systemic burden

It would be naive indeed to expect the rate of elimination of plutonium from the body to be independent of animal species, chemical and physical nature of the material administered, and route or method of administration. The effects of these factors on elimination rates have been observed in a number of experiments.

The excretion rate of systemically absorbed plutonium is extremely slow and decreases with time. This time dependence has resulted in the general practice of expressing excretion rates as logarithmic functions of the type

\[ Y = a T^{-b} \]  

where \( Y \) is the amount of plutonium excreted per day, and \( T \) is time of observation in days after administration. Only limited consideration of some of the results in dogs and man will be given.

STOVER et al. [24, 26] observed the excretion rate of intravenously administered Pu\(^{4+}\) citrate in beagles for periods up to 8 yr after injection. They found that 12% of the injected dose was excreted during the first 22 d, after which the rate levelled off rather abruptly. This necessitated fitting the data prior to and beyond 22 d with separate expressions. From 1 to 22 d after injection, the urinary \( (Y_u) \) and total \( (Y_t) \) plutonium excretion rates (in per cent of injected dose) were best represented by

\[ Y_u = 1.44 T^{-1.52} \]  
\[ (1 < T \leq 22) \]  
\[ Y_t = 6.98 T^{-1.59} \]  

Beyond 22 d, the urinary and total excretion rates were best represented as

\[ Y_u = 0.0605 T^{-0.409} \]  
\[ (T > 22) \]  
\[ Y_t = 0.223 T^{-0.485} \]  

During the first 22 d, the faecal-to-urinary ratio dropped rapidly but averaged approximately 4. Beyond 22 d, it was approximately unity out to about 4 yr.

Human excretion data have been obtained from occasional cases of occupational exposure and from 15 terminal patients administered tracer doses
of plutonium (usually Pu\textsuperscript{4+}-citrate) via intravenous injection. The latter observations have been summarized in a number of publications \cite{6,27,13,28}. No attempt will be made here to present these observations in detail or to elaborate on their shortcomings and applicability to assessment of plutonium body burdens in man. It seems adequate only to say that their primary virtue lies in the fact that they are the only data of their kind available. To some degree, excretion of intravenously-administered plutonium by man and dog is similar. The human urinary (Y\textsubscript{u}), faecal (Y\textsubscript{f}), and total (Y\textsubscript{t}) excretion rates (in per cent of injected dose) from 1 through 138 d were fit to the following power functions:

\begin{align*}
Y\textsubscript{u} &= 0.23 T^{-0.77} \quad (1 \leq T \leq 138), \\
Y\textsubscript{f} &= 0.63 T^{-1.09} \\
Y\textsubscript{t} &= 0.79 T^{-0.94}
\end{align*}

Additional data collected from three industrial exposure cases were used to adjust these expressions to T = \sim 5 \text{ yr}. The adjusted expressions for the urinary and total excretion rates were:

\begin{align*}
Y\textsubscript{u} &= 0.2 T^{-0.74} \quad (1 < T < 1750), \\
Y\textsubscript{t} &= 0.79 T^{-0.94}
\end{align*}

Appreciably different expressions are obtained when the data are fitted in the normal instead of the logarithmic plane. The amount of plutonium excreted during the first few days was less for man than for the dog (\sim 3% as compared to 12% during the first 22 d). As with dogs, there was a very rapid drop in the rate during the first 20 to 30 d, after which it levelled off abruptly. In fact, a considerably better fit to the data is obtained if the excretion values during the first 10 d are excluded. As with dogs, the faecal-to-urinary ratio was about 4 immediately after injection and dropped to unity during the first 20 to 30 d. The ratio continued to drop, however, to a value of about 0.5 at 138 d.

(b) Lung burden

There are no experimental data on the rate of elimination of inhaled plutonium by man. Observations are confined to a few cases of accidental industrial exposure \cite{29,30}. Elimination of material deposited in the lungs involves two routes: (a) absorption into the systemic circulation and subsequent excretion via the kidney and gastro-intestinal tract, and (b) movement up the bronchial tree and subsequent elimination via the faeces. The rates of elimination by both routes (as well as the amount initially retained in the lung) are dependent, of course, on the chemical and physical nature of the material inhaled and on the respiratory variables of the host. Retention or elimination of inhaled plutonium in various forms has been studied
in mice, rats, dogs, and pigs. There appears to be little consistency in
the data, in the experimental methods used, or in the methods of reporting
results. No attempt is made, therefore, to summarize all of these studies.
Among the more recent observations are those of the Hanford group [16-18,
31] on beagles inhaling $\text{PuO}_2$. In one of these studies [31], $\text{PuO}_2$ doses were
large enough to produce mortality in 55 to 412 d. From these observations,
the authors deduced that beyond two weeks the total-body retention was re­
presented by the expression.

$$p = A e^{-kt} \quad (t \geq 14), \quad (11)$$

where $p$ is the whole-body burden at time $t$ in days after exposure, and $A$
is the initial amount deposited (at $t = 0$) and excreted with the rate constant $k$.
Evaluation of the constants gave a "typical" whole-body retention curve of

$$p = 38 e^{-0.0084t} \quad (t > 14), \quad (12)$$

for a large acute inhalation exposure to $\text{PuO}_2$ particles of 0.5 - to 0.65-$\mu$
count median diameter. Since 95% of the plutonium recovered at autopsy
was found in the lungs, 4% in the bronchial and mediastinal lymph nodes,
and only about 1% in the rest of the tissues, the first derivative of this ex­
pression may be assumed to represent the rate of clearance (under these
specific conditions) of $\text{PuO}_2$ from the critical pulmonary tissues of dogs. Both $A$ and $k$ in the general expression will vary with the chemical and phy­sical nature of the inhaled plutonium, the aerosol concentration, and the
respiratory variables of the host.

3. ASSESSMENT OF PLUTONIUM BODY BURDEN IN MAN

An excellent review of the problems and methods of evaluating plutonium
exposures in man has just been published by ROBERTSON and COHN [32].
Their article has been used repeatedly and without specific reference in
preparation of the following sections.

3.1. Assessment from excretion analyses

(a) Systemic burden

As mentioned previously, very early in the development of the United
States plutonium project it was assumed that, regardless of mode of ex­
posure, plutonium would be rapidly translocated to the skeleton and pro­
duction of bone sarcoma would be the major potential industrial hazard. This
assumption prompted development of a systemic model (based on excretion
of intravenously-administered plutonium by terminal hospital patients) for
assessment of body burden from urine analyses [13, 27, 28, 33].

Following a single acute exposure occurring at known time, the body
burden may be estimated from the plutonium content ($U$) of a 24-h urine spe­
cimen (or the average of a series of consecutive samples) collected $T$ days
after exposure by the following expression derived from Eq. (9):
Industrial operations, however, usually involve intermittent or continuous low-level exposure, and attempts have been made to develop computer programmes (on the basis of the systemic model) to estimate body burdens under these conditions. A programme developed by LAWRENCE [34] assumes that the body burden due to each individual exposure can be described by Eq. (9). He then estimates a series of single intakes that would produce the observed urine concentration. He uses a method of validating the data as follows: the urinary output on a given day is used to compute the expected output on any later day. If the output on the later day is lower than expected, the previous data point is rejected. This is done on the basis that if there is an additional intake between the two days the output should be higher; in no case should it be lower. This system then assumes that the most recent data point is a valid one. The major weakness of this system is that a sample subsequently found to be invalid is capable of validating the one immediately previous.

SNYDER [35] has reported two codes, PUQUAP and PUQUAE, for the estimation of body burden under chronic exposure conditions. His programmes avoid the problem of rejection of data by assuming that intake into and excretion from the blood are continuous functions of time rather than discrete quantities. These too are based on the power function expression shown in Eq. (9). The assumption that the power function derived from the available data is sufficiently accurate that the integral will describe the case for continuous exposure is the greatest uncertainty in Snyder's approach.

It is important to point out that the body burden estimated from urine analyses by these codes does not include plutonium in the lungs and lymph nodes or material retained locally at the site of a contaminated wound. Furthermore, the presence of such reservoirs of unabsorbed plutonium may alter the parameters of the urinary excretion function. This has resulted in a number of reports pointing out limitations of the systemic model as a basis for diagnosing body burden and showing urinary excretion patterns that fail to conform to the power functions represented in Eqs. (6-10) [29, 30, 36-38]. In some of these cases, the excretion patterns were complicated by the administration of agents to enhance elimination.

(b) Lung burden

Interpretation of urine analyses on the basis of the systemic model does not include material deposited in the lung, and furthermore does not give a dependable estimate of the systemic burden because of influence of absorption from the lung reservoir on the urinary excretion pattern. HEALY [29] has proposed a lung exposure model which attempts to take these factors
PHYSIOLOGICAL PROPERTIES OF PLUTONIUM

He assumes that plutonium deposited in the lung constitutes a reservoir of material isolated from the body's normal metabolic pathways but continually being absorbed into the systemic circulation at a rate dependent upon the physical and chemical nature of the deposit and relevant physiological processes. As the material is removed from the lung either by absorption into the blood or by excretion up the bronchial tree, the size of the reservoir, and thus the amount absorbed into the blood, decreases. Assuming exponential removal of the lung burden, the quantity of plutonium remaining ($Q$) at time $t$ following and acute fixation of a quantity $Q_0$ is given by the expression

$$Q = Q_0 e^{-\lambda t}.$$  \hspace{1cm} (15)

In this expression, the overall elimination rate $\lambda$ is regarded as being composed of two components: (a) solubilization and absorption into the systemic circulation ($\lambda_s$), and (b) removal by ciliary action ($\lambda_c$). $Q_0$ specifically refers to that amount of plutonium retained in the lung after the initial rapid clearance of material deposited in the upper bronchial passages. Healy assumed that Eq. (9) describes the urinary excretion rate of each increment entering the blood and that the sum of the excretion rates of each increment gives the total excretion. It is important to note, however, that the time since administration in Eq. (9) must be taken as the time since the plutonium entered the blood and not as time of deposition in the lung. On this basis, if $R$ is the time of collection of the urine sample following deposition in the lung, then the resulting urinary excretion rate ($E_u$) is given by

$$E_u = 0.002 \lambda_s Q_0 \int_0^R e^{-\lambda t} (R - t)^{-0.74} dt.$$  \hspace{1cm} (16)

For convenience, the terms of this expression are collected and re-defined as follows:

- $E_u$ = daily excretion rate
- $\lambda$ = overall elimination rate from the lung
- $\lambda_s$ = rate of transfer to the blood (assumed equal to $\lambda$)
- $Q_0$ = quantity of plutonium retained in the lung after initial rapid clearance
- $R$ = sampling time following deposition in the lung
- $t$ = time since absorption into the blood stream.

Since the expression is not integrable, it was evaluated for individual values of $\lambda$, $R$, and $t$ by expansion of the exponential term and solving until the series converged. Healy derived similar expressions for faecal excretion and for the quantity of plutonium in the blood as a result of movement from the lung.

When exposure is by inhalation, use of this model appears to be far more realistic than use of the systemic model. Its primary difficulty lies in the choice of proper values for $\lambda$ and $\lambda_s$ in view of their dependence on the physical and chemical nature of the lung deposit, which may not be known.
under actual exposure conditions, and on relevant physiological processes in the lung which are poorly understood at present. Healy found it necessary to assume $\lambda_1$ equal to $\lambda$, and in applying the expression to an actual exposure case found that the rate of change in excretion was insufficient to provide an accurate estimate of $\lambda$, although samples were obtained for 1600 d. Figure 1 shows the fractional urinary excretion rate of plutonium on the basis of the two models, assuming a unit body burden is deposited systemically in the case of the systemic model and in the lung for the lung deposition model. In the latter case, $Q_0$ is assumed equal to unity and calculations are shown for $\lambda_1 = 0.01$ ($T/\lambda_1 = 69$ d) and $0.001$ ($T/\lambda_1 = 693$ d). A number of pertinent points may be deduced from Fig. 1. First, the data show that the level of urinary excretion following inhalation exposure is dependent on $\lambda_1$ which is related to the solubility of the material inhaled. Second, the rate of urinary excretion may remain essentially constant or actually increase for a period of time (inversely proportional to $\lambda_1$), after which it may begin to decrease with a slope greater than that expected from the systemic model. Third, the urinary excretion pattern following significant lung deposition cannot be expected to conform to that following intravenous injection for a period after exposure that is inversely proportional to $\lambda_1$. Qualitatively, at least, it may be assumed that no significantly large lung burden exists if the slope of the urinary excretion curve is essentially the same as that expected on the basis of the systemic model. The same may be assumed regarding unabsorbed material in cutaneous or subcutaneous wounds. A lesser slope at early times after exposure or a greater slope
at later times may be considered indicative of a reservoir of unabsorbed plutonium in the lungs or at the site of a contaminated wound. The question is whether \( Q_0 \) can be estimated from urine analyses on the basis of the lung exposure model. In theory, it seems possible if \( \lambda_1 \) is known for the specific conditions of exposure. Such an approach to estimation of lung burden under actual plant conditions may not be feasible because of practical limitations.

It would appear more promising in future work, however, to attempt to apply and refine the lung deposition model and to design experiments to evaluate \( \lambda_1 \) better and their dependence on appropriate physical, chemical, and biological factors than to continue to apply the systemic model to situations for which it is not adequate.

This author [27] attempted at one time to develop a method of diagnosing lung burden from urinary-to-faecal excretion ratios. The difficulties of collecting and analysing faecal samples and the wide fluctuations in faecal excretion, plus its dependence on physical and chemical nature of the deposited material and on ill-defined processes of pulmonary elimination, make the method quantitatively useless. About all that can be said is that faecal-to-urinary excretion ratios may be used in a qualitative sense to determine whether appreciable pulmonary exposure has occurred.

3.2. Body burden by external counting

(a) Systemic and lung burden

The fact that plutonium emits electromagnetic radiations has stimulated attempts to develop external counting methods of determining body burdens. Detection of plutonium in vivo by whole-body counting has been reviewed by ROESCH and PALMER [39]. Conventional whole-body counting techniques cannot be applied to the measurement of Pu\(^{239}\)body burdens. This is because the characteristic electromagnetic radiation from Pu\(^{239}\) consists predominantly of soft X-rays. There are only a few low-energy gammas. The relatively abundant X-rays are easily absorbed, the half-value layer in tissue being \( \sim 0.6 \) cm and in bone \( \sim 0.03 \) cm. This makes accurate quantitative measurements extremely difficult. With the quite low half-value layer in bone, the quantitation of skeletally-deposited plutonium by external measurements is highly unlikely.

Whole-body counting has been applied to measuring plutonium in the lungs and in the liver. RUNDO and TAYLOR [40] have used a gas flow proportional counter (argon and methane mixture) with a 150 cm\(^2\) thin Lucite window for measuring plutonium in the lungs. For a counting time of 50 min, with a source-to-detector distance of 10 cm and shielding of 2.54 cm of tissue, the minimum detectable amount of plutonium is about 15 nc.

ROESCH, et al. [39] have used a thin NaI (Tl) crystal, 11.5 cm in diameter by 0.1 cm in thickness, to measure plutonium in the liver of a subject. The minimum detectable body burden was estimated to be 300 nc. The errors in the measurements are, of course, quite large. They report somewhat better success using a crystal thickness of 0.3 cm and measuring the gamma rays from Am\(^{241}\) present in the plutonium.

