International Conference on Radiation and Health
Beer Sheva, Israel November 3-7, 1996

Program and Book of Abstracts

Ben-Gurion University of the Negev
Soroka Medical Center of the Negev
World Health Organization
International Atomic Energy Agency
A Unique On-line Radiation Monitoring System
to reduce radiation exposure in the workplace

Rotem Industries Ltd. (Israel), a leading company in the radiation monitoring field has developed a system which will help you to reduce radiation exposure in the workplace.

This system gives a very cost-effective solution which can be implemented in the following applications:

- Nuclear Medicine/Isotope Laboratories
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- Accelerators
- X-Ray Imaging Rooms
- Regular Waste Management
- PET Facilities
- Other applications involving Radiation and/or Radioisotopes

The concept of the system is simple and unique, enabling receipt of on-line monitoring of the radiation in the room, threshold alarms, and full documentation of the data.

The System will be presented during the Congress in our special booth and through an oral presentation on Monday, October 4 (please check for specific time and place).

We are looking forward to seeing you.

ROTEM INDUSTRIES LTD. P.O.Box 9046, Beer Sheva 84190, ISRAEL.
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THE FOLLOWING SPONSORS ARE ACKNOWLEDGED WITH THANKS:

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- International Association for Radiation Research
- Committee for Research and Prevention in Occupational Safety and Health of the Israel Ministry of Labour and Social Affairs

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177-0224620
PROGRAM

Sunday, November 3, 1996
10:00 - 12:00 Short Courses ("Tamar" Hall - Desert Inn Hotel)
14:00 - 17:00 "" "
20:00 "Get Together" Cocktail ("Dekel" Hall, Desert Inn Hotel)

Monday, November 4, 1996
08:00 - 09:00 Registration (Sonnenfeldt Auditorium)
Poster Mounting (Sonnenfeldt Auditorium)

09:00 - 10:00 OPENING CEREMONY
Sonnenfeldt Auditorium
Greetings
Dr. A. Braverman President, Ben Gurion University of the Negev
Dr. I. Peterburg Medical Director, Soroka Medical Center
Prof. S. Segal Dean, Faculty of Health Sciences, Ben Gurion University of the Negev
Ms. M. Ziv Israel Cancer Society
Dr. I. Turai International Atomic Energy Agency, Vienna
Dr. G. Souchkevich World Health Organization, Geneva, Switzerland
Prof. A. Serduk Minister of Health, Ukraine

10:00 - 11:00 PLENARY LECTURES
Sonnenfeldt Auditorium
Chairs: M. Quastel, J. Goldsmith, Israel
10:00 - 10:30 the Russian Radiation Legacy: Its Integrated Impact and Lessons
M. Goldman, USA
10:30 - 11:00 Fifty Years of Studying A-Bomb Survivors
A. Stewart, UK
11:00 - 11:30 Coffee Break

11:30 - 13:30 SYMPOSIUM 1: DOSIMETRY AND DOSIMETRIC RECONSTRUCTION
Sonnenfeldt Auditorium
Chairs: G. Kramer, Canada and G. Shani, Israel
11:30 - 11:55 Considerations In Assigning Dose Based on In Vivo Counting
G. Kramer, Canada
11:55 - 12:20 Thyroid Dose Reconstruction in the Ukraine: Ten Years of Study
G. Goulko, N. Chepurny, P. Jacob, I. Kairo, I. Likhtarev, B. Sobolev, and G. Voigt.
Germany and Ukraine
12:20 - 12:45 Collective Bio-Dosimetry as A Dosimetric “Gold-Standard”: A Study of Three Radiation Accidents
B. Pass, A.E. Baronov, J.E. Aldrich, P. Scallion, R.P. Gale, Canada, Russia and USA
12:45 - 13:05 Health Concerns Related To Radiation Exposure of the Female Nuclear Medicine Patient
M. Stabin, USA
13:05 - 14:00 Lunch and Poster Mounting (Menza)
14:00 - 15:10 SYMPOSIUM 2: DNA MUTATION AND RADIATION CARCINOGENESIS
Sonnenfeldt Auditorium

Chairs: E. Riklis, Israel, and J. Weiss, USA

14:00 - 14:25 Mechanism of DNA Repair
E. Priel, Israel

14:25 - 14:50 Pharmacologic Approaches to Protection Against Radiation-Induced Lethality and Other Damage
J. Weiss, USA

14:50 - 15:10 Enhanced DNA Repair: A New Modality For Improved Radioprotection and Photoprotection
E. Riklis, Israel

15:15 - 17:15 SESSION 1: PHYSICS AND HEALTH PHYSICS (Parallel to Session 2)
Sonnenfeldt Auditorium

Chairs: S. Faermann, Israel, and T. Hamilton, USA

Radiation Protection at Workplace: A New Proposition
B. Gold, and Y. Sadan. B.Ashkenazi, N. Ankri and N. Tal. Israel

Radon In Schools and Other Public Buildings: When Risk Management Can Be More Stringent Than Risk Assessment
E. Richter, J. Kleinstern, and J. Westin. Israel

Rn-222 Emanation from Rock Units and Indoor Levels in Israel: An Integrated Approach in Assessing Radon-Prone Areas

The Body Content of Pb-210: A Measure of Cumulative Exposure to Radon/Radon Progeny?
P. Roth. E Werner. W. Wahl. and W. Jacobi. Germany

The Unattached Fraction of the Radon Progeny: An Improved Method for Size Distribution Determination
G. Butterweck-Dempewolf, Ch. Schuler. and A. Reineking. Switzerland and Germany

In Vivo Measurements of Cs-137 Long Term Retention in Individuals Contaminated in the Goiania Accident
C. Oliveira, D. Melo. B. Dantas. J. Lipsztejn. and G. Laurer. Brazil and USA

A Biokinetic Model for Cesium-137
J. Lipsztejn, D. Melo. and C. Oliveira. Brazil

An Assessment of Human Exposure to Environmental Radiation in The Canadian Arctic
M. Walsh. A. Baweja. and B. Tracy. Canada

Development of a Tissue-Equivalent Lung Phantom for In Vivo Determination of Low Energy Photon Emitters
B. Dantas, G. and Rosales. Brazil

A Compressed Air Ionization Chamber for Low Exposition Rates

* Abstract not submitted
**15:15 - 17:15 SESSION 2: DNA MUTATIONS AND CARCINOGENESIS**

*Parallel to Session 1*

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<tr>
<td>Study on Carcinogenesis After Irradiation of Mice in Utero</td>
<td>K. Lumniczky, S. Antal, G. Safrany, and E. Hidvegi, Hungary</td>
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<td>A Delayed DNA Degradation Process Resembling Apoptosis Is Associated With Radiation Induced Neoplastic Transformation of Human Hybrid Cells</td>
<td>M. Mendonca, K. Howard, L. Desmond, USA</td>
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<td>Mechanisms of Radiation-Induced Gene Responses</td>
<td>G. Woloschak, and T. Paunesku, USA</td>
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<td>Revealing Molecular Genetic Changes in the Jewish Immigrants Who Came to Israel from the Chernobyl Disaster Area</td>
<td>H. Weinberg, E. Nevo, A. Korol, T. Fahima, G. Rennett and S. Shapiro, Israel</td>
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<td>Effect of Chronic Low Dose Ionizing Radiation on Chromatin Structure</td>
<td>R. Gordon, E. Novoselova, and V. Karnaukhov, Russia</td>
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<td>How Should We Assess the Action of Mixed Irradiation?</td>
<td>S. Suzuki, Japan</td>
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<td>Radiation-Induced Double-Strand Breaks In Calf Thymus DNA in the Presence of 1,2 Dihydroxy 9,10, Anthraquinone and Its Cu (I) Complex</td>
<td>S. Das, A. Saha, P. Mandal, India</td>
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17:15 - 19:00 *Poster Viewing and coffee break (Sonnenfeldt Auditorium)*
### Tuesday, November 5, 1996

#### SYMPOSIUM 3: BIOLOGICAL INDICATORS OF RADIATION EXPOSURE

**Sonnenfeldt Auditorium**

**Chairs:** A. Fischbein, Israel, and I. Emerit, France

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<tr>
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| 08:30 - 09:00 | **Indirect Action Mechanisms Responsible for Chromosomal Instability After Radiation Exposure**  
|             | I. Emerit, France                                                       |
| 09:00 - 09:30 | **Stable Biomarkers for Retrospective Biodosimetry**                    |
|             | J. Lucas, USA                                                           |
| 09:30 - 10:00 | **Assessment of Radiation Induced Injury to the Reproductive System: from the Bench to the Bedside**  
|             | A. Fischbein, Ramat Gan, Israel                                         |
| 10:00 - 10:45 | Coffee Break                                                           |

#### SYMPOSIUM 4: EPIDEMIOLOGY: THYROID CANCER

**Sonnenfeldt Auditorium**

**Chairs:** B. Modan, Israel, and E. Cardis, France

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| 10:45 - 11:10 | **Chernobyl Related Thyroid Cancer: What Evidence for Role of Short Lived Iodines?**  
|             | J. Bleuer, Y. Averkin, and Th. Abelin, Switzerland and Belarus         |
| 11:10 - 11:35 | **Lessons from Chernobyl on Radiation and Health: Thyroid Cancer and Leukemia**  
|             | E. Cardis, Iarc, Lyon, France                                           |
| 11:35 - 12:00 | **Malignant and Benign Tumors Following Radiation Exposure to the Head and Neck**  
|             | E. Ron, USA                                                             |
| 12:00 - 12:30 | **the Relationship Between the Prevalence of Thyroid Cancer and Thyroid Nodules In the Population of the Marshall Islands to Potential Exposure from Nuclear Weapons Tests**  
|             | K. Trott, M. Schoemaker, T. Takahashi, K. Fujimori, and S. Simon, UK and Japan |
| 12:30 - 13:00 | **Reconstruction of Thyroid Doses for Children With Thyroid Cancer In Belarus**  
|             | G. Voigt, E. Buglova, E. Demidchik, G. Goulko, Y. Kenigsberg, H. Müller, and H. Paratzke, Germany, and Belarus |
| 13:00 - 14:15 | Lunch (Menza)                                                           |

*Abstract not submitted*
14:15 - 16:15  SESSION 3: BIOLOGICAL INDICATORS OF EXPOSURE  (Parallel to Session 4)