KIEFER and MAUSHART [41] have used annular cylindrical proportional counters to measure plutonium in the hand or arm. They report being
able to detect 20 nc distributed in a phantom arm. They suggest that large flat anticoincidence proportional counters might be used to measure plutonium in the lungs. Such a system has not yet been attempted.

(b) Burden in contaminated wounds

Contamination of wounds has been a significant industrial health control problem. As with material deposited in the lungs, urine analyses cannot be relied on to determine quantitatively plutonium localized at the site of a contaminated wound. Early detection and subsequent surgical removal (when feasible) of such implants have become more or less standard practice [42]. External counting procedures have been developed to determine the amount of plutonium in such implants by measuring the 17-kV X-rays [43,44]. If the material is superficially deposited, these counters have a minimum detectable level of about 0.1 nc.

4. DISCUSSION AND CONCLUSIONS

Twenty years' experience with the production and processing of large quantities of plutonium in the United States has shown the primary industrial hygiene problems to be chronic or intermittent low-level inhalation exposure, a number of contaminated wounds, and a few accidental acute exposures usually involving inhalation. The industrial medical record of the plutonium industry appears almost miraculous. Perhaps fewer than 50 workers have received exposures equal to or slightly greater than the maximum permissible body burden, insofar as it is possible to assess a body burden. This enviable record is a result of the rigorous industrial hygiene and engineering control measures introduced into plutonium processing operations from the very beginning.

With such rigorous and effective industrial hygiene controls, one may question seriously the value of a difficult and expensive routine programme of assessing body burdens of personnel working with plutonium. This is not an easy question to answer. However, a workable programme of this nature would provide the ultimate proof of the effectiveness of industrial hygiene control measures. Both the Hanford and Los Alamos laboratories have uncovered potentially hazardous operations and exposure conditions through investigating high urinary excretion values of specific employees. Also, if it were possible to determine body burden with reasonable accuracy, such a programme would be highly desirable both for health protection and for medico-legal reasons. In the opinion of this author, the present capability of assessing body burden is limited to assessment of systemic burden from urinary excretion to ± 25% following an acute exposure under conditions that preclude any significant reservoir of unabsorbed material in the lungs or tissues. Even under these simple conditions, this accuracy cannot be obtained from a simple routine sampling schedule but requires careful analyses of a series of 24-h specimens collected over a period of several weeks.

At the present time, there is no proven method for assessing body burden in those cases where significant reservoirs of unabsorbed material may
be localized in lungs and lymph nodes. It is possible, however, to use the faecal-to-urinary ratio to establish the presence of a sizeable pulmonary reservoir following an acute inhalation exposure. A ratio of several times unity clearly indicates unabsorbed material in the lung. Unfortunately, the ratio cannot be related quantitatively to the size of the lung burden. It is possible also to establish qualitatively the presence or absence of a significant lung burden from the general characteristics of the urinary excretion pattern.

More critical than the occasional acute exposure case, which is always given special consideration, is the problem of the long-term employee. The Los Alamos Scientific Laboratory now has several employees who have been working with plutonium for over 10 yr. Many of these have no history of involvement in a contamination accident, exposure to excessive air concentrations, or infliction of a potentially contaminated wound. However, they consistently show positive plutonium excretion in the urine. Estimation of their body burdens by the IBM 704 FORTRAN code developed by LAWRENCE [34] gives values ranging from 25 to 100% of the maximum permissible level. It has not been possible to test the accuracy of such codes for the estimation of body burden under the conditions of very low-level chronic exposure experienced by these workers. The extent of lung and lymph-node accumulation under these conditions is an unanswered question also.

In conclusion, it may be said that there is no known satisfactory method of assessing plutonium body burden in man under the more usually encountered conditions of exposure. The greatest needs are for a method of determining body burden under conditions of very low-level chronic and intermittent exposure and a method of assessing the amount of material deposited in the pulmonary tissues. Development of methods based on external measurement of the 17-kV X-rays from plutonium may be the most promising approach to the latter need.

REFERENCES

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DISCUSSION

H. G. JONES: I have a comment regarding wounds contaminated with plutonium. Normally, as you say in your paper, these wounds are monitored by measuring the 17-keV X-rays given off by the plutonium. Although these X-rays pass through tissue fairly well, self-absorption in the plutonium itself is very important, the half-value thickness being of the order of only a few microns. In the worst case, when a sliver of plutonium is buried in subcutaneous tissue with its longest dimension at right angles to the skin surface, only a very small part of the X-rays will be measured, so that the amount of plutonium present will be considerably underestimated. This should obviously be borne in mind when clinical decisions are made, on the basis of such readings, as to whether or not wound tissue should be excised after accidents involving plutonium.

W. H. LANGHAM: That is quite true. However, the wound monitor has been very helpful in the management of contaminated wounds. In the
very early years we used to excise any wound sustained in the contaminated area, but we found that this practice kept most people from reporting their wounds. The wound monitor by no means takes out of this problem the need for good intuitive judgement on the part of the surgeon and I think his decisions should be made in consultation with a health physicist who understands the instrument and its limitations.

C. J. MALETSKOS: Do you think that other signs of radiation damage should be searched for and considered in determining the relative sensitivity of bronchial lymph nodes, lungs, liver and bone to plutonium, apart from the end-point of cancer?

W.H. LANGHAM: Most certainly so, because signs of radiation damage such as osteoporosis, osteonecrosis and even spontaneous fractures were seen in many radium dial cases who never developed tumours. These effects have also been produced in animals. Liver damage has been observed in the Utah beagles as a result of plutonium injection. Fibrosis in the lungs may be considered, too, when the route of exposure is inhalation.
ON THE ESTIMATION OF A SYSTEMIC BODY BURDEN OF PLUTONIUM*

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Abstract — Résumé — Аннотация — Resumen

ON THE ESTIMATION OF A SYSTEMIC BODY BURDEN OF PLUTONIUM. Several computer programmes have been described in the literature which use the complete urinalysis record of employees to estimate their systemic body burden of plutonium-239, i.e. the body burden exclusive of plutonium-239 in the lungs or in the contents of the gastro-intestinal tract. For each successive sample date such codes use an excretion model, suggested by Langham, to estimate the urinary excretion that would be expected to result from prior intakes that have been estimated. Any excess in the sample is considered to indicate an additional intake, or is rejected as being the result of an erroneous determination. An examination of excretion data taken under controlled conditions indicates that there is considerable fluctuation about the smoothed curves used in the excretion model, that the deviations are by less than a factor of two in the majority of cases, and that much of this fluctuation must be accepted as of biological origin and not merely the result of faulty sampling techniques. This suggests that a mathematical treatment should accept small fluctuations as not necessarily indicating additional exposure or artifacts of sampling. Such a computer code has been written and tested on the few cases where the body burden is considered to be well established. These cases suggest that this technique may be an improvement over earlier methods. The code uses one index as specifying a level below which data are not considered to be significant, and a second index specifies the degree of excess over the general trend which is considered to be due to additional intake to blood.

ÉVALUATION D'UNE CHARGE CORPORELLE SYSTÉMIQUE DE PLUTONIUM. On trouve, dans des publications spécialisées, la description de plusieurs programmes de calculatrices qui, d'après les résultats complets d'analyses d'échantillons prélevés sur les urines de travailleurs, permettent d'évaluer chez ces derniers la charge corporelle systémique de plutonium 239, c'est-à-dire la charge corporelle à l'exclusion du plutonium 239 présent dans les poumons ou dans le contenu du tractus gastro-intestinal. Pour chaque des dates de prélèvement successives, les codes sont fondés sur un modèle d'excrétion, suggéré par Langham, qui permet de prévoir l'excrétion dans les urines à laquelle on peut s'attendre, à la suite d'absorptions antérieures de quantités estimées. Tout excédent dans l'échantillon est considéré comme dénotant l'absorption d'une quantité supplémentaire, ou écarté comme étant le résultat d'une détermination erronée. Les constatations suivantes ressortent de l'examen sous contrôle des données relatives à l'excrétion de plutonium: il existe des variations considérables de part et d'autre des courbes ajustées utilisées dans le modèle d'excrétion; les écarts sont, dans la plupart des cas, de l'ordre d'un facteur inférieur à deux; les variations ne sont pas dues simplement à l'imperfection des techniques de prélèvement, mais doivent en grande partie être attribuées à une cause biologique. Pour traiter ce problème mathématiquement, il faut donc admettre, semble-t-il, que de faibles variations n'impliquent pas nécessairement une exposition supplémentaire ni un phénomène artificiel qui serait la conséquence du prélèvement d'échantillons. Sur cette base, on a élaboré un code pour calculatrices, dont on a fait l'essai sur les quelques cas où la charge corporelle est considérée comme connue. Il ressort de ces cas que cette méthode peut constituer une amélioration par rapport à celles qui étaient appliquées auparavant. Dans le code ainsi élaboré, un indice définit le niveau en dessous duquel les données ne sont pas considérées comme significatives et un autre indice définit la valeur excédentaire par rapport à la tendance générale, qui est considérée comme impliquant une absorption supplémentaire de plutonium dans le sang.

ОБ ОПРЕДЕЛЕНИИ СОДЕРЖАНИЯ ПЛУТОНИЯ В СИСТЕМАХ ОРГАНИЗМА. В литературе уже были описаны различные счетно-вычислительные программы, использующие полные данные анализа мочи рабочих для определения содержания плутония-239 в системах ор-
ganism, for example, only in light or in the contents of the digestive tract. For each subsequent sample, a model of excretion, proposed by Langham, is used to determine the expected excretion in urine after previous absorption, which was computed. Any increase in the isotope level is considered as additional absorption, or rejected as a result of incorrect determination.

The examination of the excretion data, obtained under controlled conditions, shows that there are considerable fluctuations from the smoothed curves used in the excretion model, and that the majority of these deviations are at least 200%, and that many of these fluctuations have a biological origin and not merely a result of inadequate sampling techniques. This indicates that the mathematical treatment permits small fluctuations as not necessarily indicating additional exposure or artifacts in the sampling technique. This key has been prepared and tested in very few cases in which the systemic body burden of Pu\textsuperscript{239} was considered well known. These cases appear to indicate that this method may constitute a perfection of previous methods.

Internal exposure to plutonium, particularly Pu\textsuperscript{239}, poses an important and difficult problem for the health physicist. No techniques of whole-body gamma detection have been devised that are sensitive enough to measure a systemic body burden at the maximum permissible level recommended by the International Commission on Radiological Protection (ICRP), and thus those charged with evaluating an employee's exposure must attempt to base this evaluation on interpretation of such data on excretion of the radionuclide as may be available. Whether the exposure is acute or chronic and whether the plutonium entered the body by inhalation, by ingestion, or through a wound, the problem posed is one of the most difficult for the health physicist.

Several computer codes which use an employee's urinalysis data to estimate his systemic body burden of Pu\textsuperscript{239} have been described in the literature [1, 2]. These codes and other similar ones designed by the author are based on the metabolic model devised by Langham to represent the excretion and retention in man following intravenous administration of Pu\textsuperscript{239} [3]. Briefly, Langham analysed the excretion data of some eleven terminal patients.
ESTIMATION OF SYSTEMIC BODY BURDEN

who received injections of Pu\textsuperscript{149}-citrate. He found that power functions described the general trend of the excretion data during some 138 d. By ingenious analysis he was able to indicate that probably the same functions were adequate to represent the trend of excretion data of employees over periods of five years or longer. However, the hospital cases as well as the data on employees show a considerable degree of fluctuation about the curves describing the trend of the data.

The author has designed a code which, to some extent, takes into account possible fluctuations about the trend of the data. Assuming $S_i$ is the measured amount of Pu\textsuperscript{239} in urine on day $t_i$, $i = 1, 2, \ldots, n$, the problem consists of determining intakes $I_i$ of Pu\textsuperscript{239} to blood which will account for the excretion record and be consistent with the metabolic model. The model is represented by a series of constants $U_j$, each $U_j$ being the fraction of dose of Pu\textsuperscript{239} to blood which is excreted in the urine $j$ days later. The constants $U_j$ may be computed by a formula or may be entered in the code as a table of constants.

The computer first selects a time $j_1$ preceding the first sample day $t_1$ and computes the first intake

$$I_1 = S_1 / U_1 t_{11}.$$

Thus the first sample value is accounted for exactly by $I_1$. The intake $I_1$ already produces urinary excretion

$$I_1 U_{t_{1} - 11},$$
on day $t_1$, and so the computer calculates reduced excretions

$$S'_1 = S_1 - I_1 U_{t_{1} - 11}, \quad i = 2, 3, \ldots, n.$$

Because of inaccuracies in the model or because of statistical fluctuations of the data, it may happen that some $S'_i$ are negative. If this is the case, the machine will make a second choice of time $j_2$ for the first intake. In fact, the computer will systematically try all choices of day $j_1$ for the first intake and select that one as final choice which makes the negative values of the $S'_i$, if any, as large as possible, i.e. as close to zero as possible.

Having determined $I_1$ and $j_1$, the computer examines $S'_2$. If $S'_2$ is below a certain pre-assigned value which represents a reasonable estimate of expected fluctuations of the data about the trend, the computer will ignore $S'_2$ and consider that no new intake is required. If $S'_2$ exceeds the pre-assigned level of significance, a second intake is computed, the day $j_2$ of this intake being restricted to lie between the dates of the first and second samples. Proceeding serially, the computer estimates all the intakes required to produce the urine data according to the model. In principle, this code is essentially the same as that of LAWRENCE [1] but does not reject data points and does allow for some flexibility in choosing the times for the intakes to blood and in disregarding certain fluctuations of the data as not being significant.

To test the code, data on dogs exposed to Pu\textsuperscript{239} at Hanford Biology Laboratory have been used [4]. BAIR et al. injected three dogs with plutonium


Urinary excretion following intravenous injection of plutonium nitrate

The urinary excretion data are plotted in Fig. 1 together with a curve representing an average of the data. It is apparent that there are very wide fluctuations from day to day and that the dogs differ rather markedly so far as day-to-day excretion is concerned. Nevertheless, the code mentioned above was used to estimate the intake. In Fig. 2 the daily intakes as estimated by the code are shown in the form of a bar histogram. It is clear that, despite the erratic character of the excretion data, the code did correctly find that the intake was confined largely to the first day or two. The small intakes to blood on succeeding days are the result of unusually high fluctuations of the excretion data. Thus the code did give a qualitatively correct interpretation so far as time of intake is concerned. The estimated total intake is shown together with the injected amount, and it is evident that the estimates are within a factor of 2. In view of the erratic character of the data, this is considered to be encouraging.

BAIR et al. [4] also exposed dogs by inhalation, some to plutonium nitrate (0.14 N HNO₃) and others to Pu²³⁹ O₂. The urinary excretion data of those dogs exposed to the nitrate were analysed by the code also, and the
Computer estimates of intake to blood. Single intravenous injection cases.

Computer estimates of intake to blood. Inhalation cases.
estimated intakes to blood are shown in Fig. 3. Although the time sequence is erratic, significant intakes to blood do seem to occur over a succession of days and tend to decrease with time. Thus the qualitative aspects are as we might expect. However, the large number of days of no intake undoubtedly is an artifact produced by sporadic high excretions early in the period of observation. The estimated total intake to blood is shown also on Fig. 3 together with the difference of lung deposition and the terminal lung burden as estimated by the experimenters. Again the results generally agree within a factor of 2.

It seems clear that the present methods cannot be relied upon to give more than a very rough indication of the intake to blood. There are a number of possible improvements that suggest themselves. Some preliminary smoothing of data, perhaps by the computer, might reduce the error. However, it seems likely that marked improvements will come only with a better understanding of the metabolic model and of the probable source of the wide individual differences and day-to-day fluctuations of the excretion data. It would seem that carefully controlled experiments might help in understanding these difficulties and that even if the experiments did not enable us to overcome these difficulties, we might in this way obtain a firmer estimate of the uncertainty of our method of estimation.

ACKNOWLEDGEMENT

The author wishes to acknowledge the very kind assistance of Dr. W. J. Bair for supplying to the author detailed data on the experiment analysed here, the work of G. A. Bogar of the ORNL Mathematics Division who coded the programme for the 1604 computer, and the assistance of M. R. Ford in making a preliminary analysis of the data and in interpreting the results of the computer calculations.

REFERENCES

ESTIMATION OF BODY CONTENT FOLLOWING INHALATION OF INSOLUBLE PLUTONIUM

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Abstract — Résumé — Аннотация — Resumen

ESTIMATION OF THE BODY CONTENT FOLLOWING INHALATION OF INSOLUBLE PLUTONIUM. The problem of estimating the body content of plutonium following the inhalation of plutonium oxide is of considerable practical importance and, on the grounds of the known insolubility of plutonium oxide, measurements of plutonium in urine might be considered valueless. This paper reviews the relevant published biological data from beagle dog experiments and also reviews data from two human cases. From this review it is concluded that there is evidence for believing that the body content, following an accidental inhalation, can be estimated from the measurements of plutonium excreted in urine at times greater than about 300 d after the intake. Some possible excretion methods are discussed. Finally, there is a comment on the radiological protection aspects of insoluble plutonium in the lungs and bronchial lymph nodes and it is stressed that the particular nature of the plutonium must be taken into consideration.
1. INTRODUCTION

The importance of plutonium oxide fuels in the future United Kingdom nuclear power programme has been indicated in recent papers by McINTOSH and GRAINGER [1] and KRONBERGER [2]. As larger quantities are handled and more experimental work is carried out with plutonium oxide the risk of accidental inhalation by a worker also increases. Measurements of the excretion of plutonium in the urine and faeces of workers have been used to estimate body content in cases of known intake and similar measurements made at regular intervals have been made on samples from those continuously exposed to the risk of an intake, albeit an extremely small risk. The efficacy is now being questioned of the use of plutonium excretion measurements to estimate body content in the case of inhalation of insoluble plutonium. In this paper, some of the relevant biological data on humans and animals is discussed and it is concluded that excretion measurements following inhalation can be used to make an estimate of the body content with some degree of confidence.

The best way to estimate the amount of radionuclide in the body is by direct in vivo measurement using a whole-body counting facility. However, in the case of plutonium-239 the only radiation which can be detected outside the body are the low-energy X-rays (13.6, 17.4 and 20.5 keV). These low-energy X-rays are highly absorbed in bone (over 99% are absorbed in passing through 1 cm of bone) and hence the quantity of radiation detected outside the body will depend critically on the location of the plutonium relative to the skeleton. Consequently in vivo measurements of plutonium-239 X-rays will always be difficult to interpret in terms of body content. TAYLER and RUNDO [3] describe the progress they have made on the problem of measurement of plutonium in vivo and report that they can now detect about 0.075 µc in the chest which is about four times the ICRP [4] permissible lung burden. It can be anticipated that the limit of detection so far achieved by Taylor and Rundo will be reduced by improved instrumentation but the difficulty of interpreting the measurements will always remain so there is no alternative to the use of plutonium excretion measurements to estimate the body content.

2. SIMPLIFIED MODEL FOR METABOLISM OF INHALED PLUTONIUM

In order to concentrate attention on the important aspects of plutonium metabolism a simplified model is proposed, as shown in Fig. 1. The model shows the main pathways which may be followed by insoluble plutonium initially deposited in the alveoli of the lung. In this paper the alveolar deposition refers to that material which is deposited in the lung beyond the ciliated epithelium.
INHALATION OF INSOLUBLE PLUTONIUM

Fig. 1

Proposed model to illustrate the metabolic pathways and movement of inhaled insoluble plutonium.
The numbers given in the model are the percentages of the initial intake at 900 d after intake
in beagle dogs. Where there are two values the upper refers to inhaled plutonium oxide
retained in the alveoli and the lower refers to injected plutonium citrate.

HILDING [5] describes how the probable process of clearance from the
alveoli is by phagocytic action in which the phagocyte moves with an engulfed
particle on to the ciliary escalator and is then cleared from the lung, up the
tracheobronchial tree. Cells and particles reaching the throat are swallowed
and discharged from the body in the faeces. Other particles can be found
in the lung interstitial tissue, lymphatics and pulmonary lymph nodes,
MORROW and CASARETT [6]. Some plutonium from the lung enters the
circulatory system via the lymphatic system or by direct transfer into the
lung capillaries. Plutonium reaching the circulatory system may be de­
posited eventually in the liver, bone and other tissues and some may be ex­
creted via the urine or faeces. It is usually assumed that the plutonium in
the urine is related to the amount of soluble plutonium in the body fluids and
body organs whereas plutonium in the faeces in the first few months after inhalation is related to the amount of insoluble plutonium in the lungs. Two or three years after the intake a reasonable proportion of the plutonium in the faeces may be endogenous but there is no direct evidence for this in humans at present.

3. A REVIEW OF SOME RELEVANT BIOLOGICAL DATA FROM BEAGLE DOG EXPERIMENTS

This review is not intended to be complete and a fuller survey of the literature can be found in a recent paper by ROBERTSON and COHN [7]. The most comprehensive series of inhalation experiments with plutonium oxide so far is that carried out by BAIR and his colleagues at Hanford [8, 9, 10] and some of the results of their work are summarized in Table I. In the third and fourth columns of this Table the distribution in the important body organs and the total amount excreted is given for groups of beagle dogs sacrificed 30 d after inhalation of plutonium oxide. Although the data in these two columns were from the same experimental series, which was carried out using six different particle size distributions, the data from a group of three dogs exposed to very fine particles are given separately in column 3. The considerable movement from the lung, about 50% in 30 d, was characteristic of this very small particle size only; the lung content was much less mobile for the other five particle size distributions. In fact the metabolism of the plutonium oxide in the experiments with the other five particle size distributions was very similar and consequently the data have been combined and averaged in column 4. Column 5 shows results obtained for distribution and total excretion in two dogs sacrificed about 40 weeks after inhalation. The final column gives the average values of distribution and excretion for five dogs sacrificed 900 d after exposure. In Fig. 2 the values for retention in lung, and bronchial lymph nodes together with total excretion, as given in columns 4, 5 and 6 of Table I are plotted against time of sacrifice after exposure. Although the data for very fine particles, given in column 3, are of extreme interest, these cannot be used because there are no equivalent data for times longer than 30 d after intake.

It should be noted that the data given in Table I and plotted in Fig. 2 represent a considerable condensation of the work of Bair and his colleagues. For example, data from experiments with very different particle size distributions and total lung deposition have been merged. Again, the point at 280 d post inhalation plotted in Fig. 2 is subject to considerable uncertainty because it represents results from only two dogs. There are many other pitfalls connected with this method of interpretation of data so that any conclusion drawn must be regarded as tentative and subject to change in the light of more information.

With the above reservations in mind the following comments may be made. The lung burden as plotted in Fig. 2 falls to about half in 200 d; the further fall to a quarter of the initial alveolar deposit takes another 700 d so that a simple exponential retention equation does not apply. Most of the plutonium oxide leaving the alveoli in the early period after inhalation
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Particle size, CMD</td>
<td>PuO₂</td>
<td>PuO₂</td>
<td>PuO₂</td>
<td>PuO₂</td>
</tr>
<tr>
<td></td>
<td>μm</td>
<td>μm</td>
<td>μm</td>
<td>μm</td>
</tr>
<tr>
<td>0.12</td>
<td>0.24 to 0.6</td>
<td>0.3 to 1.6</td>
<td>0.3 to 1.6</td>
<td>0.1 to 0.5</td>
</tr>
<tr>
<td>Retained amount(4)</td>
<td>0.21</td>
<td>0.3 to 10</td>
<td>0.3 to 10</td>
<td>3.1</td>
</tr>
<tr>
<td>Number of dogs</td>
<td>3</td>
<td>15</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Time after intake</td>
<td>days</td>
<td>30</td>
<td>30</td>
<td>212</td>
</tr>
<tr>
<td>30</td>
<td>30</td>
<td>23</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Distribution(5) as % of retention(4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>50</td>
<td>88</td>
<td>38</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Bronchial lymph nodes</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Skeleton</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>0.3</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>0.6</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Other tissue</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Translocated(6)</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>24</td>
<td>2.1</td>
<td>0.3</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Excretion as % of retention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Faeces</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>54</td>
<td>6.7</td>
<td>6.7</td>
<td>6.7</td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>~0.3</td>
<td>1.4</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>37</td>
<td>4.6</td>
<td>4.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(4) The retained amount refers to the particulate material which is instantaneously deposited beyond the ciliated epithelium i.e., in the alveoli.

(5) The values given in this Table are the mean values of those given in the original papers.

(6) Translocated to other tissues excluding the bronchial lymph nodes but including the urine.

(7) These values are for the percentage of the initial retention excreted per day as measured during the 14 d before sacrifice.
Data on the retention in lung and bronchial lymph nodes and excretion by beagle dogs following inhalation of plutonium oxide. These data were taken from Table I.

appears in the faeces but some also moves into the respiratory lymph nodes as indicated in the model in Fig. 1. After 900 d, the graph shows that about 58% has been excreted in the faeces, 25% of the initial alveolar deposition is still in the lungs, 14% has moved into the bronchial lymph nodes, 4% has been excreted in the urine and the remainder has been translocated to the liver, bone and other tissues. By analogy with the dogs receiving plutonium citrate injections, STOVER et al. [11], it might be expected that some of the plutonium reaching the circulatory system would be excreted in the faeces and this could amount to as much as 10% of the initial deposition as estimated by comparison with the 4% excretion in the urine. There are, however, no separate data available for the amount of endogenous plutonium in the faeces.

Plutonium moving up out of the lungs to the throat and down into the gastro-intestinal tract must account for most of the plutonium measured in the faeces and the daily faecal excretion is many times higher than the urinary excretion in the early post-inhalation period. In fact, 10 d after inhalation, in the experiments referred to in column 4 of Table I, the daily faecal excretion is about 100 times higher than the daily urinary excretion. PARK et al. [10] measured the urinary and faecal excretion in three dogs for a 14-d period prior to sacrifice at 900 d after inhalation. In two of the dogs the percentage of the initial alveolar deposit excreted per day was roughly the same for both faeces and urine but in the third dog the faecal excretion was about eight times higher than the urinary excretion. These mean values for the percentage of the initial deposit excreted per day are given in column 6 of Table I. For comparison, similar values 900 d after injection of plutonium citrate calculated from equations given by STOVER et al. [12] are roughly 0.004%/d for both faecal and urinary excretion. Hence, 900 d after either injection or inhalation the percentage of the initial intake excreted per day in the urine is the same in these dogs. In Fig. 2 the total excretion of plutonium for the dogs injected with citrate is plotted for comparison with the inhalation cases and although the total excretion was lower during the period 500-900 d, the curves are parallel indicating that
the rates of excretion had been similar. Hence this similarity of excretion after either inhalation or injection probably applies to the period of several hundred days on either side of the nine hundredth day after intake.

In order to compare the distribution and excretion of plutonium at 900 d after inhalation of plutonium oxide or injection of plutonium citrate the appropriate values expressed as a percentage of intake have been appended to the model in Fig. 1. Where there are two values, the upper refers to the inhalation case. The most striking point about this distribution is the relationship between the total urinary excretion and the retention in the body organs. In the case of the plutonium oxide inhalation, the plutonium which is translocated from the lungs and respiratory lymph nodes appears not to go to the bone and liver as might have been expected from experiments with plutonium citrate injections but is excreted in the urine and, possibly, though not separately measured, in the faeces. Hence, the plutonium complex leaving the lungs and respiratory lymph nodes must be of such a form that it is more likely to be excreted in the urine and faeces than deposited in the bone and liver.

4. RELEVANT BIOLOGICAL DATA FROM HUMANS

There are little data in the literature relevant to the problem of assessment of body contents arising from inhalation of plutonium oxide. LANGHAM et al. [13] reported the results of measurements of plutonium concentrations in tissues obtained at autopsy from nine chronically-exposed workers at Los Alamos. Their measurements show qualitatively that the relative tissue concentrations are, in decreasing order, respiratory lymph nodes > lungs > liver > bone. Similar data from the United Kingdom, SCHOFIELD [14], were 1.5 pc/g and 0.5 pc/g in lungs and liver respectively in a worker who may have been exposed intermittently to plutonium for about 10 yr. These relative tissue concentrations are such as might have been expected from the inhalation experiments with beagle dogs.

The distribution of plutonium among the body organs of two human subjects and, for comparison, two experimental series of beagle dogs, are shown in Table II. Columns 3 and 4 show how very differently the plutonium is distributed between the body organs five months after an injection of plutonium citrate, LANGHAM et al. [13], in comparison with the case of a radiation worker who was chronically exposed to plutonium oxide and plutonium nitrate by inhalation over a period of 12 yr, LANGHAM [15]. From the routine measurements of plutonium in urine carried out during the radiation worker's career, SNYDER [16] made an estimate of body contents which was found to be in agreement with the autopsy measurements. The method of analysis used by Snyder, inevitably makes use of the empirical functions derived by LANGHAM [17] for the relationship between an injected amount of plutonium citrate and its subsequent rate of excretion in urine. The distribution of the plutonium among the body organs is very different in the two human cases shown in Table II. It appears that the rate of excretion of plutonium in the urine is not greatly influenced by the difference in distribution of plutonium in the body, otherwise Snyder's analysis would not have given such an accurate estimate. The same point has already been made
<table>
<thead>
<tr>
<th>Reference</th>
<th>Langham's (a) worker</th>
<th>Radiation (a) worker</th>
<th>Beagle dogs (c) PuCl injection</th>
<th>Beagle dogs (c) PuO₂ inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>66</td>
<td>36</td>
<td>11</td>
<td>0.4</td>
</tr>
<tr>
<td>Lungs</td>
<td>23</td>
<td>48</td>
<td>1.7</td>
<td>2.8</td>
</tr>
<tr>
<td>Respiratory lymph nodes</td>
<td>-</td>
<td>7.4</td>
<td>-</td>
<td>14.1</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.4</td>
<td>0.3</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

(a) Autopsy data obtained five months after injection of plutonium citrate.
(b) Occupationally-exposed to plutonium for 12 yr prior to a radiation accident at Los Alamos.
(c) Distribution data at death, 900 d after intake expressed as a percentage of initial intake.
with reference to the beagle dogs; the last two columns in Table II emphasize the great difference in distribution 900 d after injection of plutonium citrate or inhalation of plutonium oxide which still give approximately the same rate of excretion in the urine.