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<td>Is Fish Painting Appropriate for Dose Estimation of Accidental Radiation Overexposure?</td>
<td>I. Sorokine-Durm, V. Durand, A. Le-Roy, N. Paillolle, N. and P. Voisin, France</td>
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<td>The In Vitro Micronucleus-Centromere Assay to Detect Low Doses of Radiation in Human Lymphocytes</td>
<td>A. Vral, H. Thierens, and L. De Ridder, Belgium</td>
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<td>Glycophorin-A In Liquidators from Chernobyl</td>
<td>V. Wishkerman, M. Quastel, A. Duvdevani, and J. Goldsmith, Israel</td>
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<td>Automation of the Dicentric Assay: Use of Color-Pigment Painting, Metaphase Finder and Digital-Image Analysis</td>
<td>W.F. Blakely, H. Loats, P.G.S. Prasanna and C.J. Kolanko, USA</td>
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<td>Chromosome Aberrations in Cultured Peripheral Lymphocytes from Persons With Elevated Skin Radiosensitivity</td>
<td>T. Kondrashova, T. Ivanova, and S. Katsalap, Russia</td>
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<td>Hemopoietic Progenitor Cells in Patients Affected By Chernobyl</td>
<td>N. Bilko, and V. Bebeshko, Ukraine</td>
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<td>Age Response of Stable Chromosome Aberration Frequency in Lymphocytes of Chernobyl Victims and Control Group</td>
<td>L. Vorobtsova, A. Begomasova, N. Timofeeva, and A. Pukkenen, Russia</td>
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<td>Persistence of Translocations Detected By Fish In Accidentally Exposed Radiation Workers</td>
<td>G. Stephan and S. Pressl, Institute for Radiation Hygiene of the Federal Office for Radiation Protection, Germany</td>
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<td>Genotoxic Effects of Pesticides Examined in Lymphocytes of Occupationally Exposed Vinegrowers</td>
<td>G. Joksic, M. Nikolic, V. Spasojevic-Tišma, Yugoslavia</td>
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<td>Stimulation of Immunity After Low Dose Radiation (LDR)</td>
<td>S. Liu, China</td>
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<td>Ten Years After Chernobyl: Biological Dosimetry, Oncogenesis and Multiabberant Cells</td>
<td>A. Vorobiev, N. Rivkind, and N. Shklovsky-Kordi, Russia</td>
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<td><strong>Iodine Deficiency in Belarusian Children as Possible Factor</strong></td>
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<td>Stimulating the Irradiation of Thyroid Gland During the Chernobyl Catastrophe</td>
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<td>M. Gembicki, A. Stozharov, A. Arinchin, K. Moschik, S. Petrenko, I. Khmara, and K. Bavcrstock (WHO), <em>Poland, Belarus and Italy</em></td>
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<td><strong>The Hanford Thyroid Disease Study</strong></td>
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<td>S. Davis, K. Kopecky, T. Hamilton, and B. Amundson, USA</td>
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<td><strong>Possible Influence on Radiation Exposure and Iodine Deficiency on the Molecular Events in Thyroid Cancer</strong></td>
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<td>K. Troshina, G. Gerasimov, G. Alexandrova, M. Bronstein, I. Dedov, I. Tomashevsky, T. Jennings, and J. Figge, <em>Russia and USA</em></td>
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<td><strong>Autoimmune Thyroiditis in Children Affected by the Chernobyl Accident</strong></td>
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<td>A. Poverenny, A. Shinkarkina, Ju. Vinogradova, V. Podgorodnichenko, A. Tsyb, <em>Russia</em></td>
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<td><strong>Immune Status in Children With Benign and Malignant Thyroid Tumors</strong></td>
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<td>V. Chebotarev, G. Zamotaeva, T. Davydova, G. Zubkova, N. Kotyarenko, and N. Stepura, Ukraine</td>
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<td><strong>Radiiodine Impact on the Population of Russia After the Chernobyl Accident and Its Health Effects</strong></td>
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<td>L. Zvonova, and M. Balanov, <em>Russia</em></td>
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<td><strong>Additional Dose-Forming Factor in the Thyroid Gland After Chernobyl Station Disaster</strong></td>
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<td>E. Parshkov, and I. Chebotareva, <em>Russia</em></td>
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<td><strong>Analysis of Thyroid Cancer Morbidity in Obninsk Children and Adolescents of Russia During Ten Year Period After Chernobyl</strong></td>
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<td>V. Shakhtarin, A. Tsyb, and E. Parshkov, <em>Russia</em></td>
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<td><strong>Clinical Current of Thyroid Cancer in Children, Adolescents and Young Adults Living on Radionuclide Contaminated Territories of Bryansk, Kaluga and Tula Regions</strong></td>
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<td>B. Vityurin, P. Roumantsev, A. Ilyin, and E. Parshkov, <em>Russia</em></td>
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<td><strong>Coffee Break</strong></td>
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SESSION 5: LIQUIDATORS  (Parallel to Session 6)
Sonnenfeldt Auditorium

Chairs: J. Rennart and A.F. Tsyb, Israel and Russia.

The Corporate Research Projection “Effects of Radioactive Radiation on Health—Risk and Projection Models”: First Results
W. Morgenstern, V. Ivanov, and A. Michalski. Germany and Russia

Mortality, Cancer Incidence and Thyroid Pathology Among Esthonian Chernobyl Clean-Up Workers
M. Tekkel, M. Rahu, T. Veidebaum, M. Hartshorne, P. Inskip, T. Hakulinen, A. Auvinen, E. Pukkala, and J. Boice, Jr., Estonia, USA; and Finland

Ultramorphological Abnormalities in Spermatozoa of Salvage Workers Following Decontamination Work at the Chernobyl Nuclear Reactor and Its Vicinity
N. Zabludovsky, A. Fischbein, F. Eltes, V. Smirnov, V. Grischenko, B. Bartoo, Israel and Ukraine

the Pilot Study of Clean-Up Workers from Lithuania
A. Kesminiene, G. Rimdeika, J. Kurtinaitis, W. Bigbee, and J. Boice, Jr., Lithuania and USA

On the Thyroid Cancer Prognosis After the Chernobyl Accident
L. Scheplyagina, L. Remmenik, and G. Frank, Russia

Epidemiological Investigation of Health Problem Among Participants of Clean-Up Workers Following the Chernobyl Accident (1986-1996)
V. Ivanov and A. Tsyb, Russia

Blood Pressure Association With Exposure to Chernobyl Radiation Among Liquidators Who Immigrated to Israel
E. KordvISH, J. Goldsmith, L. Merkin, and M. Quastel, Israel

the Evaluation of Time and Dose Dependent Dynamic Damages Caused By the Influence of Ionizing Radiation to Chernobyl Nuclear Power Plant Accident Clean-Up Workers in Latvia
E. Curbakova, B. Dzerve, M. Eglite, T. Farbtuha, I. Frickausa, and T. Zvagule, Latvia

the Latvian Chernobyl Clean-Up Worker's Cohort Ten Years After the Disaster
A. Stengrevics, G. Obrams, J. Tchrbakova, and R. Jensen, Latvia and USA

Internal Exposure of the People Involved in 1986 in Remedial Actions on Chernobyl Nuclear Power Plant
V. Kutkov, I. Gusev, S. and Dementiev, Russia

Cytogenetic Radiation Markers in Liquidators: Why We Are Finding Them Long After the Accident?
N. Slozina, A. Nikiforov, E. Neronova, and T. Kharchenko, Russia

Health Status of Emergency Workers Who Live in North-West Regions of Russia
I. Shantyr, I. Romanovitch, N. Makarova, and E. Saigina, Russia

Leukemia Among the Liquidators Ten Years After Chernobyl
G. Tolochko, and E. Ivanov, Belarus
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<td>Insights into the Mechanism of Radiation Damage and Radioprotection Through Their Modulation by Cytokines</td>
<td>R. Neta, USA</td>
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<td>Melatonin and Radioprotection from Genotoxicity: an <em>In Vivo - In Vitro</em> Investigation In Human Volunteers</td>
<td>Vijayalaxmi, R. Reiter, T. Herman, and M. Meltz, USA</td>
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<td>Radiomodification by Cell Cycle Arresting Drugs</td>
<td>R. Gorodetsky, L. Levivansky, I. Ringel, and A. Vexler, Israel</td>
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<td>On Thymus Carcinogenesis In the Mice After Low-Dose Irradiation</td>
<td>D. Bhattacharjee, and H. Sarma, India</td>
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<td>Biological Effect of Humic Acid Product in Rats Exposed to 60-Co Gamma Irradiation</td>
<td>J. Namenyi, A. Gachalyi, and J. Hidegi, Hungary</td>
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<td>Study on the Possibility of Melanin Application for Protection Against Radiation</td>
<td>I. Mosse, B. Dubovic, S. Plotnikova, L. Kostrova, S. Subbot, and I. Maksimenya, Belarus</td>
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<td>Studies on Liver Chromatin Structure Irradiated With Fast Neutrons</td>
<td>B. Constantinescu, and L. Radu, Romania</td>
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<td>Cancerostatic and Radioprotective Effect of the Migi-K Preparation and the Possibility of Its Use In Tumor Radiotherapy</td>
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<td>Features of Radiation Damage Accumulation Over Long Time Intervals</td>
<td>N. Beregovskaya, and I. Beregovskii, Ukraine and USA</td>
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<td>Prediction of Hormesis In Radon Carcinogenesis</td>
<td>R. Barstra, Holland</td>
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| 08:30 - 10:00| **SYMPOSIUM 5: PSYCHOSOCIAL ASPECTS**          | Sonnenfeldt Auditorium    | Chairs: J. Cwikel, Israel, and J. Havenaar, Holland | 08:30 - 08:55 Psychological Factors Affecting Health After A Nuclear Disaster
|              | **SYMPOSIUM 6: NON-IONIZING RADIATIONS**       | Hall B                    | Chairs: M. Suess, Israel, and M. Repacholi, Who, Switzerland | 08:30 - 08:55 RF Field Exposure and Cancer: What Do the Laboratory Studies Suggest?
|              |                                                 |                           |                                             | 08:55 - 09:20 Biological Effects in Animals Exposed to Extremely Low Frequency (ELF) Electric and Magnetic Fields
|              |                                                 |                           |                                             | 09:20 - 09:55 Two Year Follow-Up Study of Immigrants to Israel from the Chernobyl Area

* Abstract not submitted
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<td><strong>Hall C, Kreitman Building</strong>&lt;br&gt;Chairs: L. Epstein, Israel, and Y. Hosoda, Japan</td>
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<td>Assessing the Risk of Radon: Approaches of the Beir IV and Beir VI Committees</td>
<td>E. Double, and J. Samet, USA</td>
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<td>Lack of Association of Indoor Residential Radon Exposure and Risk of Childhood Acute Myeloid Leukemia (AML)</td>
<td>M. Steinbuch, D. Sandler, J. Buckley, C. Weinberg, and L. Robison, USA</td>
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<td>Feasibility Assessment for Epidemiologic Studies of Communities Near Nuclear Weapon Facilities in the United States</td>
<td>P. Garbe, O. Devine, and J. Smith, USA</td>
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<td>Curvilinearity in the Dose Response Curve for Cancer in the Japanese A-Bomb Survivors</td>
<td>M. Little, and C. Muirhead, UK</td>
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<td>Delayed Health Effects of Exposure to 1957 Kyshtym Nuclear Accident: Exposed Persons and Offspring</td>
<td>L. Privalova, B. Katsnelson, E. Polzik, and V. Kasantsev, Russia</td>
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<td>Conceptual Approaches to Rehabilitation of the Altai Region Population Exposed to the Nuclear Tests at the Semipalatinsk Test Site</td>
<td>V. Demin, V. Kutkov, V. Golikov, I. Keirim-Marcus, V. Rezontov, Ja. Shoiket</td>
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<td>Mortality from Malignant Tumors Among the Men Exposed to the Nuclear Test Site at the Semipalatinsk Test Site on August 29, 1949</td>
<td>A. Algazin, Ja. Shoiket, and V. Kiselev, Barnaul, Russia</td>
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<td>the Deleterious Effects of Chronic Radiation Exposure for Inhabitants of the Area Near Semipalatinsk Nuclear Test Ground</td>
<td>R. Rozenson, B. Gusev, K. Apsalikov, and V. Kantorova, Kazakhstan</td>
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10:00 - 10:30  | Coffee Break                                      |                                                                         |
10:30 - 13:00 SESSION 8: PSYCHOSOCIAL ASPECTS (Parallel to Sessions 9 & 7B)

Sonnenfeld Auditorium

Chairs: Z. Wolfson, Israel, and A. Nyagu, Ukraine

Psycho-Neurological Disorders Pathogenesis Conception of Chronical Radiation Disease

Psychosocial Status and Psychosomatic Health of Adolescents Victims Chernobyl Disaster
V. Bebeshko, and N. Korol, Ukraine

PTSD in the Population Living in the Contaminated Region After the Chernobyl Accident
M. Lebedeva, Russia

Mental Disorders Related to the Chernobyl Disaster
L. Kryzhanovskaya, and A. Utkov, Ukraine

Psychosocial Peculiarities of Liquidators and Causes of Disadaptation
0. Chinkina, Russia

Health Condition and Ability to Continue Their Professional Work in Patients Who Suffered Acute Radiation Syndrome in the Result of Chernobyl Accident
V. Bebeshko, D. Belyi, A. Kovalenko, I. Khalavka, O. Gergel, T. Fiedner, M. Weiss and B. Fischer, Ukraine and Germany

Adjusting Ability and Sensibility in Case of an Accident
J. Rozental, Israel

Psychosocial Assistance in the Aftermath of Environmental Accidents: Some Policy Considerations and an Agenda for the Future
S. Becker, Israel

10:30 - 13:00 SESSION 9: NON-IONIZING RADIATIONS (Parallel to Sessions 8 & 7B)

Hall B

Chairs: E. Ne'eman, Israel, and A. Ahlbom, Sweden

Problems of Exposure Assessment in Radiofrequency Epidemiology Research
L. Erdreich, USA

Frequency of Micronuclei in the Peripheral Blood and Bone Marrow of Cancer-Prone Mice Chronically Exposed to 2450-MHZ Radiofrequency Radiation
Vijayalaxmi, M. Frei, S. Dusch, V. Guel, M. Meltz, and J. Jauchem, USA

Effects of Electric Fields on Drosophila: Physical Model, Physiological Action and Genetic Consequences
S. Dromashko, O. Kvitko, and G. Pisarchik, Belarus

Effect of Ultraviolet Radiation on Bone Electron Structure
Yu. Dekhtyar, and A. Katashev, Latvia

the Results of an Epidemiological Study of the Health Effects of EMF Generated By Radar
Yu. Dumansky, N. Nikitina, S. Bitkin, and A. Gotz, Ukraine

Distance Sensitivity of Normal and Malignant Cells to Ultrasound In Vitro
F. Leibekowicz, Israel