Recently data have become available in the United Kingdom from an accidental inhalation of a mixture of plutonium oxide and plutonium nitrate by a radiation worker. The retained lung content was estimated by assuming that it was 1/5th of the measured faecal excretion in the four days immediately following the accident which gave a value of 0.016 µc. Another estimate of body content was based on the measured daily rate of urinary excretion of plutonium which was measured at intervals up to 700 d following the intake. These data were interpreted by a method developed by BEACH and DOLPHIN [18] in which emphasis is placed on measurements made at long times after intake. This method, like all others of its type, is based on LANGHAM'S [17] empirical relationships. The range of values obtained for the initial intake was from 0.008 µc to 0.017 µc which is in reasonable agreement with the estimate based on the faecal excretion measurements. This indicates that the amount of plutonium in the body taken in via the lungs as a mixture of plutonium oxide and plutonium nitrate, can be estimated with some degree of confidence, from the measurements of urinary plutonium excretion.

Further interesting data from the accidental inhalation case referred to above are given in Table III. In this Table the plutonium excreted in urine and faeces at two different times after intake are given for the inhalation case together with similar values obtained from the empirical equations derived by LANGHAM [17] for plutonium citrate injections. It should be noted that the daily excretion in urine is roughly the same for both sets of data when they are expressed as a percentage of the initially retained amount. The Table also shows that the faecal excretion rate is falling off more slowly following the inhalation possibly due to the fact that some plutonium is still being cleared upwards by ciliary action from the lung to the throat and from thence into the faeces. These data again show that the rate of plutonium excretion in urine following inhalation may be related to the total body content, however distributed, by applying Langham's empirical equations.

5. DISCUSSION

From the data presented, from direct measurement in the case of the dogs and by inference in the human cases, it appears that the fraction of the plutonium in the body excreted per day in the urine is roughly the same both for injections of plutonium citrate and for inhalation of a mixture of plutonium oxide and nitrate. This similarity of excretion rates probably holds from a hundred days after intake until at least 1000 days after intake. Some tentative possible explanations may be put forward in order to account for this apparently similar excretion.

Figure 3 shows diagrammatically the location of plutonium in the body and indicates two possible excretion mechanisms. These excretion mechanisms could be used to explain the similar excretion rates for a given
DAILY EXCRETION OF PLUTONIUM IN FAECES AND URINE. EXPRESSED AS A PERCENTAGE OF THE INITIAL INJECTION OR INITIAL RETENTION*

<table>
<thead>
<tr>
<th>Days post intake</th>
<th>Measured values for an inhalation case (TAYLOR [21])</th>
<th>Calculated from LANGHAM'S [17] empirical equations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measured values</td>
<td>Calculated values</td>
</tr>
<tr>
<td></td>
<td>Urine</td>
<td>Faeces</td>
</tr>
<tr>
<td>100</td>
<td>0.006</td>
<td>0.005</td>
</tr>
<tr>
<td>500 - 700</td>
<td>0.002</td>
<td>0.004</td>
</tr>
</tbody>
</table>

* The initial retention was assumed to be one-fifth of the measured amount in the faeces excreted in the first four days after inhalation.

WHOLE BODY FLUIDS

Pu.
Colloidal or particulate
in reticulo-endothelial cells or in body cells

Pu. bound to protein
in organic bone
in bone mineral

Complexing agents such as citrate or other substances X, Y, etc.

EXCRETION IN URINE AND FAECES

By "solubilization" in a complex with citrate or substances X, Y, etc.

Or, alternatively, by a direct break through the kidney or gut wall of particulate or colloidal plutonium in cells, or attached to protein.

Fig. 3

Suggested simplified model to illustrate possible mechanisms of excretion of plutonium from the body.

amount of plutonium in the body irrespective of its location by one of the following:

(a) The 'solubilization' rate and subsequent excretion of plutonium in the urine is roughly the same for all plutonium compounds and is independent of the aggregation or particle size on entering the body.

(b) A fraction of the body content of plutonium becomes engulfed by phagocytes, and
(i) chemical action within these cells forms a compound which may be excreted in the urine rather than deposited in the bone or liver, or (ii) some phagocytes containing plutonium get into the circulatory system and may pass out through the kidney.

Some discussion of these possible explanations is required. In (a) the term 'solubilization' in the case of insoluble deposits in the lung does not mean that the plutonium leaves the lung in a complexed form such as in a citrate complex because this would result in a distribution and excretion pattern similar to that observed in the plutonium citrate injection experiments. In the case of the beagle dogs it appears that the plutonium leaving the lung and bronchial lymph nodes is more likely to be excreted in the urine and possibly the faeces than it is to be deposited in the bone or liver and reticulo endothelial system generally. It seems possible that the plutonium leaving the lungs and bronchial lymph nodes is either attached to protein molecules or in a colloidal form such that it is not likely to be deposited in the bone. It seems, therefore, that the process of a simple 'solubilization' by means of a citrate complex is not plausible.

In (b) above it is assumed that after either form of intake the same fraction of the plutonium content of the body is in phagocytic cells and a small fraction of these cells may be excreted from the body. In the case of the beagle dogs this may be true, for Table II shows that, although about half the initial inhalation of plutonium has left the body after 900 d, this might be offset by an equivalent amount of the initially injected plutonium citrate being bound tightly in the bone matrix. The remainder of the plutonium in both cases might well be mainly associated with phagocytic cells in the lung and reticulo endothelial system including some in the bone marrow. The explanation for the movement of plutonium from these cells as given in (b) (i) and (b) (ii) is very tentative. However there is now evidence that cells are excreted in the urine of normal subjects, SANDERS [19], and some of these cells could contain small colloidal particles of plutonium. This suggested excretion of particles inside phagocytic cells is in accord with the large day-to-day variations in excretion rate, which have been found to be as high as a factor of 10 above the mean in some human cases.

From the foregoing discussions it is clear that more experimental data are required, particularly with regard to identifying the chemical form and possible attachment to cellular material of the plutonium excreted in the urine and faeces. Such experiments present a real challenge in measuring extremely small amounts of plutonium.

Evidence from autopsy data is the only satisfactory way of showing that the body content after inhalation of plutonium can be related to the urinary excretion rate in the manner suggested in this paper. Every effort should be made to obtain measurements of the organ content at autopsy on the body of any worker who was exposed to a plutonium inhalation hazard and who had given fairly frequent urine samples for plutonium measurement.

6. RADIOLOGICAL PROTECTION ASPECTS

If the present concepts about the critical organs go unchanged then in the case of plutonium inhalation there is some interest in the problem of
identification of the critical organ. As mentioned previously, autopsy data from chronically-exposed workers show that the concentration in the bronchial lymph nodes is greater than that measured in other organs of the body. The ICRP [4] selected the critical organ on the grounds of maximum tissue concentration and therefore the bronchial lymph nodes should logically be the critical organ rather than the lung following inhalation of insoluble plutonium. In consequence, the present \((\text{MPC})_a\) recommended by ICRP for insoluble plutonium would have to be reduced by a factor of at least 100 on account of the small mass of the bronchial lymph nodes compared with 1000 g, the mass of the lungs. A further reduction factor might have to be introduced on account of the apparently longer half-life of the insoluble plutonium in the bronchial lymph nodes. It is probably wiser not to adopt more restrictive values for the \((\text{MPC})_a\) until more evidence has been obtained on the relative effects to the whole body of biological damage to these body organs.

Current thinking in radiological protection is giving more attention to the concept that the risk of biological damage is related to the product of dose and the number of cells irradiated. In even more sophisticated concepts of biological risk, the product of the dose and the mass of potentially divisible DNA is considered to be an important parameter. The number of cells or the amount of divisible DNA irradiated by particulate material depends critically on the particle size distribution for a given quantity of activity. Table IV shows how the number of particles and the approximate number of cells irradiated by 0.04 \(\mu\)c of plutonium-239 varies with the particle size. In calculating the values given in Table IV the range of the alpha particles was taken to be 50 \(\mu\)m and the cells were assumed to have a volume of 5000 \(\mu\)m\(^3\). The cells are not all irradiated instantaneously, for example a particle of 0.05 \(\mu\)m diam. has one disintegration in it per week on average. A few large plutonium particles lodged in the bronchial lymph nodes may not give rise to as much biological risk as the same quantity of plutonium monatomically distributed on or near cells in the bone, HERRING et al. [20]. Considerations like this make it seem reasonable to retain the lungs as the critical organ for insoluble plutonium until more biological data become available about radiation damage to lungs and bronchial lymph nodes.

7. CONCLUSIONS

From the small amount of biological data available it has been suggested that measurements of urinary plutonium might still be a useful method of making an estimate of body content at long times after intake of mixtures of plutonium oxide and plutonium nitrate by using methods based on LANGHAM'S [17] empirical relationships. For beagle dogs, it is possible to predict body contents in cases of plutonium oxide inhalations from relationships developed from experiments with plutonium citrate. By analogy with the dogs, it may be possible to estimate pure plutonium oxide body contents in humans from urinary excretion measurements with some degree of confidence. Therefore measurements at frequent intervals of urinary excretion of plutonium by workers routinely engaged in laboratories processing plutonium oxide is probably the best method of ensuring that these workers are not receiving small intakes which have escaped detection by the normal environ-
THE VARIATION WITH PARTICLE DIAMETER OF THE NUMBER OF PARTICLES AND THE NUMBER OF CELLS IRRADIATED FOR A CONSTANT ACTIVITY OF 0.04 μc OF PLUTONIUM OXIDE

<table>
<thead>
<tr>
<th>Particle diam. (μm)</th>
<th>Particles (No.)</th>
<th>Cells irradiated</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>per particle</td>
<td>total</td>
</tr>
<tr>
<td>50</td>
<td>1</td>
<td>9600</td>
<td>9600</td>
</tr>
<tr>
<td>5</td>
<td>10³</td>
<td>342</td>
<td>3.4 x 10⁵</td>
</tr>
<tr>
<td>0.5</td>
<td>10⁶</td>
<td>120</td>
<td>1.2 x 10⁸</td>
</tr>
<tr>
<td>0.05</td>
<td>10⁵</td>
<td>106</td>
<td>1.1 x 10¹¹</td>
</tr>
</tbody>
</table>

mental monitoring procedures. On the other hand, the best available method of establishing the retained lung content following a known accidental inhalation is by measurement of the total plutonium excreted in faeces during the next four days. Measurements of plutonium excreted in faeces at long times after intake are difficult to interpret in terms of body content with our present knowledge; far less data for humans have been collected on faecal excretion than for urinary excretion of plutonium. Hence on balance it is probably better to continue the measurement of plutonium excretion in urine for radiological control of those working routinely in laboratories processing plutonium oxide and only to use plutonium in faeces measurements for special investigations and in those cases of known inhalation.

From the radiological protection standpoint it has been argued that in the case of insoluble plutonium it might be better to leave the lung as the critical organ rather than change to the bronchial lymph nodes which might be considered a logical change on the present concepts. The reason for this conservatism is the fact that we do not sufficiently understand the biological risks associated with particulate material in the body.

ACKNOWLEDGEMENTS

The author wishes to acknowledge suggestions helpful or otherwise made to him by his colleagues, Drs. I. S. Eve, K. P. Duncan and S. Jackson, in the course of long conversations which were held at times when we should have been working on other problems.

REFERENCES

DISCUSSION

É. POCHIN: I would certainly agree with the view expressed both by Dr. Dolphin and by Dr. Wright Langham*, namely that one should hesitate before regarding the pulmonary lymph nodes as the critical organ for plutonium. The pulmonary lymph nodes, which weigh a total of about 20 gram in man, constitute a relatively small mass of tissue; in addition, the irradiation of lung tissue by particulate inhaled plutonium must be extremely non-homogeneous, and since one is dealing with alpha-tracks, the irradiation by cell will be even more non-homogeneous. If one compares mean irradiation of total lung cells with mean irradiation of total lymphoid cells, the irradiation of the pulmonary lymph nodes can be regarded as the non-homogeneous irradiation of about one fiftieth of the total mass of lymphoid tissue and one gets a ratio of 15:2. Dr. Langham's post-mortem data, on the other hand, give a ratio of about 15:100, comparing lung concentrations with pulmonary lymph nodes. So one must clearly be careful about making a sudden change from one critical organ to another.

* LANGHAM, W.H., "Physiological properties of plutonium and assessment of body burden in man", these Proceedings.
DETERMINATION OF PLUTONIUM BODY BURDENS FROM MEASUREMENTS OF DAILY URINE EXCRETION

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Abstract — Résumé — Аннотация — Resumen

DETERMINATION OF PLUTONIUM BODY BURDENS FROM MEASUREMENTS OF DAILY URINE EXCRETION.

The original data from 16 human experiments, as reported by Wright Langham and others, have been re-analysed using a simple compartment model. The functions obtained from this analysis, relating the body burden to the daily excretion in urine following an injection, are used in proposed mathematical models for the slow release of soluble plutonium into the blood stream from a wound site or the lungs. The results of calculations on the model for various hold-up times at the wound site or lungs are presented graphically.

The presently available data on the biological variation between men and in the day-to-day plutonium in urine excretion in an individual are analysed and discussed with special reference to the best design of a routine urine sampling programme.

DETERMINATION DE LA CHARGE CORPORELLE DE PLUTONIUM D'APRÈS LES MESURES OPÉRÉES SUR LES EXCRÉTIONS URINAIRES QUOTIDIENNES. Les auteurs ont procédé à une nouvelle analyse des données initiales tirées de 16 expériences sur des sujets humains, décrites par Wright Langham et d'autres auteurs, au moyen d'un modèle à compartiment unique. Cette analyse permet de définir les chargés corporelles en fonction de l'excrétion quotidienne dans l'urine. À la suite d'une injection, ces fonctions sont utilisées dans des modèles mathématiques proposés pour la libération lente dans le sang de plutonium soluble à partir d'une blessure ou des poumons. Les auteurs donnent une représentation graphique des résultats des calculs faits sur le modèle pour divers temps de rétention au niveau de la blessure ou des poumons.

Les poumons analysent et examinent les données dont on dispose actuellement sur les variations biologiques de la quantité de plutonium contenue dans l'urine selon les individus et, pour un même individu, en fonction du temps, en s'attachant particulièrement à établir le meilleur programme d'échantillonnage régulier de l'urine.

ОПРЕДЕЛЕНИЕ СОДЕРЖАНИЯ ПЛУТОНИЯ В ОРГАНИЗМЕ ПУТЕМ ИЗМЕРЕНИЯ СУТОЧНОГО ВЫДЕЛЕНИЯ С МОЧОЙ. В работе Р. Лангхэм сообщается, что с помощью простой модели произведен анализ данных экспериментов на 16 людях. Функции, полученные при этом анализе, устанавливают связь между содержанием изотопа в организме и суточным выделением его с мочой после инъекции и используются для предлагаемых математических моделей медленного выделения растворимого плутония в кровеносное русло из раны или легких. Представлены графически результаты расчетов на модели для различных сроков задержки изотопов в ране или легких.

Предлагается анализ и обсуждение имеющихся в настоящее время данных по биологическим и климатическим вариациям у отдельных людей и колебаний выделения плутония у одного человека в разные дни, в особенности, создание наилучшего практического плана взятия проб мочи.

DETERMINACIÓN DE LAS CARGAS CORPORALES DE PLUTÓNIO A PARTIR DE MEDICIONES DE LA EXCRECIÓN DIARIA DE ORINA. Los autores, por medio de un modelo de compartimiento simple, han vuelto a analizar los datos originales procedentes de dieciséis experimentos realizados sobre seres humanos por Wright Langham y otros. Las funciones obtenidas por este análisis, que relacionan la carga corporal con la excreción diaria en la orina después de una inyección, se utilizan en modelos matemáticos que proponen los autores para el paso lento del plutonio soluble desde una herida o desde los pulmones a la corriente sanguínea. La memoria presenta en forma de gráfico los resultados de los cálculos efectuados en el modelo para diversos tiempos de retención en la herida o en los pulmones.
1. INTRODUCTION

In the atomic energy industry a considerable amount of effort is expended in obtaining samples of urine and analysing them for plutonium. Interpretation of these measurements of plutonium in terms of body content is very difficult. LANGHAM [1] used data obtained from human experiments to derive a simple power law equation to relate urinary excretion rate to body content. Many reports have been published in the literature (LANGHAM [1], HEALY [2], SANDERS [3], LAWRENCE [4], SNYDER [5] and LISTER [6]) in which the equations derived by Langham were used to estimate body content in particular cases of plutonium contamination.

In the present paper mathematical models have been developed to represent the metabolism of plutonium and these are based on a re-assessment of the original human data from LANGHAM [1]. The models take into account the fact that plutonium may be released continuously to the rest of the body from the site of entry which may be, for example, the lungs or a wound. This idea of slow continuous release to the body was first suggested by HEALY [2] and in the present paper the original ideas have been developed and extended.

HAMMOND [7] noted that very large variations occurred in the daily urinary excretion of plutonium and new data are given on this biological variation in the present paper. These new data have been analysed by sampling and statistical techniques to determine the size and nature of the biological variation. This information has been used to determine the effect of combining two or more sequential samples in order to lower the biological uncertainty and increase the precision of the estimated value of the average excretion rate.

2. EXCRETION OF PLUTONIUM IN URINE AFTER INTRAVENOUS INJECTION

Many series of animal experiments, SCHUBERT et al. [8] BELIAYEV [9] STOVER et al. [10] and LINDENBAUM et al. [11], have been carried out in which plutonium citrate complexes were administered by injection. After a few days most of the injected plutonium was found to be located in the liver and bone. Immediately following the injection of plutonium citrate in these animal experiments the rate of excretion of plutonium in the urine was found to be high but it fell off rapidly during the first few days. This suggests that the initial excretion was probably plutonium in a citrate complex, similar to the injected material. After the first few days most of the plutonium citrate had been deposited in the bone, liver and other body organs or had become bound to protein in the blood and other body fluids and the rate of plutonium excretion in urine is reduced to a low level. The data for the rate of plutonium excretion in urine by humans following an injection of plutonium
citrate, as described by LANGHAM [1], have been re-analysed with the object of distinguishing between the initial rapid excretion rate of plutonium citrate and the much lower excretion rate of metabolized plutonium. From this analysis an equation was obtained which had two components as follows:

\[ Y_u(t) = 0.410 \exp(-0.67t) + 0.1610^{-0.68}, \]  

where \( Y_u(t) \) is the percentage of the initially injected amount excreted per day on day \( t \). This equation is plotted in Fig. 1 on a log-log graph. The first component of this equation has a half-life of one day and accounts for the rapid excretion of about 0.6% of the injected amount and is probably unmetabolized plutonium citrate. The second component is a power function with an index slightly smaller than that given by LANGHAM [1], i.e. 0.74, and this component is thought to represent metabolized plutonium excretion.

Data on the concentration of plutonium in blood following a plutonium citrate injection, LANGHAM [12], have been analysed and the following equation gave a reasonable fit to the data:

\[ B(t) = 4.3 \exp(-0.33t) + 0.105 \exp(-0.009t), \]  

where \( B(t) \) is the concentration of plutonium expressed as a percentage of the injected amount per litre of blood on day \( t \) after injection. The half-lives of the two exponential components are 2 d and 80 d. The short half-life component may be compared with the short half-life of the first component of the urinary excretion, in Eq. (1). This shows that the plutonium excretable through the kidney is initially decreasing with a half-life of one day whereas the amount of plutonium in the blood is decreasing with a two-day half-life. This suggests that plutonium in blood is quickly becoming non-excretable through the kidney which agrees with experience from animal experiments where it is known that the injected plutonium citrate complex is rapidly converted into protein-bound plutonium which cannot pass through the kidney.

3. EXCRETION AFTER DELAYED RELEASE OF PLUTONIUM TO THE BLOOD

Systemic contamination with plutonium may occur by retention in the lung following inhalation, HEAL Y [2], by direct absorption at the site of a wound, HAMMOND [7], burn, LISTER [6], or other skin trauma, WILSON and SILKER [13]. The rate of movement of plutonium from the site of entry depends on both the physico-chemical form of the plutonium and the physiological conditions at the site. For example, delayed movement from a wound site is indicated in data reported by HAMMOND [7] in which the excision of a sliver containing plutonium from the wound site some months after a puncture wound was accompanied by a significant drop in the urinary plutonium excretion. HEAL Y [2] also reported data which indicated a delayed transfer of plutonium to the body from the lung. A full description of the mechanism of delayed transfer is not needed for the purposes of this paper; it is suffi-
Log-log plot of \( Y_u(t) = 0.41 \exp(-0.67t) + 0.16t^{-0.68} \), where \( Y_u(t) \) is the percentage of the initially injected amount excreted per day, on day \( t \). This equation was found to give the best fit to the human data, LANGHAM [1]. The two components of the equation are illustrated by broken lines.

It is convenient to assume that the radionuclide enters the blood according to some putative monotonic decreasing function of time \( I(t) \). If an amount \( q \) is initially retained at the site of entry then the amount released to the blood at a subsequent time \( t \) is \( q \, I(t) \). The daily excretion of plutonium \( E_u(t) \) is then

\[
E_u(t) = q \int_0^t I(\tau) \, Y_u(t-\tau) \, d\tau
\]

where \( Y_u(t) \) is the power function component of Eq. (1).

Various particular functions may be substituted for the completely general monotonic decreasing function \( I(t) \). The two elementary functions that have been considered in this paper are: a simple negative exponential function and a power function of negative index. The exponential function represents the simplest type of release mechanism in which the rate of release is a constant fraction of the quantity present. This function may be thought to represent an over-simplification of the actual release mechanisms and so the power function was also used. The power function may be considered to represent approximately a set of exponential functions of both decreasing fraction and decreasing release rate. However, it should be emphasized
Log-log plot of the predicted daily urinary excretion rate of plutonium assuming an exponential release of plutonium to the rest of the body from the site of entry. Curves are given for half-lives of the exponential release function ranging from 1 to 1000 d.

That the two functions were chosen for mathematical convenience rather than with any special knowledge of the biological mechanism of release.

The function given above, Eq. (3), was solved for the simple single exponential function with half-lives of the transfer mechanism of 1, 10, 25, 50, 80, 120, 365, 500 and 1000 d. The results obtained are shown graphed on a log-log scale in Fig. 2. For comparison, the power function component of Eq. (1) is shown drawn with a broken line in this figure. The values of the function (3) were also obtained when the transfer from the site of entry was assumed to be a power function. The chosen representative values of the index were:

-2.000, -1.231, -1.177, -1.151, -1.137, -1.126, -1.105 and -1.091,

The choice being based somewhat arbitrarily on the criterion that half the retained amount would be transferred to the blood in times similar to those
TABLE I

TIME TAKEN TO TRANSFER VARIOUS AMOUNTS OF THE INITIALLY RETAINED PLUTONIUM FROM THE SITE OF ENTRY TO THE BLOOD FOR SEVERAL VALUES OF THE INDEX OF THE POWER FUNCTION

<table>
<thead>
<tr>
<th>Index (b)</th>
<th>Time taken to transfer</th>
<th>Transferred after 50 yr (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>half (d)</td>
<td>three quarters (d)</td>
</tr>
<tr>
<td>2.000</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1.231</td>
<td>10</td>
<td>202</td>
</tr>
<tr>
<td>1.177</td>
<td>25</td>
<td>1260</td>
</tr>
<tr>
<td>1.151</td>
<td>50</td>
<td>5000</td>
</tr>
<tr>
<td>1.137</td>
<td>80</td>
<td>12 400</td>
</tr>
<tr>
<td>1.126</td>
<td>120</td>
<td>30 000</td>
</tr>
<tr>
<td>1.105</td>
<td>365</td>
<td>271 000</td>
</tr>
<tr>
<td>1.100</td>
<td>500</td>
<td>524 300</td>
</tr>
<tr>
<td>1.091</td>
<td>1 000</td>
<td>2 065 000</td>
</tr>
</tbody>
</table>

chosen for the exponential function. In order to illustrate the power function release in more detail Table I has been compiled. This Table shows that although the half period for release has been chosen to be the same for both exponential and power functions the release rate becomes much slower for the power function at times longer than the half period. This is illustrated by the values in column 3 which give the time required to release to the blood three-quarters of the initial intake. The last column shows the amount released during 50 yr. For example, the power function of index -1.177 is chosen to give a release to the blood of half the initial intake in 25 d but the time taken to release three-quarters of the initial intake is 1260 d and even after 50 yr 16% of the original intake is still present at or near the site of entry. Hence, a practical consequence of the use of the power function to represent a release to the blood is that some of the intake is permanently retained at or near the site of entry into the body.

Figure 3 shows the curves obtained by integration of Eq. (3) with the general release function represented by a power function with the indices as given in Table I. In these calculations the total amount retained at the site of entry, all of which will be theoretically allowed to eventually enter the blood, is 0.04 μc. This is the ICRP [14] maximum permissible body burden of plutonium referred to bone as the critical organ.

The following general points may be made about the two families of curves given in Figs. 2 and 3:

(a) The predicted initial excretion rate for all the curves in Fig. 2 is less
than would be expected on the basis of the excretion equation given by LANGHAM [1].

(b) All the curves in Fig. 2 predict that the urine excretion rate will reach a maximum value at some time after intake which depends on the assumed half-life for the exponential release. The longer the half-life the greater the time after intake that the peak is reached.

(c) All the curves in Fig. 2 converge on the power function component of Eq. (1) at long times after intake.

(d) The curves in Fig. 3 predict a lower initial excretion rate than the power function component of Eq. (1) but in contrast to the curves in Fig. 2 they reach a peak within one or two days of the intake.

(e) The curves in Fig. 2 are all significantly non-linear on the log-log plot throughout the period of 10 000 d whilst the curves in Fig. 3 rapidly become linear in appearance. From about 10 d after the initial intake the apparent indices of the excretion curves in Fig. 3 range from about 0.59 to 0.65.

The curves in Figs. 2 and 3 have no real foundation because the mechanisms of transfer from the site of entry are not understood. However, it is certain that delayed release does occur in some cases as shown by the data of HEALY [2] and HAMMOND [7], previously referred to. If a monotonically decreasing release function is applicable, and this might be con-
sidered the most readily acceptable of all the assumptions made in these calculations, then some general conclusions can be inferred from the shape of the curves. The most important general conclusion is that the initial rate of excretion of plutonium in urine is expected to be more dependent on the rate of release from the site of entry than on the amount of plutonium at the site. Hence measurements of plutonium in urine made shortly after intake are probably less reliable in terms of estimating the body content than measurements made at long intervals after intake. Unfortunately the original data from the human experiments for excretion of plutonium following a plutonium citrate injection is least reliable at periods beyond one year.

4. SOURCES OF UNCERTAINTY IN THE MEASUREMENT OF THE URINARY EXCRETION RATE OF PLUTONIUM

One of the principle objections to the interpretation of a single measurement of urinary excretion of plutonium is the existence of a typically large uncertainty. There are four important sources of uncertainty in any measurement which are as follows:

(a) the biological variation in the daily amount of plutonium excreted;
(b) the determination of a 24-h sample of urine;
(c) the quantitative chemical analysis of urine for small amounts of metabolized plutonium; and
(d) the background contamination level.

By far the largest of these uncertainties is the biological variation and, for the purposes of this paper, the others may be neglected by comparison. The reasons for this biological variation, which is quite frequently of the order of a factor of 10 or more, are not known. However, HAMMOND [7] suggested that they might be due to temporary kidney damage because he found a large variation of the order of 200 in the excretion rate in an individual six weeks after intake was accompanied by albumin in the urine. To obtain some information about the type and size of this biological variation a study was made of the urinary excretion rate in a few workers who had been involved in the processing of plutonium at some previous time. An almost continuous urine collection for the normal working week was instituted for these men. Those workers whose urine record showed no statistically significant curvilinear trend in urine excretion during the period of the investigation were selected for inclusion in this study.

Frequency histograms of the data were formed for each of the selected individuals. Typically all these were found to be positively skew and of the log normal type. The raw data were then subjected to a logarithmic transformation, normalized to a transformed mean excretion rate of 1 pc/d and then amalgamated into a single histogram. Other such histograms were developed by adding the raw data sequentially in pairs, trios and tetrads for each individual. Hence four histograms were obtained; the first is shown in Fig. 4. A log normal curve was fitted to the raw data shown in Fig. 4 and this shows that the histogram departs slightly from the curve. This slight departure was due to the presence of more extremely large values than would be expected in this type of distribution. It was felt that this excess of large values indicates the presence of significant contamination in a very small
Fig. 4

Histogram of 357 measurements of plutonium in urine samples normalized for each individual to 1 pc per sample and amalgamated. The full line represents a log-normal curve found to give the best fit to the data.

Percentage of urine samples. Following a discussion of CRAMER's [15], it is possible to suppose the size of a daily excretion of plutonium to be the net result of a number of small independent influences acting in an ordered sequence upon an initial amount. If the influence of any one factor is proportional to the instantaneous amount of the plutonium the distribution of the eventually excreted amount will be log normal. However, an exact biological interpretation of this distribution is not possible at present and is not necessary for the purposes of this paper. There was some evidence, not statistically significant in the sample under investigation in the current work, which suggests that the individual raw data could be regarded as a stationary Markov process with an error-component. However, if this autocorrelation is ignored the exact frequency distributions formed by sequentially adding urine samples can be theoretically calculated. Unfortunately, in practice, the definite integrals formed proved intractable to the current writers. Nevertheless, the central limit theorem suggests that continued amalgamation of this sort would result in frequency distributions that were increasingly nearer to the Gaussian form. The four frequency distributions found were plotted cumulatively on log-probability graph paper and the extent of the confidence limits determined for the levels of probabilities of 90%, 95% and 99%. These confidence limits can be expressed as a factor by which the median value must be multiplied to get the upper confidence limit and divided to get the lower confidence limit. In Fig. 5 this factor was plotted against the number of raw data added sequentially for the three different confidence limits. The shape of these curves may serve as a guide to the advantages of amalgamating sequential urinary excretion data in order to minimize the biological error associated with a single urine sample. It can
Fig. 5
Plot of the confidence factor against the number of amalgamated samples for three different confidence limits. For example, in twenty single urine samples the curve for 95% confidence indicates that on the average a measurement of plutonium in one sample would be a factor of six different from the median measured value of plutonium in a large number of samples.
be seen that, for the reasonable assurance of 95% confidence, there is a decrease of just over one in this factor if two consecutive samples are collected, whilst for the far more restricted case of 99% confidence there is still a great advantage in the collection of three or more consecutive samples before analysing a conveniently sized aliquot for plutonium content. Furthermore, the curves in Fig. 5 suggest that 10 or more sequential samples might have to be added together before the 90% confidence factor approaches the value 2.