Application of RF Regulation: the General Policy in the IDF
A. Dudyevany, and N. Amite, Israel

Behavioral Effects Caused by Microwave Exposure
A. Smolva, Ukraine

Radio Frequency Exposure Near High Voltage Lines
M. Vignati, and L. Giuliani, Italy

XIII
Chairs: T. Schlesinger, Israel, and E. Ivanov, Belarus

the Ukrainian/American Ocular Study: Current Perspectives of an Extensive Cohort Study of Cataract Incidence

B. Worgul, Y. Kundiev, P. Vitte, P. Medvedovsky, G. Parhomenco, A. Ruban, I. Sergienko, I. Likhtaryov, V. Chumak. Ukraine and USA

Chernobyl Exposure and Hemoblastoses in Belarus

E. Ivanov, G. Tolochko, L. Shuyaeva, R. Jaroshevich, V. Lazarev, V. Ivanov, N. Shapovalvuk, G. Vinokurova, and N. Raspopova. Belarus and Israel

Principles of Collection and Analysis of Health Data from Belarusian Children Who Were Exposed to Radiation as a Result of the Chernobyl Accident


Epidemiological Estimation of Malignant Neoplasms in Territories of Russia Radiocontaminated from the Chernobyl Accident

L. Remennik, V. Mokina, V. Chissov, and G. Petrova. Russia

Evaluation of the Radiation Factor in Population Coming to Israel from Effects of the Chernobyl Zone

E. Lyass, and D. Borohov. Israel

Radiation Induced Cerebral Meningioma: A Comparative Study

L. Lupu, I. Shelef, P. Tiberin, and Y. Hertzanu. Israel

Synergistic Interaction of Ionizing Radiation With Other Harmful Agents and Environmental Health Criteria

V. Petin, G. Zhurakovskaya, L. Komarova. Russia

Morphofunctional Status of Upper Sections of Digestive Tract for Children from Regions Subjected to Radionuclide Contamination

G. Rimarchuk, L. Schlepyagina, A. Vycherova, T. Tyurina, and G. Plaksina. Russia

the Non-Linear Effects of Influence of Low Dose Radiation on Reserve of Defensive Functions of Hematopoiesis: Biomedical Data and Risk Assessment

V. Janenko, K. Atoev, V. Khmelovsky, O. Vorobiev, and V. Klimenko. Ukraine

Study of Remote Consequences of Chernobyl Accident and Prevention By Using Antioxidant Preparations

N. Oganesian, I. Emerit, A. Pogosian, K. Asrian, and A. Carapetian. Armenia

Biological Antioxidants of the Dead Sea for the Treatment of Local Radiation Lesions

N. Kuhyna, A. Tsyb, M. Bardychev, V. Andreev, V. Berdov, and F. Lyass. Israel and Russia

Spa Treatment and Recuperation in Israel for Participants In the Elimination of Chernobyl

A. Chernovsky, A. Godovich, F. Lyass, I. Shapiro, E. Krakov, and G. Markarov. Israel and Russia

13:00 - 14:00

Lunch (Menza)

14:00 - 19:00

Outing to Sde Boker and to Ein Ovdat

20:00

Departure for a Nabatean Dinner at Mamshit (Ancient Nabatean City) - Optional
**Thursday, November 7, 1996**

### SYMPOSIUM 9: OCCUPATIONAL AND CHRONIC EXPOSURE

**Sonnenfeldt Auditorium**

**Chairs:** B. Gold, Israel, and D. Goldsmith, USA

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<td>Combined Effect of Radiation and Other Agents</td>
<td>W. Burkart, Germany</td>
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<td>08:55 - 09:20</td>
<td>The NASA Space Radiation Health Program</td>
<td>W. Schimmerling, USA</td>
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<td>09:20 - 09:45</td>
<td>Joint Cancer Risks Among Workers Having Silica, Smoking and Radon Exposures Must Be Examined</td>
<td>D. Goldsmith, and J. Goldsmith, USA and Israel</td>
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<td>09:45 - 10:10</td>
<td>A Study of Deterministic Health Effects of Radiation Exposure in Chelyabinsk: 65 Nuclear Workers</td>
<td>N. Wald, USA</td>
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10:10 - 10:30

**Coffee Break**

### SYMPOSIUM 10: CONSEQUENCES OF THE CHERNOBYL EXPOSURE

**Sonnenfeldt Auditorium**

**Chairs:** J. Iscovich, Israel, and T. Hakulinen, Finland

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<td>UACOS: The Ukrainian/American Chernobyl Ocular Study</td>
<td>B. Worgul, USA</td>
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<td>11:45 - 12:10</td>
<td>Chernobyl: 10 Years After</td>
<td>A. J. Gonzalez, Austria</td>
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<td>12:10 - 12:30</td>
<td>Lessons Learned in the Study of Immigrants to Israel Who Came from Areas of Russia, Belarus and the Ukraine Contaminated by the Chernobyl Accident</td>
<td>M. Quastel, J. Goldsmith, J. Cwikel, L. Merkin, V. Wishkerman, S. Poljak, E. Kordysh, I. Emerit, and G. Kramer, Israel</td>
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### SESSION 11: RISK ANALYSIS AND HEALTH POLICY

**Sonnenfeldt Auditorium**

**Chairs:** J. Goldsmith, Israel, and K. Atoev, Ukraine

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<td>Risk Assessment of Radiation Effect on Immune and Endocrine System</td>
<td>K. Atoev, V. Janenko, V. Rykhtovsky, and E. Kostelnyak, Ukraine</td>
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<td>Estimation of the Long-Term Internal Exposure of the Russian Population Due to Radiation Accidents</td>
<td>M. Balanov, G. Bruk, and V. Shutov, Russia</td>
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<td>Incompatibility of Individual and Population Risk Estimations for Radiation</td>
<td>J. Goldsmith, Israel</td>
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<td>Analysis of Errors Occurred for Assessment of Health Status In Individuals Involved In Radiation Accidents</td>
<td>A. Guskova, Russia</td>
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<td>Modern Approaches to Implementing Radiation Protection Measures for People Residing In the Contaminated Areas of the Republic of Belarus</td>
<td>V. Ternov, I. Vasiljeva, J. Kenigsberg, Belarus</td>
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<td>Analysis of Medical Consequences of Radiation Accidents (Review of Publications In the Journal, “Medical Radiology and Radiation Safety”)</td>
<td>S. Yarmonenko, Russia</td>
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*Abstract not Submitted*
12:30 - 13:50  SESSION 12: RADIOBIOLOGY AND RADIOPROTECTION  
Hall B

Chairs: E. Riklis, Israel, and R. Neta, USA

Special Discussion: Perspectives of Radiobiology
With I. Tuari, IAEA, Vienna; E. Riklis, Israel and B. Laster, USA

Antioxidant (Ubiquinone-9) Protection of Immune System and CNS Under Chronic Low Dose Irradiation
E. Novoselova, N. Semiletova, V. Makar, T. Semenova, and N. Medvinskaya, Russia

Biologic Basis of Hyperthermia In Cancer Treatment: Investigations of Blood Oxygen Mechanisms During Hyperthermia
V. Zinchuk, Belarus

Radiation Accelerates the Terminal Differentiation of Senescent Human and Mouse Fibroblasts
O. Kvitko, L. Zhukova, and I. Koncva, Belarus

Low Dose-Rate Ionizing Radiation-Induced Disorders of K+ Transport Modulation By Serotonin In the Nervous Tissue
I. Kulikova, and A. Dvoretsky, Ukraine

Molecular Level Study of Functional Disorders in the CNS After Low Dose Irradiation
T. Ananieva, and A. Dvoretsky, Ukraine

Antimutagenic Prevention and Modulation of Individual Radiosensitivity With Pharmaceutical Preparations
A. Vaglenov, A. Karadjov, E. Yaneva, V. Petkova, and S. Laltchev, Bulgaria

13:50 - 14:50  Lunch (Menza)

14:50 - 16:20  PANEL DISCUSSION: RISK ANALYSIS
Sonnenfeldt Auditorium

Chairs: E. Lubin, Israel, and V. Bond, USA

A Markedly Different Approach to Risk Assessment
V. Bond, USA

Modern Radiation Policy: Prevention, Monitoring and Compensation
B. Modan, Israel

The Probability of Causation as a Basis for Compensation Scheme for Radiation Linked Diseases
T. Schlesinger, Israel

Who Radiation Emergency Medical Preparedness and Assistance Network (Rempan)
G. Souchkevitch, WHO, Switzerland

A Decade After Chernobyl: Results, Problems and Tasks
A. Tsyb, Russia

16:20 - 16:40  Coffee Break

16:40 - 17:40  SUMMATION
Sonnenfeldt Auditorium

Chairs: M. Quastel, and J. Goldsmith, Israel

Brief Subject Summaries
E. Riklis, Israel (Radiobiology)
J. Cwikel, Israel (Psychosocial)
E. Cardis, France (Long-Term Effects)

Summation of Entire Conference
K. Baverstock, WHO, Italy

20:00  Closing Banquet, Desert Inn Hotel (Optional)

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<td>Thyroid Gland in Children of Ukraine in 10 Years After the Chernobyl Accident</td>
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<td>V. Bolshakov, D. Lyubashevsky</td>
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Adaptive Response of Blood Lymphocytes of People Living in Regions Contaminated with Radionuclides
G. Afansjev, I. Pelevina, N. Semenov. Russia

Methods of Biological Dosimetry in Persons Exposed to Conditions Associated with the Chernobyl Accident
A.B. Semov, E.L. Iofa, V.A. Shevchenko. Russia

Late Effects in Cell Populations after Low Level Irradiation
I. Pelevina, V. Gotlib, N. Semenov. Russia

Specific and Non-Specific Reactivity of Small Mammals Inhabiting Radiocontaminated Territory for One Hundred Generations, as Compared to those from Fluorocontaminated Areas
M. Chibiryak, N. Lyubashevsky. Ekaterinburg. Russia

The Genetic Adaptation of Small Mammals to a Radiocontaminated Environment as the Basis for an Extrapolation to the Health of Human Descendants
N. Lyubashevsky, M. Chibiryak, E. Grigorkina, V. Starichenko. Russia

Individual Features of Skeletal Metabolism of Radionuclide (Theoretical and Applied Aspects)
V. Starichenko, N. Lyubashevsky. Russia

Reconstruction of the Dose accumulated in inhabitants of Russian Regions Contaminated with Radionuclides as a Result of the Chernobyl Accident

Change of Oncological Characteristics in Rats after Chernobyl Accident
N. Nedopitanskaya, E. Bagley, E. Reshavskaya N. Kornuta. Ukraine

Individual Accumulated Doses in Persons Irradiated as a Result of the Chernobyl Accident Determined by Tooth Enamel EPR Technique
I.A. Ivannikov, V.G. Skvotov, V.F. Stepanenko, A.F. Tsyb, V.A. Sokolov. Russia

Aberrant Lymphocyte Blood Level, Immune Competence, Health, Tumor Development and Life Span of Animals after Radionuclide Corporation
A. Monakhov T. Yakovleva, V. Anisimov. Russia

SPECT Reconstruction From a Small Number of Projections
C. Niculue C. Turnacu, T. Cracinescu. Romania

Rn-220 and Rn-222 Risk Assessment: Methodology and Results
I. Yarmoshenko, M. Zhukovsky, a. Ekidin, a. Vozhakov. Russia
Radiation and Non-Radiation Risks in the Urals
A. Ekidin, I. Yarmoshenko, A. Vozhakov, Russia

Changes in Electrolyte and Trace Element Metabolism of the Chernobyl Clean-Up Workers
V. Zaichick, L. Lyasko, Russia

Effective Radiation Dose to the Patient from Radonuclide Diagnostic Procedures in a Nuclear Medicine Department
E. Dzjuk, J. Chas, M. Marciniak, Poland

The Study of Radiation Damage and Repair of Hypoxic Tumor and Normal Cells by the Micronuclear Test
M. Levitan, S. Kosin, L. Eidus, Russia

Clinical Findings of Autoimmune Thyroiditis in Children Exposed to 1-131
I.M. Khmara, H.V. Shemajkena, M.V. Tchajkovsky, Belarus

Chromosome Mutations in Rodents Inhabiting the Urals Regions Contaminated by Radioactivity

The Late Cytogenetic Consequences in Human Victims of the Chernobyl Catastrophe
O. Belyakov, A. Bogomasova, V. Kravtsov, I. Vorobbtsova, Russia

Effects of Low Dose Radiation on Fluorescent Properties of Liver Microsomes
V. Buko, A. artukevich, a. Maskevich, L. Zavodnik, K. Ignatenko, Belarus