5. PROGRAMMES FOR SAMPLING THE DAILY EXCRETION OF PLUTONIUM IN URINE

Following the discussions and results obtained in the previous sections of this paper some consideration is now given to sampling programmes for determining the urinary excretion rate of plutonium. There are clearly two situations, each of which requires a sampling programme. The first is that following a known accidental intake, and the second is that where workers are routinely engaged in laboratories and factories processing plutonium. These situations will be considered separately.

(a) Sampling following a known accidental intake

The curves shown in Figs. 2 and 3 indicate that the rate of urinary excretion of plutonium varies rapidly during the first few weeks after intake. The manner in which the urinary excretion varies will depend on the mode of entry of the plutonium into the body and the mechanisms by which it is released into the rest of the body. In order to establish this initial rapidly varying excretion pattern the most comprehensive sampling programme should be instituted immediately the accidental intake is recognized. It should be noted, however, that whilst the data on the urinary excretion of plutonium obtained during this initial period will not necessarily be of great value in ultimately assessing the body content, it might give valuable information about the rate of transfer of the plutonium from the site of entry to the rest of the body. The body content may be more reliably estimated from excretion measurements made at longer times after intake. However, it has been emphasized in section 4 that a large biological uncertainty is associated with each single measurement of plutonium excreted in 24 h and therefore to lessen the effect of this uncertainty some sequential collection of urine over several days is essential.

(b) Sampling of workers routinely engaged in plutonium processing

Normally measurements of plutonium in the air and on the surfaces in the working areas of laboratories and factories processing plutonium should give early warning of any release of plutonium into the environment. Hence, sampling of the urine of workers engaged in routine processing is carried out to ensure that no intakes of plutonium have occurred which were undetected by the environmental sampling. In fact, if plutonium is unex-
pectedly found in the urine of the workers it is an indication that the environmental monitoring devices have not been adequate. The object of a sampling programme is, therefore, to ascertain whether the urinary excretion rate of plutonium by a worker is above or below a certain value known here as the warning level. Further discussion of the value chosen as the warning level is not essential in this paper and, indeed, is outside its scope. It is only necessary to state that if the urinary excretion rate is above this level some action must be taken by the management. It is clear from the discussion in section 4 that the degree of biological variation is such that a single measurement could, by chance, be spuriously above the warning level whilst the actual median excretion at that time was below the warning level. This could lead to the unnecessary instigation of special procedures, such as taking the worker away from contact with plutonium and carrying out a programme of intensive sampling for plutonium in his urine. Such procedures carried out unnecessarily could be both uneconomic for management and unsatisfactory for the worker. In order to decrease the possibility of a single measurement being spuriously above the warning level every effort should be made to obtain the best estimate of the plutonium excretion rate. This can be done by collecting sequential samples of urine over a week or even longer periods. Thus a sampling programme based on the collection of a single 24-h urinary excretion at, say, monthly intervals, might be less satisfactory for both management and men than a programme based on less frequent collection of a much larger quantity of urine.

6. CONCLUSIONS

The mathematical models developed in sections 2 and 3 of this paper culminating in the theoretically idealized functions for the urinary excretion rate of plutonium, as shown in Figs. 2 and 3, have the following limitations:

(a) the models are based, as indeed all similar work must be based, upon the biological data from the small series of human experiments reported by LANGHAM [1]; and

(b) the aptness of the models is limited by the assumption that the movement of the plutonium from the site of entry to the rest of the body can be represented by a monotonic decreasing function of time.

The first limitation will not be overcome until more human data become available from planned experiments or from relating measurements of plutonium content in body organs obtained at autopsy with plutonium in urine measurements made during life. The second limitation will gradually be overcome as a greater understanding is gained of the mechanisms of plutonium transport from the site of entry to the rest of the body. In the meantime, the two monotonically decreasing functions of time chosen to represent release from the site of entry to the rest of the body may serve to indicate how the expected urinary excretion rate may differ from that obtained in the human experiments where a solution of plutonium in a citrate complex was injected.

In section 4, the biological variation in the daily plutonium excretion was analysed and its influence on the planning of a programme of urine sampling was discussed in section 5. No attempt has been made to explain
this biological variation but obviously more work is required on the mechanisms of plutonium excretion which might throw some light on this problem.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the helpful discussions they have held on the subject matter of this paper with their colleagues Drs. Duncan, Eve and Jackson. They also wish to thank Mr. H. Howells and Mr. J. Arkley who facilitated access to some of the original data used in the analysis of the biological variations.

REFERENCES


DISCUSSION

J. RUNDO: There is increasing evidence for very long retention times of various materials, including plutonium and other heavy elements, in lung. This could lead to an extremely high radiation dose to lung before the plutonium leaves it. The dose would perhaps be higher than that delivered to bone, since the lung maximum permissible level is only 16 nc compared with 40 nc for bone.

G. W. DOLPHIN: I think one should always bear in mind, in this work, that one is protecting people from biological damage, not from dose, and so far our data show that the bone is the critical organ - the organ in which the osteosarcomas occur.
THE INTERPRETATION OF DATA RELATING TO PLUTONIUM CONTAMINATION. The authors present data for plutonium levels measured in various samples after heavy contamination through the skin and report on the progress of elimination during the year following contamination. They also present data resulting from measurements after very slight contamination, and attempt to interpret them.

INTERPRÉTATION DE RÉSULTATS OBTENUS APRÈS CONTAMINATION PAR LE PLUTONIUM. Présentation des résultats de dosages du plutonium sur divers prélèvements à la suite d'une contamination importante par voie transcutanée. Évolution de l'élimination pendant la première année qui a suivi cette contamination. Présentation des résultats et essai d'interprétation à la suite d'une contamination très légère.

ИНТЕРПРЕТАЦИЯ РЕЗУЛЬТАТОВ, ПОЛУЧЕННЫХ ПОСЛЕ ЗАРАЖЕНИЯ ПЛУТОНИЕМ. Излагаются результаты измерения плутония в различных образцах после тяжелого заражения через кожу. Списывается эволюция выделения в течение первого года после заражения.

INTERPRETACIÓN DE RESULTADOS OBTENIDOS A RAÍZ DE UNA CONTAMINACIÓN POR PLUTONIO. El autor expone los resultados de la determinación del plutonio en diversas muestras tomadas después de una contaminación importante por vía transcutánea. Estudia la evolución de la eliminación durante el primer año siguiente a dicha contaminación. Expose los resultados consecutivos a una contaminación muy ligera y procura interpretarlos.

L'exposé des deux cas de contamination par le plutonium que nous présentons a un double but: a) montrer l'importance de l'aide apportée par le laboratoire dans le diagnostic et le traitement, b) insister sur les grandes difficultés d'interprétation des résultats.

I. RÉSULTATS DE LABORATOIRE POUR UN CAS DE CONTAMINATION DE LA MAIN PAR LE PLUTONIUM

Dans une première partie, nous présentons l'ensemble des résultats de laboratoire obtenus en un an et demi sur un cas de contamination accidentelle par le plutonium. Les premiers résultats ont été présentés à Vienne en 1963, à la réunion sur le diagnostic et le traitement consécutifs aux contaminations radioactives [1].

Il s'agit d'une blessure à la main occasionnée par des éclats de verre et des débris de gants contaminés avec du nitrate de plutonium 239 hexavalent en solution à pH 1.

Le Laboratoire de radiotoxicologie est intervenu dans les tâches suivantes: mesurer l'activité présente dans la main et dans les divers prélèvements biologiques, fournir des indications sur l'évolution de la radio-
activité au cours du temps et en fonction du traitement, établir le bilan de la contamination.

A. Mesures de la main

Elles ont été faites au moyen d'un détecteur de rayonnement X à cristal mince d'iode de sodium, associé à un ensemble de comptage à deux bandes, l'un étant centré sur la bande de 17 keV du plutonium, l'autre sur une bande d'énergie supérieure.

Les premières estimations ont fixé l'ordre de grandeur de la contamination externe et interne de la main à 60 μc environ. Une première décontamination abaisse le niveau à 15 μc.

L'emploi du détecteur X, collimaté, a permis de préciser les zones de contamination externe et interne de la main. Après une intervention chirurgicale, qui a nettoyé correctement deux zones actives, la contamination résiduelle de la main est encore de 5 μc.

Une nouvelle étude, par scanning a été effectuée pour localiser le plus parfaitement possible l'activité et préparer au mieux une nouvelle intervention chirurgicale. Cette nouvelle intervention a permis de ramener la contamination à 2 μc environ.

Après cette phase aiguë, les mesures ont été effectuées mensuellement de façon systématique pour contrôler l'évolution du dépôt de la contamination au niveau de la main. La figure 1 montre la variation de l'activité en fonction du temps; la courbe en pointillé indique le taux de comptage et la courbe pleine l'estimation en μc.

Théoriquement, ces deux courbes devraient être dans le même rapport sur toute leur longueur. Pratiquement, les difficultés d'étalonnage sont telles que l'on peut difficilement appliquer le même facteur a posteriori sur toutes les valeurs de comptage, et nous sommes amenés à présenter ces deux courbes sans pouvoir affirmer laquelle représente le plus exactement l'évolution de la contamination au niveau de la main.
De nombreux facteurs interviennent pour rendre cette mesure délicate: a) la localisation exacte de l'agent contaminant est inconnue, et il est par suite assez difficile de choisir un étalon ayant une géométrie et une absorption comparables; b) il a pu se produire une certaine migration de l'agent contaminant dans les tissus, et leur reconstitution après l'intervention chirurgicale a certainement modifié les conditions d'absorption du rayonnement; c) l'étalon choisi est une source de plutonium liquide dans un tube bouché en lusteroid de 12 mm de diamètre. Il a évolué avec le temps car le liquide s'est évaporé, d) pour la mesure même, il faut choisir un compromis sur la distance: avec l'éloignement, le nombre de coups comptés diminue, et l'influence du mouvement propre peut devenir prépondérante; par contre, le rapprochement de la main, qui améliore le rapport taux de comptage sur mouvement propre, pose de façon aiguë à la fois le choix d'un étalon convenable et le problème exact de la distance entre le détecteur et la main; e) l'évolution possible de l'appareil de mesure.

L'ensemble de ces difficultés permet de comprendre l'imprécision, non seulement de la détermination de la quantité réelle présente à un moment donné, mais également celle de l'évolution, bien que les courbes paraissent satisfaisantes à première vue.

B. Mesures dans le sang

Les activités trouvées dans le sang au départ, ont permis de faire un certain nombre de contrôles: a) l'activité est pratiquement en totalité dans le sérum, et les hématies lavées avec du sérum physiologique ne montrent pas d'activité notable, b) des électrophorèses de sérum sur papier ont montré la répartition de l'activité indiquée au tableau 1. Il y a donc bien une fixation préférentielle au niveau des globulines, mais il n'est pas possible d'affirmer que la différence entre les deux sérums soit vraiment représentative.

La figure 2 montre l'évolution de l'activité dans 3 l de sérum durant le premier mois. L'action du DTPA a été très effective, puisque la concentration du Pu dans le sang a diminué d'un facteur 10 environ après la première série de traitement.

D'autres dosages en série ont également permis de juger l'action du DTPA au cours du temps et d'orienter le traitement. La figure 3 représente deux courbes faites trois mois et quatre mois après l'accident, en utilisant deux rythmes d'administration du DTPA: tous les deux et tous les quatre jours.

Il semble d'une part que le pourcentage de diminution d'activité du sérum dans les heures qui suivent la perfusion, soit d'autant plus faible qu'il y a plus de temps passé depuis la contamination. Ceci est confirmé par les dernières mesures effectuées après dix-huit mois, dans lesquelles la diminution trois heures après administration de DTPA est faible.

D'autre part, le pourcentage de diminution sera d'autant plus grand qu'il y a eu un intervalle de temps plus grand entre les injections de DTPA. Dans une autre série de DTPA (non indiquée sur la figure 3) effectuée un mois après l'accident avec injection journalière, l'activité sanguine est restée sensiblement constante au niveau inférieur obtenu après la première injection.
TABLEAU I
RÉPARTITION DE L'ACTIVITÉ α

<table>
<thead>
<tr>
<th>Temps depuis l'accident</th>
<th>Albumines</th>
<th>Gloubines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>α1</td>
<td>α2</td>
</tr>
<tr>
<td>1 j</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>2 j</td>
<td>12</td>
<td>9</td>
</tr>
</tbody>
</table>

Figure 2
Evolution de l'activité dans 3 l de serum durant le premier mois.

G. Mesures dans l'os

Sur un fragment de trois grammes de crête iliaque prélevé trois mois après l'accident, des dosages de plutonium et de calcium ont été effectués. Pour une teneur totale de 1000 g de calcium dans l'individu, la quantité de plutonium présente dans le squelette serait de 3,2 μc.
INTERPRÉTATION DE RÉSULTATS

D. Mesures dans l'urine

Les mesures sont faites aussi souvent que possible depuis l'origine. Bien qu'il ne soit pas dans notre intention de décrire les essais effectués pour trouver le rythme d'injections et les doses de DTPA qui semblaient les mieux indiquées, il faut remarquer que les mesures sur l'urine ont permis de contrôler l'efficacité du traitement. Après deux séries de quatre injections de 1 g de DTPA et une période transitoire de recherche, un traitement systématique au rythme d'une injection hebdomadaire à 0.25 g a paru satisfaisant.

La figure 4 montre l'élimination journalière au cours du premier mois. Dans la figure 5, chaque point de la courbe représente l'excrétion cumulée à la suite de 4 ou 5 injections, ce qui correspond à peu près à des intervalles d'un mois. Sur le même graphique de la figure 5, l'activité du sérum a également été portée. On constate que depuis plus d'un an il existe un certain parallélisme entre la concentration dans le sang et l'élimination sous l'influence du traitement.

Après une injection unique, l'action du DTPA est importante pendant 48 h (figure 6), mais il semble qu'elle subsiste sous une forme plus discrète pendant longtemps.

Etant donné la fréquence d'administration du DTPA, nous ne disposons que de très peu de valeurs représentant l'excrétion naturelle du plutonium. Trois valeurs seulement ont été obtenues avant tout traitement, soit 3600 pc le jour de l'accident, 4000 le lendemain et 2200 le deuxième jour. De plus, par la suite, nous avons quelques valeurs obtenues hors des périodes d'injection, mais elles sont assez mal groupées, comme le montre le tableau II.
Élimination journalière dans les urines.

Il semble peu probable qu'elles correspondent à l'excrétion réelle en période de repos.
INTERPRÉTATION DE RÉSULTATS

Figure 6
Action d'une injection de DTPA sur l'excrétion urinaire.

TABLEAU II

VALEURS REPRÉSENTANT L'EXCRÉTION NATURELLE DU PLUTONIUM

<table>
<thead>
<tr>
<th>Nombre de jours depuis l'accident</th>
<th>Nombre de jours depuis la dernière injection de DTPA</th>
<th>Nombre de mesures</th>
<th>Valeurs extrêmes (pc/24 h)</th>
<th>Moyenne (pc/24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>environ 30</td>
<td>7</td>
<td>350-1170</td>
<td>500</td>
</tr>
<tr>
<td>210</td>
<td>de 12 à 40</td>
<td>4</td>
<td>430-660</td>
<td>550</td>
</tr>
<tr>
<td>420</td>
<td>30</td>
<td>2</td>
<td>135-205</td>
<td>170</td>
</tr>
</tbody>
</table>

E. Mesures sur les matières fécales

Durant le premier mois, les prélèvements ont été recueillis de façon systématique et ont donné les résultats représentés sur la figure 7. Là encore, l'action du DTPA a été très manifeste lors des premiers traitements. Le maximum d'excrétion a, en général, été constaté entre le troisième et le cinquième jour suivant l'injection. Une expérience de marquage a été faite en donnant un colorant par voie buccale au moment de l'injection. Le maximum d'intensité de coloration correspond au maximum d'élimination de radioactivité par les selles.
Figure 7
Mesures sur les matières fécales.

Par la suite, les prélèvements de matières fécales n'ont pas été recueillis de façon aussi systématique que les prélèvements d'urine, et les valeurs d'élimination cumulées après le premier mois sont plutôt estimées que mesurées réellement.

F. Bilan

Le cas présenté est assez complexe: il s'agit d'une contamination locale qui produit secondairement une contamination interne de l'organisme. Bien que des centaines d'examens aient été effectués, la mesure de la contamination réelle est très difficile et incertaine.

Les mesures locales sur la main (fig. 1) conduisent à des interprétations différentes pour la période d'élimination et pour les quantités présentes selon la façon d'exploiter les résultats. L'erreur peut atteindre 50% et il est impossible de dire si la quantité éliminée par le traitement depuis le soixantième jour est égale ou supérieure à la quantité qui a disparu de la main contaminée.

La mesure sur l'os est certainement excellente au point de vue technique, mais son interprétation est également très sujette à caution, surtout du fait des hétérogénéités de concentration non seulement dans les différents os, mais à l'intérieur d'un même os.

A partir des mesures effectuées sur le sang avant essai de décontamination, on peut tenter une estimation en admettant que la contamination
INTERPRÉTATION DE RÉSULTATS

Le membre le plus important a eu lieu au moment même de l'accident. Les données de la littérature montrent que l'on trouve dans le sang après 24 h de 5 à 25% de la quantité injectée. Ceci nous conduirait à estimer la contamination initiale entre 5 et 1 µc. Cinq mois après injection intraveineuse, LANGHAM [2] retrouve environ 0,2% de la dose injectée dans le sang. Si on admet que ce facteur est valable malgré les traitements et que la différence de voie d'injection, l'activité initiale déposée dans l'organisme était égale à 3,5 µc; il faut alors ajouter les quantités excrétées sous l'influence du traitement soit environ 2 µc, dont on retranche 0,5 à 1 µc qui ont quitté la main. La contamination initiale réelle aurait été 4,5 à 5 µc.

Pour les urines des premier et deuxième jours après la contamination, la courbe de Langham conduirait à une contamination de l'ordre du microcurie. Après 540 j, en estimant l'élimination de base journalière à 200 µc, la quantité initiale aurait été de 10 µc. Le DTPA s'est montré très efficace puisque l'élimination urinaire initiale de plutonium a été multipliée par 100 (fig. 4). Si l'on admet que l'action du DTPA, lors de la première série d'injections, a permis d'éliminer de 10 à 40% du plutonium, la quantité présente dans l'organisme aurait été comprise entre 12 et 3 µc. Quant à son action dans la phase chronique, on peut admettre que la période générale d'excrétion est environ 10 fois plus rapide qu'en l'absence de traitement.

Les analyses de matières fécales ont permis de mettre en évidence une action marquée du DTPA au cours du premier traitement, puisque l'élimination fécale initiale de plutonium a atteint 25% de l'excrétion urinaire. Elle correspond sans doute à l'excrétion par le foie. Il est à remarquer par rapport aux courbes de Langham, que l'excrétion fécale a été toujours inférieure à l'excrétion urinaire.

La figure 8 montre l'excrétion cumulée de l'activité dans les dix-huit mois qui ont suivi la contamination. On constate que le tiers de l'activité excrétée jusqu'à ce jour l'a été au cours du premier traitement par le DTPA.
En conclusion, on constate que l'interprétation des résultats est très délicate, et selon les bases auxquelles on se réfère l'incertitude de la quantité de plutonium présente peut atteindre un facteur 10.

II. CONTAMINATION PAR DES POUSSIÈRES DE PLUTONIUM OU D'OXYDE DE PLUTONIUM

Le deuxième cas présenté concerne une contamination par des poussières de plutonium ou d'oxyde de plutonium dispersées à la suite d'une explosion chimique dans une boîte à gant. Il y avait eu contamination externe et une légère activité avait été mise en évidence sur des prélèvements nasaux.

Les résultats d'analyse concernant les urines, les matières fécales et le sang sont présentés dans le tableau III.

On voit que si les premiers résultats urinaires et sanguins étaient négatifs, les suivants obtenus à partir des matières fécales posaient un problème puisqu'elles contenaient environ 140 000 pc de plutonium.

En effet, dans l'hypothèse d'une contamination digestive pure, la CIPR [3] admet un passage dans le sang de $3 \times 10^{-5}$. Dans le cas présent, ce facteur conduit à une contamination interne pratiquement nulle de 5 pc.

Au contraire, dans l'hypothèse d'une contamination respiratoire, la quantité excrétée par les matières fécales représenterait 62% de la quantité inhalée, et la fraction restant dans les poumons serait de 12%. Dans ce cas 27 000 pc resteraient fixés dans les poumons, avec possibilité de passage ultérieur dans les fluides de l'organisme.

C'est pourquoi, de nouveaux examens ont été entrepris pour avoir des informations complémentaires. Il s'est avéré que trois semaines après la contamination une légère excrétion fécale de plutonium subsistait, et qu'une injection de DTPA au 14ème jour faisait apparaître du plutonium dans l'urine.

Interprétation des résultats

1. Contamination pulmonaire

Nous avons interprété les résultats en admettant, d'après les valeurs indiquées par BAIR [4], que la diminution de l'activité au niveau pulmonaire se produit avec une période d'un an. Les calculs effectués à partir de l'élimination fécale chronique (moyenne 0.8 pc/j) conduisent dans cette hypothèse à une charge pulmonaire de 400 pc.

2. Contamination interne autre que pulmonaire

La charge systémique peut être calculée à partir des résultats urinaires. L'ensemble de ces résultats est négatif en l'absence d'injection de DTPA, à l'exception d'un prélèvement effectué le lendemain de l'accident. On a estimé que ce prélèvement correspond en volume à la moitié de l'émission journalière normale. Ainsi la quantité réellement éliminée aurait été de 0,2 picocurie environ dans la journée. La courbe de LANGHAM [5] in-
TABLEAU III

ANALYSES DES URINES, DES MATIÈRES FÉCALES ET DU SANG

<table>
<thead>
<tr>
<th>Jour</th>
<th>Urines (pc)</th>
<th>Matières fécales (pc)</th>
<th>Sang</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Résultats</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td>N. S.</td>
</tr>
<tr>
<td>1</td>
<td>N. S *</td>
<td></td>
<td>N. S.</td>
</tr>
<tr>
<td></td>
<td>N. S</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>N. S</td>
<td>32 600</td>
<td>N. S.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>86 000</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>19 700</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>N. S</td>
<td>240</td>
<td>N. S.</td>
</tr>
<tr>
<td>4</td>
<td>N. S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>N. S</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>1,3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2,2</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>3,4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>14 (DTPA)</td>
<td>2</td>
<td>1,5</td>
<td></td>
</tr>
<tr>
<td>15 et 16</td>
<td>1,3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td></td>
<td>1,2</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td></td>
<td>0,8</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td></td>
<td>0,35</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td></td>
<td>0,8</td>
<td></td>
</tr>
</tbody>
</table>

* N. S. = résultat non significatif.
dique une excrétion urinaire de 0,4% le premier jour, après contamination par injection. La quantité fixée par l'organisme, en dehors du poumon serait ainsi de l'ordre de 50 pc. Ce résultat est peut-être fortuit, mais l'excrétion de plutonium après injection de DTPA s'est montrée tout à fait positive. En admettant avec NORWOOD [6] que le DTPA augmente l'excrétion urinaire d'un facteur 50 à 100, et avec LANGHAM [5] que l'excrétion normale le quatorzième jour est de l'ordre de 0,03%, la quantité fixée dans l'organisme serait de 130 à 65 pc.

3. Contamination globale

La contamination globale serait donc de l'ordre de 500 pc, soit 400 pc au niveau pulmonaire et 100 dans les autres parties du corps.

En conclusion, nous avons admis que le mode de contamination était mixte, avec prédominance digestive très marquée.

III. CONCLUSION

Nous avons essayé de montrer les difficultés rencontrées dans l'interprétation des résultats de laboratoire en prenant deux cas réels en exemple. Bien souvent les données expérimentales de base font défaut, ou au contraire leur accumulation pose un délicat problème de choix par suite de l'éventail de valeurs proposées. Nous souhaitons que, au cours de leurs études expérimentales sur les problèmes de contamination ou de décontamination, les chercheurs s'efforcent de dégager le maximum de renseignements pratiques dont nous voudrions disposer lorsqu'il s'agit d'interpréter les résultats d'examens consécutifs à des contaminations non expérimentales.

RÉFÉRENCES


DISCUSSION

W.N. SAXBY: I would like to support your plea for collection of the maximum amount of information from cases under study, incidents, research projects, etc. Data should be obtained from faeces, urine, blood and, where relevant, breath samples. Body-radioactivity measurements should also be obtained and, in the case of plutonium inhalation, measurements made with the newly developed Pu X-ray counter.
RESEARCH WITH A VIEW TO ESTIMATING THE BODY BURDEN OF RARE EARTHS ON THE BASIS OF EXCRETA MEASUREMENTS. Body burden can be estimated directly from excreta measurements only if the chemical nature of the element involved is the sole factor governing distribution and rates of exchange in the body. Many authors have already called attention to the way in which metabolism and elimination rates are affected by various parameters, such as the nature of the anionic radical, the valency of the element, the physico-chemical state of the contaminating form and the channel and manner of contamination.

The authors show that these factors mainly affect the initial kinetics of distribution in the body during the very first minutes. Using high-speed recording techniques and varying several experimental parameters, they studied the effect of these parameters on initial kinetics, the subsequent evolution of contamination in the various tissues and elimination processes. In particular, they recorded the kinetics of bile and urine elimination, blood purification and the radioactivity level of various organs (liver, kidneys, lungs).

In order to relate the body burden to the quantities of radioisotope eliminated, it is necessary to know the amounts present in the various compartments, their rates of exchange and the times required for elimination by the various channels. In an attempt to clarify these points, the authors devised a test using a chelating agent which modifies the equilibria between compartments and directs all available cerium towards the elimination channels. By comparing the elimination values measured before and during the test, they attempt to calculate the total body burden and its distribution. They also discuss ways of applying this test at various stages in contamination.

For relier la charge corporelle aux quantités de radioélément éliminé, il est nécessaire de connaître le taux de charge des divers compartiments, leurs vitesses d'échange et les périodes d'élimination par les diverses voies. Pour essayer de préciser ces points, les auteurs ont cherché un test en utilisant un chélateur qui modifie les équilibres entre compartiments et dirige tout le cérium mobilisable vers les voies d'éliminations. En comparant les valeurs d'élimination mesurées avant et pendant ce test, ils essaient de calculer la charge corporelle globale et sa répartition. Ils discutent les modalités d'application d'un tel test à divers moments d'une contamination.

* Stagiaires Euratom
INVESTIGACIONES EXPERIMENTALES PARA EVALUAR LA CARGA CORPORAL DE TIERRAS Raras POR ANÁLISIS DE LAS EXCRETA. La evaluación directa de la carga corporal a partir de la medición de las excreta es idóneo posible si la naturaleza química del elemento considerado constituye el único factor determinante de la distribución topográfica y de las velocidades de intercambio en el organismo. Numerosos autores han destacado ya la importancia de ciertos parámetros, como la naturaleza del radical aniónico, la valencia del elemento, el estado físico-químico de la forma contaminante, la vía y el modo de contaminación, en la evolución del metabolismo y de las velocidades de eliminación.

Los autores muestran que estos factores repercuten esencialmente en la cinética inicial de la distribución en el organismo durante los primeros minutos. Utilizando técnicas de registro ultrarrápidas y modificando buen número de parámetros experimentales, estudian la repercusión de esos factores en la cinética inicial, la evolución ulterior de la contaminación de los diversos tejidos y los procesos de eliminación. En particular, han registrado las cinéticas de eliminación hepática y urinaria, la depuración sanguínea y la radioactividad de diversos órganos (hígado, riñón, pulmón).

Para establecer una relación entre la carga corporal y las cantidades de radioelementos eliminadas, es preciso conocer la proporción de carga de los diversos compartimentos, sus velocidades de intercambio y los períodos de eliminación por las diversas vías. Para tratar de aclarar estos puntos, los autores han preparado una prueba en la que utilizan un agente de quelación que modifica los equilibrios entre compartimentos y engloba todo el cero movible hacia las vías de eliminación. Comparando los valores de eliminación medidas antes y después de la prueba, tratan de calcular la carga corporal global y su distribución. Examinan las modalidades de aplicación de tal prueba en diversos momentos de una contaminación.

L'eliminación du cérium 144 introduit dans un organisme vivant est conditionnée non seulement par des paramètres biologiques, mais aussi par ses modalités d'introduction ainsi que par l'état physico-chimique sous lequel il est administré à l'organisme [1, 2, 3, 4].

En outre, l'efficacité du traitement par le DTPA en impose l'utilisation dans le cas d'une contamination sévère, et ceci va entièrement modifier l'excrétion du cérium [4].

Le travail présenté est la synthèse des recherches expérimentales entreprises pour voir quelles étaient les relations entre l'excrétion fécale ou urinaire et la charge corporelle pour diverses structures physico-chimiques des solutions de cérium. Nous avons aussi cherché quelles étaient les modifications apportées par le DTPA suivant ses modalités d'administration.
Les recherches ont été menées avec des rats Wistar, et nous avons utilisé outre les techniques classiques de mesure de prélèvements ou de comptage global, des techniques cinétiques permettant l'enregistrement simultané pendant les vingt quatre premières heures de l'activité du sang, de l'urine et de la bile, ainsi que de divers organes comme le foie, l'os, le poumon et le rein.