Investigations of Internal Exposure to Teeth Tissues by autoradiography, Thermoluminescent Dosmetry (TID), Electron Spin Resonance (ESR), Spectroscopy and Mathematical Methods
E. A. Shishkina, E.A. Ignatiev, N.M. Lyubashevsky, a.A. Romanyukha, T.A. Betenckova, Russia

Long Term investigation of the Chernobyl-Originated Cesium-137 in Different Soil Types
P. Szerbin, Hungary

Reliability of the Retrospective EPR Dosimetry with Tooth Enamel
A. Brik, V. Radchuk, Ukraine

Genotoxicity Assessment of Environmental Radiochemical Exposures
S.D. Ivanov, E.G. Kovanko, Russia

Inhalation of the Chernobyl Aerosol as a Pathway for the Public Exposure
V.A. Kutkov, P.A. Vlasov, A.M. Skryabin, R.I. Pogodin, Russia

Lipoperoxidation, Spontaneous Chemoluminescence and Antioxidant Activity of Blood Serum and Tissues in Stress
V. Baraboj, S. Zhadko, Ukraine

Belarussian Mass Media and Post Chernobyl Public Stress Formation
V.S. Lazarev, E.P. Iivanov, Belarus

Nature of X-Ray induced Mutations in Chronically Unstable Genetic Systems of Drosophila Melanogaster

Detection of Groups with Genetically Determined Cancer Risk Among the Population Living in Chernobyl Radiocontaminated Areas
G. Porubova, E. Guzenko, G. Lobko, Belarus

Chernobyl Digest-interdisciplinary Information Bank of Chernobyl Problem Investigations (Belarus, Russia, the Ukraine)
E.N. Makeeva, S.E. Dromashko, I.A. Panich, Belarus

Lymphocytes of Slightly Exposed in Terms of Patters of Expected Diseases

Incidence of Disease among Children Exposed to Radiation as a Result of the Chernobyl Accident in the Republic of Belarus
L. Lomat, a. Okeanov, M. Quastel, S. Rozin, G. Galburt, Belarus and Israel

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The Effect of Internal Irradiation With I-131 on Thymic Function and Therapeutic Possibilities
AG.A. Zamotaeva, Ukraine

Functional Thyroid Pathology and Hypoprolactinemia in Chernobyl Accident Clean-Up Workers
E.L. Strukov, L.B. Dryguina, A.M. Nikiforov, Russia

Tumour Markers in Clean-Up Workers of the Chernobyl Accident Workers in the Late Post-Accident Period
L.B. Dryguina, E. Strukov, R. Fedortseva, Russia

Non-specific Resistance in Infants from Radioactively Unfavorable Regions of the Republic of Belarus
M.M. Zafranskaya, Belarus

To the Issue of Forms of Social Psychological Care
T.N. Melnichouk, Russia

Attitude Specificity and Psychological Distress of the Population Involved in the Accident
D. Plyplina, Russia

Use of Computer Technology in Assessing Hazard of the Combination of Radioactive and Chemical Contamination
E.A. Podrushnyak, A.N. Stroy, Z.L. Voloshchenko, L.M. Golovina, M.V. Naboka, Ukraine

Cytogenetic Damage in Peripheral Lymphocytes of Teenagers From the Radioactive Contaminated Territories of Ukrainian Polissia
A.P. Kravchuk, E.S. Zubko, L.V. Boltina, A.N. Ohrimovich, Ukraine

Territories of Russia Polluted on Account of the Chernobyl Accident: Thyroid Cancer in Adults and Children
L. Remennik, V.I. Chissov, V.I. Mokina, L. Scheplyagina, Russia

Adaptation Defence Reactions of Children who were Exposed to Radiation
G.V. Plaksina, G.V. Rimarchuk, L.A. Scheplyagina, Russia

Model for Optimal Follow-Up Collection
G. Molan, M. Molan, Slovenia

The Hematological Effects of Low-Dose Exposure
N.I. Lozitska, Ukraine

Properties of the Hot Particles Discovered in Kiev after the Chernobyl Accident
V.G. Lozitskij, Ukraine

Whole Body Cs-137 Content in Slovak Population at the End of the Decade after the Chernobyl Accident
M. Fulop, A. Lahham, P. Ragan, Slovakia

Method of Biological Dosimetry in Chernobyl Conditions
S. Stajic, V. Vjetrov, Yugoslavia

Analysis of Patient Doses during Mamography in Slovakia
D. Nikodemova, V. Laginova, I. Gomola, Slovakia

A Model for Estimation of Morbidity Dynamics among Populations affected by Radiation
A.I. Michalski, W. Morgenstern, V.K. Ivanov, Russia and Germany

Use of Sorbents and Antioxidants for Prophylaxis and Therapy of Children Living in Zones Contaminated with Radionuclides as a Result of the Chernobyl Accident
S.V. Vekovshinina, V.L. Kulinichenko, Ukraine

Effect of Transfected EBV EBNA-1 on the Radiation Survival Curve of BaLB/C 3T3 Cell Line
Y.S. Tyan, M.M. Wu, S.K. Lee, China (ROC)

An Adaption-like Response to the Induction of Chromosome Aberrations in Rabbit Peripheral Blood Lymphocytes by an Acute Exposure (3 Gy) Following Low Level (0.5 Gy/Day) Chronic Exposure
P. Fedorocko, P. Brezani, N.O. Mackova, Slovakia
Thyroid Status in Children Living in Radioisotope Contaminated Region of Russia (Consequent to the Chernobyl Accident)

Mobilization of Cs-134 By Prussian-Blue in Normal and Pregnant Rats Continuously Exposed to Radiocesium.
J. J. A. Gachalyi, J. Namenyi, Hungary

Remote Consequences of Radiation on the Central Nervous System of Primates and Men
N. Kholodova, G. Kuznetsova, Russia

Thyroid State in Exposed Children and Adolescents with Acute and Chronic Radiation after Chernobyl Accident
M. Kapilyeva, Belarus

Fluorescent Study of Immune System Cells under Low Doses of Gamma Irradiation
L. A. Sergiyevich, Russia

The Basic Question of Urals Radioecology
N.A. Karnaukhova, Russia

Health Effects of Super High Frequency Electromagnetic Fields
A. Smolya, Yu. Dumansky, Ukraine

Multiaberrant Cells in Chernobyl Liquidators
N. Rivkind, V. Dorokhov, N. Schklovsky-Kordi, Russia

Radiation Dose and the Health of Chernobyl Liquidators
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ORAL PRESENTATIONS
The recent availability of information about the consequences of radiation exposures in the former Soviet Union add new insights and possible answers to several important questions regarding radiation and its impacts on occupational and public health. The 1986 Chernobyl accident, now 10 years old, has initiated a major and early increase in childhood thyroid cancer resulting from ingestion of $^{131}$I by young children living in the heaviest contaminated areas of Belarus, Ukraine, and Russia. There have been no significant additional cancer or other medical effects reported to date in the affected populations and clean-up workers. A major psychological stress has been observed in those thought to be exposed, independent of radiation dose.

The early days of the atomic energy program in the former Soviet Union were accompanied by some unfortunate events. Their first atomic blast in Semipalatinsk in 1949, exposed more than 25,000 people to significant doses of fission products, especially $^{131}$I. The late 1940s and early 1950s saw the evolution of the nuclear materials production facilities near Chelyabinsk in the South Ural Mountains, and resulted in major releases to the environment and significant overexposure to thousands of workers. Chronic radiation sickness in exposed workers was observed early on and increases in leukemia and cancers have been documented. Especially unique are the series of plutonium inhalation related lung cancers and fatalities in workers who were exposed in that first decade. Villagers downstream from the plant consumed high levels of $^{137}$Cs and $^{90}$Sr and manifested increases in leukemia from internal and external exposures. Although the 40-year-long data base for retrospective dosimetry and epidemiology studies are just beginning to be integrated and evaluated, it appears that there may be graded, significant dose rate amelioration factors for cancer and leukemia risks in workers and the general population relative to the risks derived from the Japanese A-bomb survivors. Even for Pu-induced lung cancers in workers, such a dose rate effect may be evident. The long term consequences of chronic radiation sickness are now being described for the first time and also have a 4 decade follow-up.

These lessons give us new insights about the consequences of protracted radiation at high and low doses and rates. These unique findings may provide a sound basis for more realistic, and possibly lower, risk estimates for occupational health in activities related to medicine as well as the handling of nuclear materials and nuclear facility decommissioning, decontamination, and demilitarization.
Both the Radiation Effects Research Foundation (RERF) and a host of radiation protection committees are firmly of the opinion that a lengthy follow-up of A-bomb survivors has provided the world with reliable sources of risk estimates for genetic, teratogenic, and carcinogenic effects of ionizing radiation. On this assumption, the risk of brain damage is negligible for exposures within 8 weeks of conception, and the cancer risk is lower for exposure after than before 30 years of age. However, independent analyses of A-bomb data have found evidence of unsuspected biases in the RERF study cohorts, and made new uses of the records of acute injuries of 5-year survivors. When added to other variables, the injury data made it possible to see that sensitivity to cancer effects of A-bomb radiation was much greater towards the beginning and end of the life span than during the intervening years. The very different impression left by repeated RERF analyses of A-bomb data shows that we are urgently in need of more reliable sources of risk estimates for low dose effects, and has also given a strong boost to the Oxford Survey of Childhood Cancers (OSCC data) and surveys of workers in the US nuclear industry (Hanford and Oak Ridge data).
CONSIDERATIONS IN ASSIGNING DOSE BASED ON IN VIVO COUNTING.

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The dose estimate based on the measurements from an in vivo count can only be as accurate as the results obtained from that measurement. If the in vivo measurement grossly underestimates the amount of activity present, then the dose will be underestimated by a corresponding factor and the resulting health risk will be predicted too low. If, on the other hand, the in vivo result is overestimated, the dose estimate will also be overestimated by a corresponding amount, and the health risk will be inflated. This could cause severe anxiety in the subject and, consequently, lead to other health problems.

The Human Monitoring Laboratory (HML) has been investigating the effect of heterogeneous lung depositions on the result of an in vivo count. A lung counter is usually calibrated using a realistic torso phantom that contains lungs that have the radioactivity distributed homogeneously. However, in occupational or accidental exposures the radioactive contaminant is often associated with aerosol particulates. These particulates do not deposit themselves homogeneously when inhaled and the deposition pattern is directly related to particle size, lung function and working conditions.

Monte Carlo simulations have been used to estimate the errors that can be encountered during lung counting if it is assumed that the deposition is homogeneous, when in fact it is not. A virtual chest phantom was created and four germanium detectors were modelled to correspond to the lung counting system in the HML (70 mm diameter by 30 mm thick). The lungs were loaded with activity corresponding to 70 deposition patterns and 1,000,000 photons were followed. The detector efficiencies for 20, 40, 60, 120, 240, 660, and 1000 keV were calculated for a homogeneous deposition and these efficiencies were used to estimate the bias when the deposition was heterogeneous. A bias of 800% was not unusual.

Whole body counting is also prone to errors. These can arise from the activity distribution and/or size of the subject. The latter is highly geometry dependent and, for example, a bias result of 200% can be obtained when measuring children in a chair geometry using a calibration factor based on reference man. The error introduced by assuming the activity is homogeneously distributed, when in fact it is not, is to a lesser extent also geometry dependent. Sometimes the error can approach 100%, however, most types of whole body counter will generate an error much lower than this.

Thyroid counting is the least prone to error. If the measurement is performed correctly, biases can usually be kept well below 100%. However, if the measurement is made with a collimator or if the detector is in contact with the subject’s neck biases exceeding 200% can be obtained.

All three in vivo techniques will be reviewed and the sources and magnitudes of the errors, which will affect the dose estimate and the predicted health risk, will be discussed.
THYROID DOSE RECONSTRUCTION IN THE UKRAINE: 10 YEARS OF STUDY.

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Present estimations of thyroid doses are based on \(^{131}\)I activity measurements in thyroids and \(^{131}\)I activity measurements in milk, air and water. Additionally correlations of the thyroid doses with \(^{137}\)Cs deposition and locations were used to assess doses in the territories without monitoring measurements. Several population groups are considered:

- People with short time period of intake (leaving contaminated area within 5 days);
- People with long time period of intake (being not evacuated and staying in contaminated area longer than 5 days);
- People evacuated, but staying in contaminated area longer than 5 days;
- People exposed in utero;
- People from "non-contaminated" area;
- Liquidators.