Les enregistrements nous ont permis de préciser l'influence de nombreux facteurs sur les premières minutes de la contamination qui conditionnent le devenir du cérium. Ils ont montré que même pour des techniques d'administration aussi standardisées que possible, il existait de fortes variations individuelles et qu'il était préférable de travailler animal par animal plutôt que par comparaison de lots d'animaux.

I. ÉTATS DU CÉRIUM EN SOLUTION

Le cérium peut exister en solution sous trois formes:

a) Une forme monodispersée dans laquelle le sel est ionisé. Cette forme est exclusive pour pH = 2. Elle est alors homogène. Nous l'appelons monomérique.


c) Des formes complexées dans lesquelles le cérium est masqué chimiquement. Elles existent en présence notamment de l'anion citrate et des chélateurs, EDTA, DTPA, etc.

L'introduction de l'une de ces solutions dans un milieu biologique, dont le pH avoisine 7 avec un fort effet tampon, modifie les structures du cérium. Le métabolisme de la forme monomérique, qui n'est stable qu'aux pH très acides, sera particulièrement influencé par le processus de neutralisation. En revanche, celui de la forme polymérisée sera étroitement dépendant de ses structures initiales. Enfin, les facteurs dominants du métabolisme des formes complexées seront la stabilité du complexe en milieu biologique et le métabolisme propre du chélateur.

II. DEVENIRS DU CÉRIUM

L'étude de la cinétique biologique des solutions de cérium administrées par voie intraveineuse est essentielle pour la compréhension du métabolisme de cet élément, et surtout la cinétique de la forme monomérique qui est la seule directement incorporable par les organes critiques.
(Page 1)

Au cours des secondes qui suivent l’injection intraveineuse rapide du monomère, trois phénomènes peuvent être observés:

a) une incorporation immédiate par les cellules des organes critiques, foie et os,

b) une capture de ions cérium dans le sang par des substances probablement protéiques,

c) la polymérisation du cérium en milieu biologique.

1. Incorporation immédiate

Au cours des 20 premières secondes, les enregistrements rapides mettent en évidence une localisation de 30% de la radioactivité injectée dans le foie. Sur les images autoradiographiques obtenues à ce stade, il apparaît qu'il s'agit de l'incorporation par les hépatocytes, d'une phase monodispersée. Dans le même temps, 10% de la quantité injectée est retenue dans le squelette. En moins de 15 min cette fraction ne pourra plus être remise en circulation par un chélateur. Elle a été incorporée.

2. Liaisons au niveau du sang

De nombreux auteurs ont mis en évidence, avec des résultats différents, l'existence d'une liaison cérium-protéine. En ce qui concerne la vitesse d'épuration sanguine du cérium monomérique, nous avons observé une répartition très nette de nos rats d'une même souche Wistar en deux lots: dans l'un, la charge sanguine après injection intraveineuse tombe à 10% en moins d'une heure. Dans l'autre, 4 à 5 h sont nécessaires pour obtenir le même résultat. Nous pensons que dans ce dernier lot le support protéique sanguin est plus efficace car du cérium libre dans la circulation ne peut échapper si longtemps aux processus de polymérisation et de capture. La mise en évidence des supports est difficile car la liaison est très labile et est généralement rompue au cours du déplacement électrophorétique mis en œuvre pour la révéler. Il semble que plusieurs molécules sanguines puissent jouer ce rôle de transporteur du cérium monomère.

3. Polymérisation

La neutralité du milieu sanguin provoque la polymérisation du cérium monomérique qui a échappé aux processus précédents. Les micelles formées sont probablement de très petite taille car on ne les retrouve pas dans les cellules du système réticulo-endothélial. Ce cérium faiblement polymérisé est retenu au niveau des capillaires du muscle, du poumon et de la rate, notamment. La concentration tissulaire y reste faible. Il se produit également une charge rénale.

4. Répartition secondaire

Dans les heures qui suivent ce processus cinétique initial, se produit une répartition secondaire du cérium dans l'organisme. Le cérium retenu
CHARGE CORPORELLE EN CÉRİUM

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dans les tissus est lentement dépolymérisé, pris en charge par le sang et
dirigé vers le foie et l’os [6, 7]. Ce phénomène conduit à une charge hépa-
tique de 70 à 80% et osseuse de 15 à 20%.

5. Excrétion

Le cérium absorbé par la cellule hépatique sera intégralement dirigé
vers la voie biliaire, et compte tenu de la très faible absorption digestive
(<10⁻⁴) on peut considérer qu’il ne repassera plus dans le milieu sanguin.
Le cérium osseux est éliminé dans le torrent circulatoire mais très lente-
ment puisque la période biologique de décroissance osseuse est supérieure
à 500 j chez le rat; Ces faits commandent le processus d’élimination qui
s’effectue par deux voies: urinaire et fécale.

L'excrétion urinaire intéresse deux fractions: une partie du cérium
monomérique et une partie du cérium polymérisé. Chez le rat cette élimi-
nation rénale intéresse 1 à 2% de la quantité injectée pendant les deux pre-
miers jours. Par la suite, une partie du cérium libéré par la décharge
de l'os est vraisemblablement éliminée par cette voie, mais, très faible,
elle est difficilement appréciable.

Le cérium éliminé dans les fécès provient de l'excrétion biliaire du
cérium, correspond d'une part au monomère directement assimilé et de
l'autre au cérium de dépolymérisation secondaire transporté par le sang.
La décroissance hépatique suit sensiblement une courbe exponentielle de
période 12 j.

De ce schéma général quelques points importants sont à retenir:
a) seul le cérium monomérique libre ou transporté peut être incorporé
dans les cellules hépatiques et osseuses. C'est de même la seule forme
que puisse éliminer le rein. Il en résulte que d'une façon générale, pour
être éliminé par les voies urinaires ou biliaires, le cérium doit nécessaire-
ment passer par l'état monomérique libre ou complexé.
b) le cérium monomérique libre ou transporté incorporé par le système
hépatique ou l'os. On peut considérer que le foie incorpore 3 à 4 fois plus
de cérium monomérique circulant que l'os. La connaissance de la charge
hépatique à un instant donné peut permettre une appréciation de la charge
osseuse.

L’influence de la voie d’introduction sur le métabolisme découle des
considérations précédentes. Dans le cas d’une contamination locale par
du cérium monomérique, qu’elle soit pulmonaire, intramusculaire, sous-
cutanée, intra-péritonéale, une faible fraction du monomère passe immédia-
tement dans la circulation et y suit la cinétique décrite. Le reste est poly-
mérisé sur-place (7, 8, 9). Nous allons examiner maintenant le métabolisme
du cérium polymérisé.

B. Forme polymérisée

L'épuration sanguine du cérium polymérisé est très rapide, en 10 min
elle atteint 90% de la quantité administrée. Elle met en jeu des mécanismes
essentiels, la colloïdopexie par le système réticulo-endothélial et le pié-
geage au niveau des systèmes capillaires. L'importance relative de ces
deux phénomènes dépend essentiellement de l'état de la solution injectée,
de son degré de vieillissement. Il s'agit en définitive essentiellement de la taille et de la charge des micelles. Et l'on sais que la vitesse d'évolution de ces paramètres aux changements de pH est lente.

Comme le révèlent les autohistoradiographies, la fixation initiale par le processus de colloïdopexie s'effectuera dans les cellules de Klüpfel du foie, dans le squelette, dans la rate, et d'une façon générale dans tous les organes comportant des cellules du système réticulo-endothélial.

Le piégeage au niveau du système capillaire s'effectuera d'abord au niveau du poumon car c'est le premier système de ce type irrigué par le sang au sortir du cœur droit. Le mécanisme de cette fixation reste obscur, il semble seulement sur les autoradiographies qu'elle soit extracellulaire. Ce piégeage peut être très important et l'on peut notamment observer la fixation de 80 à 90% du cérium polymère administré dans une solution chlorhydrique fraîchement préparée et à pH 10.

A la fin de cette répartition initiale commence un lent processus de dé-polymérisation, tant dans le système réticulo-endothélial qu'au niveau des capillaires. Le mécanisme de cette évolution n'est pas simple: la dépolymérisation s'effectue jusqu'à une réduction de taille des micelles qui permet un relarguage dans la circulation. A ce moment, une certaine fraction du polymère, empruntant la voie sanguine ira se fixer dans d'autres organes. C'est ainsi que la charge pulmonaire, presque constante pendant un jour ou deux, diminuera brutalement au bénéfice du foie et de l'os, et ceci par vagues successives. Nous assistons véritablement à un changement discontinue d'organes de rétention. Parallèlement et en même temps, la dépolymérisation se poursuit et réduit le cérium à l'état de monomère sous lequel il pourra être transporté dans la circulation et, soit assimilé, soit éliminé. La répartition du cérium monomère ainsi formé entre le foie, l'os et le rein, dépendra du lieu de sa libération. Les premières cellules assimilatrices rencontrées par le torrent sanguin qui le véhicule, en captèrent la majeure partie.

Ainsi, le métabolisme du cérium administré par voie veineuse sous forme de polymère n'est pas significativement différent du cas de contamination locale. Dans l'un et l'autre cas, en plus d'une fraction diffusant rapidement, nous observons l'existence d'un stockage de cérium polymérisé dont la lente transformation aboutit à un apport chronique de cérium monomérique aux organes critiques.

L'élimination urinaire qui reste faible, provient d'une part du cérium monomérique passé dans la circulation au moment de l'injection ou de la contamination, et de l'autre du cérium de dépolymérisation rejeté dans le sang d'une façon discontinue. Inconstante et comportant des variations importantes au cours du temps, l'élimination urinaire quotidienne ne saurait donner aucun élément sur l'état de contamination de l'organisme.

Le foie, en revanche, joue véritablement un rôle d'intégrateur d'une fraction du cérium monomérique, qui a circulé dans l'organisme tant au moment de la contamination qu'au cours de processus qui suivent. L'élimination fécale, d'origine biliaire, permet donc mieux de formuler une appréciation sur la quantité de cérium monomérique existant dans l'organisme et par là d'évaluer la charge osseuse probable.
C. Formes chélatées

Le métabolisme du cérium véhiculé par un chélateur dans l'organisme peut être totalement différent des schémas précédemment décrits. En effet, le métabolisme du complexe est identique à celui du chélateur, on sait qu'un cation chélaté est chimiquement masqué. C'est ce que l'on observe notamment avec des chélateurs stables en milieu biologique comme le DTPA et le TTHA. L'élimination est rapide et complète. En revanche, avec des supports tels que l'EDTA ou l'anion citrate, une fraction seulement du cérium suivra le métabolisme du chélateur car ce dernier, instable en milieu biologique, libérera du cérium en tel ou tel point de l'organisme. C'est pourquoi les études métaboliques menées avec du citrate de cérium ne sont guère représentatives du devenir du cérium en milieu biologique. C'est pourquoi aussi l'introduction de l'EDTA dans un organisme contaminé peut être plus dangereuse qu'utile car la fraction de cérium véhiculée par le chélateur est le plus souvent libérée au niveau du squelette, aggravant par là, la contamination.

D. Modifications apportées par l'introduction d'un chélateur après la contamination

Dans les cas de contamination sévère, cas où l'estimation de la charge corporelle est la plus intéressante, l'utilisation d'un chélateur comme le DTPA s'impose, étant donné l'efficacité de cette thérapeutique.

L'introduction de DTPA, en injections uniques ou répétées, va modifier le devenir du cérium et rendre encore plus complexe l'estimation de la charge corporelle à partir des excréta.

Nous avons cherché à préciser quelles étaient les modifications apportées par le chélateur à l'excrétion du cérium. Nous avons étudié les territoires de dispersion du DTPA, les différentes vitesses d'échanges et les modalités de son élimination.

Le DTPA se disperse dans le sang et les liquides extracellulaires. L'excrétion rénale qui représente 99% de l'administration est terminée en quelques heures. L'excrétion biliaire, de l'ordre de 1%, dure plusieurs jours. Est éliminé par l'urine le cérium qui se trouve dans le sang et les liquides extracellulaires. La voie biliaire n'existe que pour le cérium incorporé par les hépatocytes et dont l'excrétion n'est pas augmentée mais accélérée. Le DTPA accélère aussi in situ le processus de dépolymerisation.

E. Estimation de la charge corporelle

Dans le cas de contamination grave par blessure, il est pratiquement impossible d'obtenir une décontamination totale de la porte d'entrée.

L'excrétion quotidienne sera donc la somme de deux éliminations: élimination du cérium que a diffusé au moment de la contamination et élimination de la fraction dépolymerisée relarguée par la porte d'entrée.

L'estimation de la charge osseuse ne peut se faire par différence que si l'on connaît la quantité de cérium dans la plaie ou le poumon, sa vitesse de dépolymerisation et le pourcentage de cette fraction éliminée chaque jour.
La discontinuité des mécanismes de dépolymérisation rend illusoire la mesure de la charge corporelle par la mesure de l'excrétion urinaire. L'intégration de l'élimination fécale, par contre, donne un ordre de grandeur de la quantité totale du cérium assimilable qui a circulé dans l'organisme, donc de la charge osseuse.

Si l'on utilise le DTPA:

a) Comme test diagnostic: une injection unique pratiquée peu de jours après une contamination montrera, si l'élimination urinaire est fortement augmentée, la présence d'un foyer local de contamination. L'excrétion fécale cumulée donnera un ordre de grandeur du cérium osseux.

b) En cas de traitement continu, nécessité par la présence d'un foyer local que l'on ne peut exciser, l'excrétion urinaire sera surtout le reflet de la dépolymérisation au niveau du foyer, alors que l'excrétion fécale cumulée donnera également un bon ordre de grandeur du cérium osseux.

En conclusion, nos recherches expérimentales sur l'estimation de la charge corporelle par la mesure des excrétas ont montré que pour le cérium, l'excrétion urinaire dépendait de nombreux facteurs, alors que l'excrétion fécale cumulée pouvait donner des résultats valables, dans le cas notamment de contamination par blessure.

De plus, l'utilisation d'une thérapeutique par chélateur rendra impossible l'estimation de la charge corporelle par la mesure de l'excrétion urinaire et l'excrétion fécale, qui n'est qu'accélérée et non pas augmentée reste dont la seule possibilité d'estimer la charge osseuse.

**RÉFÉRENCES**


**DISCUSSION**

N. A. TAYLOR: Can you give me any information on the valency state of the cerium in your experiments? Is it trivalent or quadrivalent?

J. REMY: We think it was trivalent cerium. However, this problem of valency is not simple, and it appears that the valency can change according to the pH.

G. SEEGER: Can you give me the chemical formulae of the DTPA and the TTHA, and what concentrations do you use?

J. REMY: As far as the DTPA is concerned, we use calcic DTPA, and the animals are injected with 2 mg/d, usually contained in 0.5 cm³ of distilled water or physiological serum.
SYMPOSIUM ON THE ASSESSMENT OF RADIOACTIVE BODY BURDENS IN MAN
HELD AT HEIDELBERG, 11 - 16 MAY 1964

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