150,000 \(^{131}\)I activity measurements in thyroids are basic data for the dose reconstruction in the Ukraine. These measurements were performed mainly among people from an area up to 100 - 150 km far from Chernobyl. In most cases only one single measurement for each person was carried out. Quality and uncertainties of these activity measurements were assessed and a model for the individual dose estimations was developed. This model include:

- assumed deposition on the considered territory occurred during one single day;
- intake for the short-time period of stay on the contaminated territories represented by a single intake function;
- intake for the long-time period of stay on the contaminated territories represented by the time-dependent milk contamination;
- reference anatomical, metabolical and radioecological parameters.

On the basis of obtained estimations the age-dependent thyroid doses were assessed for areas with direct measurements. The results were extrapolated to the territories without direct measurements using the correlation with \(^{137}\)Cs deposition and coordinates of the locations.

Further investigations will be connected with:

- Development of a model for the individual thyroid dose reconstruction on the basis of \(^{131}\)I activity measurements in thyroids and realistic intake function
- Development of a model for the individual thyroid dose reconstruction on the basis of questionnaire data
- Development of a model for the thyroid dose reconstruction on the basis of \(^{129}\)I activity measurements, atmospheric dispersion model and questionnaire data.
COLLECTIVE BIO-DOSIMETRY AS A DOSIMETRIC "GOLD-STANDARD": A STUDY OF THREE RADIATION ACCIDENTS

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Quantification of the biologically relevant dose is required for the establishment of cause and effect between radiation detriment or burden and important biological outcomes. Most epidemiological studies of unanticipated radiation exposure fail to establish cause and effect because of an inability to construct a valid quantification of dose for the exposed population. No one bio-dosimetric technique (biophysical or biological), however, meets all the requirements of an ideal dosimeter. The present study combines new results with previously published data in order to establish a collective bio-dosimetry for the victims of three radiation accidents. This process is necessary as planning of a comprehensive dosimetry is rarely done at the initial stages of a radiation accident. Radiation dose and distribution for acute exposures is estimated by physical measurements using Electron Spin Resonance (ESR), biologic dosimetry and computer simulation. ESR is used to detect free radicals produced by radiation in dental enamel and clothing of the victim. Biologic techniques study chromosome aberrations in blood lymphocytes and the kinetics of granulocyte production following the exposure.

In the present study one victim of the Chernobyl nuclear accident, one victim of an unspecified accident involving gamma and neutron radiation, and one victim of an accidental exposure to a Cobalt-60 sterilization source, were studied for radiation dose determination.

The ESR calibration curve technique determined that the victim of the Chernobyl nuclear accident was exposed to 8.0±1.0 Gy. This result agrees well with dose estimates using the ESR additive dose technique and cytogenetics. This individual, a fireman who fought the fire in the Chernobyl reactor from the roof of the building, died of acute radiation sickness.

The second victim sustained an accumulated absorbed dose to dental enamel of 7.2±1.0 Gy, as determined by the ESR calibration curve technique. This result is in good agreement with ESR additive dose measurements, computer simulation and personal dosimetry. Neutron radiation was estimated to account for 25% of the total dose. This individual lived for 17 years following the accident.

The third victim reported on here entered a gamma-radiation chamber used for sterilizing medical supplies. The Cobalt-60 source (specific activity, $8 \times 10^5$ Ci) had not retracted properly. The total exposure time was estimated at 1 to 2 minutes. Dose estimates using computer modeling, chromosome aberrations in lymphocytes, blood granulocyte kinetics, pooled biologic dose estimates, and ESR in dental enamel and clothing material (using the additive dose technique), indicated an exposure range of 9 to 16 Gy. The ESR calibration curve technique in dental enamel determined the exposure to be 13.7±1.4 Gy, in good agreement with the other estimates. Although, for the accidents discussed, there was good agreement between the ESR calibration curve and additive dose techniques, an investigation indicated that there can be significant variability in the ESR sensitivity of enamel to radiation between teeth of different individuals.

The 50% lethal dose to bone marrow in humans is 3 to 4 Gy. Hematopoietic suppression is considered irreversible with doses exceeding 8 Gy. Partial hematopoietic recovery was achieved with the third subject, however, using supportive measures, transfusions, and hematopoietic growth factor but no transplants. The patient died 113 days following the accident from radiation pneumonitis infection instigated by diffuse and focal fibrosis of the lungs.

There are abundant reports in the scientific literature that present reasonable results for absorbed and biologically relevant doses associated with radiation accidents. In each case, the strengths and weaknesses of the techniques used are exploited. However, dosimetric external validity requires some concept of dosimetric "truth." Consensus may be the best approximation to this truth. Thus, it is important to accumulate and analyze studies that apply collective dosimetry to the analysis of acute radiation exposures or to lower levels of radiation exposures found in occupational and general populations at risk.
HEALTH CONCERNS RELATED TO RADIATION EXPOSURE OF THE FEMALE
NUCLEAR MEDICINE PATIENT

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The female nuclear medicine patient brings special concerns to the consideration of the balancing of risks and benefits of ionizing radiation in this application. Being slightly smaller than her male counterpart, on average, she tends to receive higher radiation doses to most organs given the same administrations of radioactive materials. As her gonadal tissue is located within the body, close to many abdominal organs (including the intestines and urinary bladder), it usually receives a higher absorbed dose than the corresponding tissue in males. In addition, absorbed dose to the female breast is more strongly related to cancer formation than in breast tissue of males. Most anthropomorphic phantoms used in internal dosimetry readily account for these differences (except that male breast dose is not well modeled); however this paper reports a systematic review of these differences in many nuclear medicine procedures and their potential implications.

An entirely separate area of importance exists when the patient may be pregnant or nursing. In this case, additional safety concerns for the unborn child or breastfeeding infant arise. Our center has performed systematic studies of (1) the types and quantities of radiopharmaceuticals routinely administered to women of childbearing years, (2) current knowledge of the amounts of different radiopharmaceuticals that may cross the placenta, as reported in human and animal studies, (3) absorbed dose estimates for the fetus at all stages of pregnancy, using the pregnant female phantom series (ORNL/TM-12907, 1995), (4) current knowledge of the fractions of administered radiopharmaceuticals which may appear in the breast milk of the lactating patient, and (5) absorbed dose estimates to newborns and 1-year-old infants from ingestion of radiopharmaceuticals excreted in breast milk assuming different periods of time that breastfeeding may be interrupted.

In this talk, all of these areas of concern for the female nuclear medicine will be addressed, with the pertinent results to date reviewed, and recommendations for dealing with practical aspects of the related safety issues discussed.

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PHARMACOLOGIC APPROACHES TO PROTECTION AGAINST RADIATION-
INDUCED LETHALITY AND OTHER DAMAGE

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Studies on mechanisms of radioprotection are leading to a more rational use of protectors for
different applications. In considering the feasibility of radioprotectors that act through various
mechanisms, it is necessary to distinguish the application desired, e.g., protection against
accidental acute high-dose radiation injury, low doses over a long period of time, or high-LET
radiation during space flight, as well as protection of normal tissues of cancer patients who are
undergoing therapy. Protectors can be generally classified as either sulfhydryl compounds,
other antioxidants, and receptor-mediated agents (e.g., bioactive lipids, xanthine derivatives,
immunomodulators, and cytokines). This review will focus on comparative radioprotection
and toxicity studies in mice using synthetic chemical agents, and chemical and biological
mechanisms of protection by the various agents will be discussed. Studies on gamma and
neutron-irradiated mice indicate that the phosphorothioates WR-2721 and WR-151327 provide
the best protection against hematopoietic and gastrointestinal damage compared to other
sulphhydryl agents and other classes of radioprotectors. Other animal data suggest that low
doses of phosphorothioates may provide protection against both radiation-induced mutagenesis
and carcinogenesis. The superiority of phosphorothioates appears to be related to their high
affinity for DNA, and the similarity in structure of phosphorothioate metabolites to
polyamines, and consequent effects on processes related to DNA structure and synthesis.
Examples of the potential utility of combinations of phosphorothioates with pharmacologic
agents approved for other purposes will be presented. Drug tolerance levels are available from
clinical trials using WR-2721 (ethylol) and provide a basis for discussions on the disadvantages
of phosphorothioate administration outside of a clinical setting. Low doses of chemical
protectors may nevertheless be potentially useful in accident scenarios when used in
combination with therapeutic measures. The assessment of potential prophylactic measures
should take into account compatibility with therapeutic measures currently in use or that might
be available in the near future for the treatment of radiation injuries. These include antiemetics,
purified stem cells, granulocyte colony-stimulating factor and other cytokines.
ENHANCED DNA REPAIR—A NEW MODALITY FOR IMPROVED RADIOPROTECTION AND PHOTOPROTECTION

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Classical radioprotection which began in 1949 by Harvey Patt, has reached a deadlock where the maximum protection factor attained by various chemicals is around 2. Furthermore, the compound considered to be the best, WR-2721, is too toxic to be of general use in emergency situations.

A more important mode of protection is offered by the biological parameters of DNA repair capacity, enabling cells with a high repair capacity to be far more resistant to radiation than cells with deficient repair capabilities.

A formula of enhanced DNA repair was offered in 1981 by Riklis as a model for improved protection, combining DNA repair capabilities with chemicals that enhance these capabilities. This property of enhanced repair is particularly of importance for protection from the genetic effects of low level and chronic radiation due to its antimutagenic effects.

The enhancement of DNA repair was first demonstrated by the addition of WR-2721 when added even after exposure to ionizing radiation and to UV radiation (Riklis 1983). Later, some natural non-toxic compounds were found to have the same effect. Thus the vitamin nicotinamide at a low concentration of 3 mM can enhance DNA repair synthesis with up to 5 fold dose dependent increase in $^3$H-thymidine uptake into damage sites.

In solar radiation, UVA mimics the effects of ionizing radiation in terms of oxidative damage, which cause DNA single strand breaks. UVB, like UVC radiation produces specific photoproducts which are repaired through excision repair (Riklis 1965). Recently, a combination of nicotinamide and certain antioxidants was developed, affording a unique system for enhancement of DNA repair after exposure to either solar radiation or ionizing radiation.

Such a combination has been included in a preparation named EDNAR (Enhanced DNA Repair), which provides better protection from sun light, a skin protection system without the need for chemical filtering sunscreen. The lotion shows also antimutagenic and anti-inflammatory properties. This offers a new dimension to solar protection and to skin protection from radiation (Riklis 1995). The possible internal use of EDNAR to replace classical (but toxic) radioprotectors is being considered.

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The goal of radiation protection is to limit the probability of radiation induced diseases in persons exposed to radiation and their progeny, to a degree that is reasonable and acceptable in relation to the benefits from activities that involve such exposure.

Modern radiation protection practice requires that exposure be kept to levels which are as low as reasonably achievable (ALARA).

The implementation of a radiation safety program depends also upon the judgments and perceptions of the radiation safety personnel.

Persons employed or involved with the use of ionizing radiation in medicine are one of the largest groups of occupational exposed individuals. Often, there is also a direct relationship between the reduction of exposure to patient and reduction of the exposure to workers.

The radiation exposure in medicine is mainly in three departments:
1. Diagnostic Radiology: Fluoroscopic procedures, radiography and special examinations like angiography, cardiac catheterization and others.
3. Oncology: Brachytherapy, external beam units, administration of isotopes for metastatic lesions in bone.

Since most procedures that cause radiation exposure in medicine are clearly justified and there is a direct benefit to the exposed individual, less attention has been given to the optimization of protection in medical exposure than in most other applications of radiation sources.

In the 9th International Congress of IRPA, held in Vienna on April 14-19, 1996, the optimization and justification of medical exposure received increasing attention with the realization that there is considerable potential for reducing doses to the patient and medical workers.

The Medi-SMARTS system provides a useful tool for the qualified health or medical physicist, to evaluate the patient, personnel and family exposures in the hospital, especially in the nuclear medicine, and oncology departments with some potential aspects in diagnostic radiology. The Medi-SMARTS system is designed to measure and collect radiation data automatically and continuously from workplaces.

Radiation is monitored by variety of detectors in order to obtain detection of different radiation sensitivities and energies. Results are transferred from a Data Process Unit (DPU) by a RS-485 communication network. Each DPU can present the level of radiation locally, execute local alarms etc. The data is collected by a PC located in the control room. Special user friendly software displays the results on-line on a room map, saves data in files, process and print results and reports. All information is documented in the computer for future analysis and investigation.

The Medi-SMARTS will be presented in detail at the International Conference on Radiation and Health - Beer Sheva, Israel November 3-7, 1996.
RADON IN SCHOOLS AND OTHER PUBLIC BUILDINGS: WHEN RISK MANAGEMENT CAN BE MORE STRINGENT THAN RISK ASSESSMENT

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The Jerusalem Talpiot School Radon Episode (1) was a sentinel event calling attention to the need for establishment and implementation of a nation-wide policy on radon exposures for school buildings, community and recreation centers, public buildings, day-care centers, live-in institutions, and multiple use buildings. In Talpiot, community initiative prompted the discovery of extremely high radon levels in the school building and the discovery of a “hot” room in which a 39 year old female teacher with metastatic breast cancer had worked for some 15 years; another worker, a janitor in his 50’s with multiple myeloma had worked much of the time in the basement. Another school in the same area was also found to have “hot spots”. Geologic maps of phosphate deposits in Israel and the West Bank suggest that many other sites, including residential dwellings, could be at risk from indoor radon exposure, notably east of the Jerusalem watershed. The hypothesis that radon leaks from ground sources resulted from release of new fissures produced by a recent earthquake could not be tested because baseline data was lacking.

A nation-wide policy first has to define threshold exposure levels for control and emergency closure. Risk assessments based on interpolation from uranium miner studies and community case-control studies vary; the EPA Standard (150 Bcq m-3) has been criticized for being both too stringent (based on lifetime indoor exposures) and too lax (accepts too high a cancer risk; ignores possibly special risks of children). But the fact that exposures in most points in the Talpiot School could readily by brought down to levels seen nation-wide (30-40 bcq m-3) using standard recommended control procedures states the case for a uniform nation-wide standard below 75 bcq m-3. Considerations of prudence, including prevention of the presumed special risks of children, support the case for this recommendation, because epidemiologic studies still lack the power and precision needed to define a health-based time-weighted threshold for radon exposure.

A community radon standard for public buildings has to include surveillance and monitoring routines, prioritization of high-risk areas, construction specifications for high-risk areas with phosphate deposits, remedial guidelines, follow-up evaluation, quality control supervision of laboratories, information delivery based on right-to-know and community participation, education on the special risks from radon for smokers, and possibly governmental guarantees of compensability for future lung cancer victims with past childhood exposures to “hot” environments. Since much of the West Bank area of the Palestinian Authority sits on phosphate deposits, joint projects for surveillance may be indicated.

**Rn EMANATION FROM ROCK UNITS AND INDOOR LEVELS IN ISRAEL - AN INTEGRATED APPROACH IN ASSESSING RADON-PRONE AREAS**

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The objectives of the recent study are: a) comparison between indoor radon measurements and underlying rock formations, denoting “radon-prone areas” from these two complementary view points; b) obtaining a statistically well-founded estimation for the radon levels to which the populations in such radon-prone areas are exposed, and hence - the expected rise in mortality rates in those areas.

A map of radon emanation from rock units in Israel had been published, (Shirav et al, 1993), indicating regions of high radon potential. From a geological/geochemical point of view, supported by alpha-track measurements of the pore gas, rocks belonging to the Mount Scopus Group (upper Cretaceous age), have the highest radon potential (average ~90,000 Bq/m³), due to an appreciable amount of phosphorite and uranium (up to 150 ppm). These rocks are exposed over approximately 25% of Israel’s area, with some heavily populated cities built on them.

All available indoor measurements which were carried out between 1989 and the end of 1994 (total of 31,842) were stored in a computerized file, indicating zip code and radon level in Bq/m³ units for each of them. The data were sorted according to zip codes, grouped into single populated areas, and geographical coordinates (Israel grid) were added to every location, as well as a geological code, indicating the rock formation which underlies the area. The arithmetic mean, geometric mean and the percentage of measurements higher than 200 Bq/m³ were calculated for 179 built-up areas, in which more than 80% of the Israeli population resides.

Analysis of the resultant comprehensive database, coupled with GIS (Geographical Information System) capabilities, shows a significant correlation between indoor radon level and underlying bedrock. The average radon level in buildings located on the Mount Scopus Group is 79 Bq/m³, compared to 50 Bq/m³ for all other regions. Estimating 75/25% ratio for personal indoor/outdoor stay, these values correspond to exposure levels of 61 Bq/m³ and 40 Bq/m³, respectively. For the majority (86%) of the locations built on these radon-prone rocks, 1-36% of the measurements exceed 200 Bq/m³ (the Israeli action level), whereas only in 45% of all other built-up areas, 1-21% of the measurements exceed this level.

Indoor radon levels (for low radon areas) computed from the recent database are in agreement with former publications (i.e.: Margaliot, 1993). The significantly higher radon level for radon-prone areas in Israel suggest an additional ~2.5-6.0% of lung cancer deaths due to radon exposure for residents of these regions (based on the BEIR IV model, 1988). This finding will be further compared with the Israel cancer registry.

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THE BODY CONTENT OF $^{210}\text{Pb}$: A MEASURE OF CUMULATIVE EXPOSURE TO RADON/RADON PROGENY?

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The content of the long-lived $^{222}\text{Rn}$ daughter $^{210}\text{Pb}$ in the human body has been proposed as a measure of cumulative exposure to radon/radon progeny for occupational and residential environments. However, there are various sources that contribute to the $^{210}\text{Pb}$ accumulation in the body. For a reliable interpretation of any measured $^{210}\text{Pb}$ value, it is imperative that the significance and variability of these different sources are sufficiently well understood. In this study, the accumulation of $^{210}\text{Pb}$ in the human body was modelled for a variety of exposure conditions, applying the most recent knowledge on lead metabolism in man.

The results indicate that for normal residential situations, cumulative exposure and hence dose and risk estimates for radon cannot be derived from the body content of $^{210}\text{Pb}$, since the short-lived $^{222}\text{Rn}$ daughters contribute only about 0.5 mBq per day or 2% of the total daily $^{210}\text{Pb}$ accumulation under these conditions (vs. 12% from the direct inhalation of $^{210}\text{Pb}$ and 86% from ingestion). Due to the necessary assumptions and the associated uncertainties in every component that contributes to the accumulation of $^{210}\text{Pb}$ in the body, such estimates seem to be of limited significance even in high radon environments. The largest uncertainty at increasing Rn levels arises from insufficient data on the direct inhalation of $^{210}\text{Pb}$ under these circumstances. Indoor measurements of airborne $^{210}\text{Pb}$ show a nearly proportional increase with equilibrium equivalent radon concentration (EEC). It therefore seems reasonable to expect significantly increased values of indoor $^{210}\text{Pb}$ air activities in many dwellings. The establishment of a relationship between the body content of $^{210}\text{Pb}$ and the cumulative exposure to short lived Rn daughters requires a more detailed knowledge of the short and long term behaviour of lead in the body, knowledge of the airborne concentrations of $^{210}\text{Pb}$ and short lived $^{222}\text{Rn}$ daughters in indoor atmospheres and their variabilities.
THE UNATTACHED FRACTION OF THE RADON PROGENY: AN IMPROVED METHOD FOR SIZE DISTRIBUTION DETERMINATION

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The exposure due to the inhalation of radon decay products amounts to about half of the annual dose received by the general population. The deposition in the human respiratory tract and thus the inhalation dose is strongly dependent on the size of the inhaled particles.

The size distribution of the airborne radon decay products is determined by production from radioactive decay, cluster formation with water vapour and trace gases, attachment to ambient aerosol particles, and deposition on room surfaces. The resulting size distribution of airborne radon progeny under realistic living conditions can be separated in two distinct modes: The ultrafine cluster or unattached fraction of 1-4 nm diameter and the attached mode associated with ambient aerosol particles in the diameter range of 200 to 400 nm. 30 to 90 percent of the inhalation dose is associated to the unattached fraction, depending on inhalation pattern and size characteristics of the ultrafine clusters. The knowledge of the size distribution in the ultrafine cluster mode is therefore necessary for a more precise dose estimation. Recent measurements showed a bimodal size distribution structure of the unattached fraction.

Size fractionating measurements in the nanometer size range are performed with diffusional methods, e.g. tube or wire screen diffusion batteries. Results of these measurements consist of the convolution integral of the size distribution and the penetration function of the instrument.

Non-linear approximation algorithms like the Simplex- or EM-algorithm are used to estimate size distributions of the unattached fraction which reproduce the measured values. The performance of these methods is unsatisfying, especially when a bimodal solution is needed. The lack of performance is due to the poor size resolution of the diffusional method, yielding a large amount of local minima for a wide range of parameter sets.

Therefore a random walk technique has been developed as alternative approach, which has been successfully tested with theoretical values and measurement results.
IN VIVO MEASUREMENTS OF $^{137}$Cs LONG TERM RETENTION IN INDIVIDUALS CONTAMINATED IN THE GOIANIA ACCIDENT

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A radiological accident occurred in September 1987 in the city of Goiania-Brazil, due to the exposure to a 50.9 TBq $^{137}$Cs source used for medical therapy. This accident resulted in internal and external contamination as well as irradiation of members of the public. Some people had radiation burns after rubbing the fragments of the source on their skin. Successive skin decontaminations were carried on until there was no external detection of $\beta$ radiation. In August 1990, with the objective of verifying the long term retention of Cs in the scars, a detection system to perform in vivo measurements in specific regions of the body, with enough sensitivity to discriminate between surface and deep contamination, based on the ratio $K_a / K_\beta$ ($^{137}$mBa characteristic x rays) was set up in Goiania. This system was also used to obtain information of the distribution of residual activities of $^{137}$Cs in the body, 3 years after the intake. The detector applied in this set of measurements system consisted of a HPGe type N, collimated with a 20 cm x 0.5 mm layer of copper. Ten people were selected for this study based on their remaining $^{137}$Cs body burden, which was obtained using a 8” x 4” Nal(Tl) detector, and on the presence of radiation burn scars. The selected individuals lay down on a thin matrix under the detection system. The HPGe was positioned over and close to the region of interest, which was different for each patient. Depending on the number of scars, caused by the radiation burns and the activity still present, the evaluation could last from 4 to 8 hours. Two of the subjects showed the presence of Cs activity in wound sites. Seven of the individuals showed high levels of x-ray activity in the surface area above the liver. Measurements of these low energy x-rays (≈30 keV) from an organ as deep in the body as the liver indicates a significant amount of activity in that organ and also that Cs is probably not homogeneously distributed, 3y after the intake.
A BIOKINETIC MODEL FOR $^{137}$Cs


In September 1987, an accident involving the stealing and breaching of a Cs-137 teletherapy source in Goiânia, Brazil, resulted in the contamination of several children and adults. Some of these individuals had high levels of contamination, allowing the retention of Cs-137 to be studied for 5y after the accident.

An improved biokinetic model for Cs was developed based on an analysis of the data of seventeen children, 1-10y old, 10 adolescents, four females and six males, 15 adult men and 15 adult women. The transfer of Cs-137 from mother to fetus through the placenta was estimated from data from two pregnant women. The retention of Cs-137 in one of the babies that was born with measurable activity was also included in this study.

In addition to the data on Cs-137 retention from the individuals contaminated in the Goiânia accident, data from a study on the metabolism of Cs-137 in immature, adult and aged Beagle dogs and data from the literature were used in the formulation of the Cs-137 biokinetic model presented. The whole-body retention of Cs is described by the sum of three exponential terms, the first one representing the fast clearance of Cs from plasma in the urine, the second one reflecting the turnover rate of Cs in the tissues and organs of the body and the third one representing the very long retention in the subcellular fraction in the skeletal muscle tissue. The retention model is based on a step function of body weight. When compared to this model, the ICRP publication 56 (1989) biokinetic model for the retention of Cs-137 underestimates the effective dose for the 2-5y old children, and overestimates the dose for infants, adolescents and adults.
AN ASSESSMENT OF HUMAN EXPOSURE TO ENVIRONMENTAL RADIATION IN THE CANADIAN ARCTIC

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The primary objective of the study was to review and integrate the diverse data on environmental radioactivity levels in the Canadian Arctic and to provide radiation dose estimates from both natural and artificial sources. A related objective was to assess the relative contributions of different exposure pathways.

A database of approximately 7000 records was compiled for radioactivity analyses of various environmental media (abiotic and biotic) as well as radiation field measurements conducted since 1988. The study revealed that there is a paucity of Canadian data for radionuclide concentrations in small game and edible vegetation as well as for Po-210 in marine mammals. The data on indoor radon levels were also found to be inadequate.

In order to examine the radiation exposure patterns in the Canadian Arctic, doses were calculated for residents of five aboriginal communities representing the diverse geographical locations, distinct ethnic populations and dissimilar dietary habits of this vast region. Estimated annual doses to the typical adult inhabitant were significantly elevated (2 to 9 mSv) compared to the doses to most Canadians as represented by the non-native resident of the city of Yellowknife (1 mSv). Calculated doses to one-year old infants and to adult members of a critical group, that relied almost entirely on country-food diets, were even higher. The doses arise primarily from the consumption of caribou meat. One single radionuclide, Po-210, contributed from 57% to 72% of the total dose. This large contribution from Po-210 arises, in part, from the recent recommendations of ICRP-67 wherein a significant increase in the dose conversion factor was recommended.

In Phase II of the study, in order to refine the dose estimates, the data were analyzed to include left-censored measurements. In addition, statistical techniques were employed to more precisely calculate the doses from key exposure pathways. These analyses modified the annual dose estimates by up to 2.5 mSv but did not alter the general exposure patterns. Substitution of non-Canadian data where Canadian data were lacking generally had a modest effect on dose estimates with the exception of the doses resulting from the ingestion of Po-210 from marine invertebrates.
DEVELOPMENT OF A TISSUE-EQUIVALENT LUNG PHANTOM FOR IN VIVO DETERMINATION OF LOW ENERGY PHOTON EMITTERS

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The calibration of the IRD-CNEN whole body counter for the in vivo determination of low energy photon emitters requires the use of artificial structures to simulate the organ size and shape, its density and the distribution of the radionuclide. Therefore, a physical anthropomorphic lung phantom was produced with foamed poliurethane as the tissue equivalent material. The cast was obtained by plasting an inert LLNL lung phantom. After curing, the structure was sliced in 10 pieces and filter paper inserts were cut in the size of each section. To each set of 10 paper inserts, known amounts of a single radionuclide were added, simulating an uniform distribution within the organ. This procedure was applied to each radionuclide of interest, i.e. Am-241, U-238 and Pu-239. The advantage of this assembly is that an unique lung set can be used to calibrate for various radionuclides. It also allows non uniform distributions to be easily simulated so as to calibrate the detection system for specific situations.
A COMPRESSED AIR IONIZATION CHAMBER FOR LOW EXPOSITION RATES


The compressed air ionization chamber (CAIC) has been developed since Gray (1931). The use of different CAIC types could be found in the literature, but only a few models are available. Therefore a CAIC portable, capable of measuring very low exposition rates with a good resolution is necessary in many low level radiometric surveys. In this paper two aluminum chambers with different volumes (23 cm$^3$ and 150 cm$^3$) were constructed. Calibrations at pressures at 25atm and 14atm were made respectively in such a way to minimize the dependence with energy. In the range from 40 keV to 1.25 Mev using a 150cm$^3$ chamber it was possible to measure exposition rates near to those found for the background. The results show a gain in current greater than 10 times when compared to a conventional ionization chamber. The two chambers have shown a good linearity for low exposition rates; however corrections due the recombination process, must be done, for values above of 0.1 $\mu$C/kg.s. A good performance has been obtained as the two chambers were used for analyzing the direct and scattered X-rays beams.
Among Japanese survivors of the A-bomb explosions, exposed in utero, significant increase in cancer incidence was observed. For studying radiation caused carcinogenesis, mice were irradiated in utero and occurrence of tumors followed. Irradiation with fission neutrons (0.5 Gy) caused 5-6-fold tumor incidence. After gamma rays, depending on dose and period of pregnancy, 28-50% cancer incidence was found compared with 22% in unirradiated animals. Most of the tumors were observed in lymphoreticular system, liver, lung and uterus. In lymphoreticular tumors elevated expression of H-ras oncogene was verified in 22% of tumor samples and of myc in 26%. Decreased expression of the p53 gene was found in 18% of lymphoreticular tumors as well as in 57% of malignant lung tumors. Mutations at codon 12 of K-ras gene was proved in two out of 6 lung tumors and at codon 6J, of H-ras gene in 60% of malignant liver adenocarcinomas. No point mutations were seen, however, in benign liver tumors. Loss of heterozygosity (LOH) of p53 and mts genes was also detected: 43% and 10% in lymphoreticular tumors, 60% and 20% in malignant liver tumors, 29% and 14% in lung adenocarcinomas and 18% mts LOH in malignant uterus tumors.
A DELAYED DNA DEGRADATION PROCESS RESEMBLING APOPTOSIS IS ASSOCIATED WITH RADIATION INDUCED NEOPLASTIC TRANSFORMATION OF HUMAN HYBRID CELLS

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The HeLa X skin fibroblast human hybrid cell assay is a useful model to study the molecular changes associated with, and mechanism of, radiation-induced neoplastic transformation in a human cell based system. Analysis of gamma ray-induced tumorigenic segments (GIM’s) of the non-tumorigenic hybrid CGLI indicate that damage and/or loss of fibroblast chromosomes 11 and 14 are strongly correlated with neoplastic transformation. This has led to the proposal that it is the radiation-induced loss of tumor suppressor genes located on those chromosomes which is at least one of the transforming events in these hybrid cells. The mechanism of how these tumor suppressor loci are lost or inactivated remained unclear. Since it had been shown that appearance of IAP positive neoplastically transformed foci in this system is delayed after radiation exposure (most foci begin to appear after day 9 post-irradiation) immediate loss or tumor suppressor gene deletion appeared unlikely. Further investigation revealed the delayed appearance of foci post-irradiation correlated with the establishment of plateau phase in the transformation flasks and with the onset of the expression of delayed heritable damage or lethal mutations. We proposed that the delayed expression of heritable damage is a result of genomic instability and have begun to investigate the nature of this delayed genomic instability process. We found that a DNA degradation process resembling apoptosis is evident beginning around day 8, post-irradiation in this system and the data suggest that induction of this process is associated with the radiation-induced neoplastic transformation of these human hybrid cells. We now propose that in this system there is a slow buildup of genomic damage or loss over time (10-12 cell divisions post-irradiation) which has two relevant outcomes:

1. Cell death due to the induction of an apoptotic like process in cells which have undergone large scale genomic damage or loss.

2. Neoplastic transformation of a small subset of survivors which have lost fibroblast chromosomes 11 and 14 (tumor suppressor loci) but have not acquired enough genetic damage to induce the apoptotic response.
During the past several years, work from our group has identified genes induced by cellular stresses such as ionizing radiation, UV, EMF, etc. We have shown that the pattern of gene induction is dependent upon radiation quality, type, dose, exposure kinetics, and cell type. Recently, we have examined mechanisms responsible for these responses. In the process of identifying genes differentially expressed in cells exposed to ultraviolet (UV) radiation, we identified a transcript having a 25-bp region that is highly conserved among a variety of species, including *Bacillus circulans*, pumpkin, yeast, *Drosophila*, mouse, and man. In the 5' region (flanking region or UTR) of a gene, the sequence is predominantly in +/- orientation with respect to the coding DNA strand; in the coding region and the 3' region (UTR), the sequence is most frequently in the -/+ orientation. In two genes, the element is split into two parts; however, in most cases, it is found only once, with a minimum of 11 consecutive nucleotides precisely matching the original sequence. The element is found in a large number of different genes with diverse functions, from human ras p21 to *B. circulans* chitosanase. Gel shift assays demonstrated the presence of a protein in HeLa cell extracts that binds to the sense and antisense single-stranded consensus oligomers as well as to double-stranded oligonucleotide. It is speculated either that this element binds to protein(s) important in maintaining DNA in a single-stranded orientation for transcription, or alternatively, that this element functions as a repressor.

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REVEALING MOLECULAR GENETIC CHANGES IN THE JEWISH EMIGRANTS WHO CAME TO ISRAEL FROM THE CHERNOBYL DISASTER AREA

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Radiation events such as the Atomic bomb have been claimed not to have yielded significant genetic defects. The accident in the Chernobyl atomic plant has created a different long term exposure to low radiation doses. It is thus our intention to evaluate the possible genetic consequences of such type of exposure, with the powerful tools of molecular genetics. Thus, the aim of this research is to reveal molecular genetic changes (e.g. de novo mutations), which occurred in people exposed to ionizing radiation in the Chernobyl area. The analysis involves DNA isolated from different individuals and families (both parents and offspring born before and after the disaster). Because of the small size of the experimental sample one has to use tools enabling the simultaneous testing of hundreds of genomic regions. DNA fingerprinting based on minisatellite markers or microsatellite markers may be a suitable molecular genetic tool to address this problem. PCR seems to be a most promising technique for high sensitivity analysis employing microsatellites.

Two PCR methods used in this study were: AP-PCR (Arbitrary Primed PCR, hot start) and RAPDs (Random Amplified Polymorphic DNA). The separation of the amplification products was conducted employing PAGE (Poly Acrylamide Gel Electrophoresis) and Silver Staining (SS). Band pattern was detected by SS in order to increase the sensitivity as compared to that of ethydium bromide staining. So, combinations have been made between AP-PCR and SS and between RAPDs and SS. The following experiments were conducted. In the first step about 200 PCR primers were screened. One hundred of these primers were 10-mers used for RAPD-PCR amplifications, the other 100 were microsatellite primers used for AP-PCR amplifications. About 52 primers from both groups appeared to give a good resolution (40 to 50 clear bands) and reproducibility. Two hundred RAPD reactions have been conducted for the families mentioned above, looking for resolution and reproducibility. Until now twenty seven primers have been used to analyze the families mentioned above, looking for appearance of new bands in children born after the disaster as compared to the DNA profiles of their parents and sibs born before the disaster. Usually such new bands ranged in size from 200 bp to 900 bp, although new bands of 2-3 kb were also detected. In total six out of 27 primers resulted in DNA profiles manifesting new band(s) in the child born after the exposure. The revealed changes in the DNA profiles were tested for reproducibility in three independent PCR runs. These consistent results point towards a possible influence of low dose radiation on the genetic material.
EFFECT OF CHRONIC LOW DOSE IONIZING RADIATION ON CHROMATIN STRUCTURE

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Background. Acute γ-irradiation with doses lower than 0.05 Gy is known to stimulate lymphocyte function. The effect of exposure to chronic low dose treatment was studied considerably less. Chromatin is presumed to be the primary target for ionizing radiation. The types of DNA damage vary. One type produced by high doses of radiation may occur predominantly in the DNA sites enriched with A-T basepairs. On the other hand, liver and spleen DNA of the animals exposed to prolonged irradiation in the Chernobyl zone had high content of low molecular fractions enriched with G-C basepairs. The main aim of our investigation was to reveal changes in lymphocyte chromatin in rats exposed to chronic low dose irradiation and to estimate their capability to recover after treatment.

Methods. For this purpose we had to use a technique most sensitive to the chromatin state and capable to distinguish DNA base content. Our work was carried out by means of fluorescent microscopy combined with phase contrast imaging. The microfluorimeter used in our work permits us to analyze the degree of radiation-induced damage of the DNA structure in individual cells. We used fluorescent dyes Hoechst, 33258 (H58) and Acridine orange (AO) differing in the mode of the binding to DNA. H58 was chosen for its sensitivity to base content since it formed specific complex with DNA sites enriched with A-T pairs. Intercalating stain AO is able to proclaim the extent of helicity and the stability of the DNA-protein complex. Three groups of Wistar male rats were investigated: control one; animals irradiated with two different dose-rates ~ 0.43cGy/day (total doses: 11cGy, 21cGy, 35cGy), and 3.0cGy/day (total doses: 50cGy, 140cGy, 200cGy). In both experimental groups measurements were carried out immediately after exposure. In the experiments with dose-rate 0.43cGy/day long-term effect of radiation was studied as well.

Results. The fluorescence intensity of H58-DNA complex in T lymphocytes decreased considerably in comparison with control in both experimental groups. Dose rate of 0.43cGy/day caused the maximum loss of the fluorescence after 11cGy cumulative dose. In the case of dose-rate 3cGy/day the increase of cumulative dose resulted in fluorescence decline. Thus, we found the disparate kinetics of fluorescence intensity of H58-DNA complex for two different dose rates. Both red and green fluorescence intensities of AO-DNA complex diminished after chronic exposure to a low dose of radiation. This may be explained with reduction whether of single- and double-stranded sites in DNA or of number of sites accessible for the dye binding. Various types of damaged T-lymphocyte states were detected: 1) Cells where the plasma membrane and most cytoplasm organelles remained morphologically intact during irradiation. In those cells considerable chromatin condensation and nuclear fragmentation could be observed; probably, those were apoptotic cells; 2) the cells with destroyed plasma membrane, cell organelles and the nucleus; they might be assigned to necrotic cells. The cell repair capacity was followed during long-term experiments. We have revealed a significant repairing effect for all cumulative doses investigated. Differences between chronic and acute irradiation were studied using the same total dose of 50cGy at various dose rates. Chronic irradiation dose seemed to induce more profound destructive processes in DNA as compared with acute irradiation.

Significance. Thus, usage of fluorescent dyes possessing different modes of binding to DNA showed chronic low dose irradiation induced not only A-T basepair destruction but considerable conformational reconstruction (chromatin condensation and possibly fragmentation) and/or degradation of the total DNA. Comparing fluorescent and phase contrast images we may suggest that chronic low dose γ-irradiation induced both modes of cell death in lymphosites: apoptosis and necrosis.
HOW SHOULD WE ASSESS THE ACTION OF MIXED IRRADIATION?

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The combined modalities of radiation are often used and sometimes occur in nature. However, it is not clear whether these combined effects are synergistic, because definition of the term “synergism” is confusing. It is, of course, desirable that the definition should be simple and reasonable. The definitions of synergism which have been used to date are examined with respect to the effect of mixed irradiation on cells with different types of radiation, and it is shown that they are not appropriate and misleading. This is probably attributable to simply treating the resultant phenomena (cell survival in most cases) without adequately taking into consideration knowledge of underlying biological mechanisms in defining the synergism in mixed irradiation. This paper discusses the inappropriateness of these definitions.

The action of mixed irradiation is defined as synergistic by various ways, which are given below.

1. $S(D_1 + D_2) < S(D_1)S(D_2)$, where $S(D_1)$ and $S(D_2)$ are the surviving fractions of cells irradiated with doses $D_1$ and $D_2$ of radiation types 1 and 2, respectively, and $S(D_1 + D_2)$ is the surviving fraction of cells irradiated with dose $D_1$ of radiation 1 and then with dose $D_2$ of radiation 2.

2. $E > 1$ from probabilistic backgrounds ($P_{exp} = P_1 + P_2 - P_1P_2$, $E = P_{obs}/P_{exp}$), where $P_1$ and $P_2$ are the separate probabilities of the effect after exposure to radiation types 1 and 2, respectively, and $P_{exp}$ and $P_{obs}$ are the expected and observed probabilities of the effect after exposure to a combination of radiation types 1 and 2, respectively.

3. Below the “envelope of additivity” in isobolograms (i.e., iso-effect curves) If one plots the various pairs of doses of two types of single irradiation that add up to a certain survival value, one obtains two lines or curves according to two modes of addition of the second doses. The addition is performed by taking the increments in dose starting from zero (mode 1) or from the dose that gives the survival with the first irradiation (mode 2). Area surrounded with curves in modes 1 and 2 is named “envelope of additivity”.

4. $S(y_i + x) < S(x_i + x)$; ICRU’s definition

When radiation X reduces survival, a dose $y_i$ of radiation Y that reduces survival to $S(y_i)$ is equivalent to dose $x_i$ of radiation X, i.e., $S(y_i) = S(x_i)$.

Inappropriateness of these definitions of “synergism” is briefly explained in the following.

1. The equation is always satisfied with survival curves with a shoulder including even a survival curve with a single irradiation as a special case of mixed irradiation. One exception is that two survival curves are semilogarithmically linear ($S(D_1 + D_2) = S(D_1)S(D_2)$ in this case).

2. This definition is basically the same as (1), since Ineq. $S(D_1 + D_2) < S(D_1)S(D_2)$ can be easily obtained by substituting $1-S$ for $P$ in Ineq. $E > 1$. Incorrectness of (1) and (2) is attributed to the misunderstanding that each radiation acts independently.

3. Survivals of mixed irradiation with two types of radiation were the same irrespective of their sequence. According to these definitions, however, action of mixed irradiation with radiation 1 plus 2 is called synergistic and that with radiation 2 plus 1 additive (3) or antagonistic (4).

These inappropriate definitions may have made some people think that mixed irradiation is more effective than a single type of irradiation from an ordinary sense of the term “synergistic”. In this sense, however, there has been no evidence for synergism of mixed irradiation.

In conclusion, to avoid misunderstanding, the concepts (1)-(4) should not be used as a definition of the synergism of mixed irradiation, even if there is no simple substitute, and the terms synergism and synergistic should also not be applied to mixed irradiation unless a reasonable definition and evidence are provided. Therefore, to assess risks of environmental, accidental or space radiations, which are often two or more, from the effects of single irradiations, action of mixed irradiation must be further studied including a definition of the synergism.
RADIATION-INDUCED DOUBLE-STRAND BREAKS IN CALF THYMUS DNA IN THE PRESENCE OF 1,2 DIHYDROXY 9,10 ANTHRAQUINONE AND ITS Cu(II) COMPLEX.

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DNA is usually considered to be the most critical cellular target while considering the lethal, carcinogetic, mutagenic effects of drugs, radiation, environmental and other chemical agents. These agents damage DNA by altering the bases or by disrupting the sugar-phosphate backbone. Base damage can have disastrous consequences for a cell and at times low levels of base damage are difficult to quantify by physical or chemical methods. However, DNA double strand breaks can be detected with great sensitivity by monitoring the rate of strand unwinding. Exposure of cells or DNA to ionizing radiation, besides other forms of damage, is known to increase the unwinding rate of large DNA molecules through the breaking of hydrogen bonds. This can be interpreted to say that the radiation-induced strand breaks are responsible for increase in the unwinding rate and that an increased rate of DNA unwinding can be used as a sensitive measure of strand breaks. The unwinding can be monitored directly using ethidium bromide as a fluorescent probe (after Morgan and Pulleyblank) which binds selectively to double-stranded DNA and is now a well established technique.

Anthracyclines and their metal complexes have been tried in chemotherapy of cancer and studies have shown that these have been effective in controlling tumours. However, studies with these compounds as radiomodifiers is not well pursued. We intend to find out whether hydroxyanthraquinones, core molecule of the anthracyclines, and its metal complexes are able to act as radiosensitizers. We have shown that Cu(II), Ni(II) and Fe(III) complex of 1,2 dihydroxy 9,10 anthraquinone act as effective radiosensitizers using uracil and thymine as our target molecules. In this present study the double strand breaks in calf thymus DNA (Sigma Chemical Company) have been monitored for fluorescence with ethidium bromide after exposure to $^{60}$Co $\gamma$-rays both in the presence and in the absence of 1,2 dihydroxy 9,10 anthraquinone (DHA) and its Cu(II) complex. Cu(II) forms a well defined 1:3 complex with DHA and the physicochemical characteristics of the complex have been reported elsewhere. The dose was varied from 2 gray to 15 gray. The experiment was carried out at pH 7.0 using phosphate buffer at a temperature of 28°C. It was found that the quinone and its Cu(II) complex both act as effective radiosensitizers to the double strand breaks of DNA upon exposure to radiation. The experiment revealed that the enhancement ratio for double strand breaks in calf thymus DNA was 1.29 in the presence of DHA while it was 2.0 in the presence of the Cu(II) complex. This result indicates the complex to be more efficient in radiosensitization in comparison to the quinone towards double-strand breaks.
INDIRECT ACTION MECHANISMS RESPONSIBLE FOR CHROMOSOMAL INSTABILITY AFTER RADIATION EXPOSURE

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Plasma from patients, irradiated accidentally or for therapeutic reasons, contain, for many years afterward, clastogenic factors (CF), which induced also chromosomal breakage in dividing lymphocytes from unexposed donors. CF were detected in a high percentage of plasma samples from Chernobyl accident recovery workers, even in those who received radiation doses lower than the allowable cumulative dose of 0.25 Gy.

CF can be produced by irradiation of blood in vitro, with a dose of 0.5 Gy/min from a 137 Cs source at a rate of 0.46 Gy/min. While serum irradiated in absence of cells was not clastogenic, irradiation of cells in PBS yielded clastogenic supernatants. If the irradiated cells were washed and resuspended in fresh culture medium, the continued to release CF. The formation as well as the chromosome damaging effects of CF were preventable by superoxide dismutase.

CF are found also in a variety of other pathological conditions, where their formation and clastogenic action are related to increase superoxide production. These include chronic inflammatory diseases with autoimmune reactions, asbestos workers, AIDS patients, as well as the congenital breakage syndromes ataxia telangiectasia, Bloom’s Syndrome, and Fanconi anemia.

Identified clastogenic components of CF are lipid peroxidation products, cytokines (in particular TNF alpha) and nucleotides, in which adenine is deaminated to hypoxanthine (ITP, IDP). Certain components of CF stimulate superoxide production by neutrophils and monocytes. Produced via superoxide and stimulating further superoxide production by competent cells, CF are autosustained, what explains their persistence of years after the radiation event. They may represent risk factors for the development of late effects in irradiated persons.
STABLE BIOMARKERS FOR RETROSPECTIVE BIODOSIMETRY

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Chromosome translocations are linked to human carcinogenesis and inherited genetic disorders. Because such health detriments may require decades to appear, the persistence of translocations in tissues is of great interest. Recent advances in chromosome staining using fluorescence in situ hybridization (FISH) facilitate fast and reliable measurement of reciprocal translocations, a kind of DNA damage linked to both prior exposure and risk. In contrast to other biomarkers available, the frequency of reciprocal translocations in individuals exposed to whole-body radiation is stable with time post exposure, has a rather small inter-individual variability, and can be measured accurately at low levels. Inversions, also stable aberrations, are difficult to measure. The ratio of inversions to translocations (F value) is believed to be a discriminator between high- and low-LET radiation exposure (i.e., it is believed to be a signature for radiation quality). Here, we discuss results from our studies demonstrating the stability of the translocation frequency with time after exposure (about 30 y post exposure) in whole-body exposed rhesus monkeys. These results, together with measurements of previously exposed humans, provide a basis for the use of reciprocal translocations in radiation dose reconstruction. In addition, a FISH-based method to measure inversions in lymphocytes is introduced; and our preliminary data on F-values measured in vitro for low- and high-LET radiations support the radiation quality signature theory.
CHERNOBYL-RELATED THYROID CANCER: WHAT EVIDENCE FOR ROLE OF SHORT-LIVED IODINES?

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In Belarus alone, about five hundred cases of thyroid cancer have been diagnosed and treated so far among persons exposed to radioactive contamination from the Chernobyl nuclear accident when they were children or adolescents. There is little doubt that radioactive iodine isotopes emitted during the nuclear explosion and subsequent fire must have been instrumental in causing malignancy in this particular organ. Comparison of the observed geographic distribution of Chernobyl-associated thyroid cancer incidence rates by districts and of contamination maps by radioactive fallout shows indeed a better fit for estimated 131-iodine contamination than for 137-cesium doses, but information has so far not been detailed enough to formally test this correlation by statistical methods.

Since in the past, 131-iodine used for medical purposes had not been shown to be carcinogenic in humans, and in view of the unusually short latency period between exposure and clinical manifestation of cancer, the suspicion has been voiced that not only 131-iodine, but also energy-rich shorter-lived radiiodines may have played a role in post-Chernobyl thyroid carcinogenesis. Measurements of these isotopes are not available, but reconstruction of geographic distributions based on meteorological observations immediately following the accident could provide a basis for comparison with 131-iodine distributions. In this presentation, data from the Epidemiological Cancer Register for Belarus will be used to present geographic and time trends of thyroid cancer incidence rates for the period 1986 through 1995 among persons exposed as children and adolescents, and these will be compared with maps of estimated radiiodine contamination for different days following the accident and under different assumptions. Tentative conclusions will be drawn from the available evidence, and further research needs will be discussed.
LESSONS FROM CHERNOBYL ABOUT RADIATION AND HEALTH: THYROID CANCER AND LEUKAEMIA

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This paper summarises the on-going follow-up of populations exposed as a result of the Chernobyl accident and the main results to date, and proposes directions for future studies to provide information on some of the outstanding questions in radiation and health. Apart from the dramatic increase in thyroid cancer in those exposed as children, there is no evidence to date of a major public health impact of the radiation exposure from the Chernobyl accident in the three most affected countries. Although some increases in the frequency of cancer in exposed populations have been reported, these results are difficult to interpret, mainly because of differences in the intensity and method of follow-up between exposed populations and the general population to which they are compared.

Only 10 years have passed since the Chernobyl accident and it is essential that monitoring of the health of the population be continued through the use of improved population registries. Careful studies of selected populations and diseases are also needed in order to study observed or predicted effects. Studies of liquidators will provide important information concerning the effects of exposure protraction and perhaps of radiation type in the relatively low dose (0-500 mSv) range. The dramatic increase in thyroid cancer in young people, moreover, provides a unique opportunity to increase our understanding of factors—genetic and environmental—which modify the risk of radiation induced cancer.
MALIGNANT AND BENIGN TUMORS FOLLOWING RADIATION EXPOSURE TO THE HEAD AND NECK

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The development of thyroid cancer is a well known late effect of childhood head and neck irradiation. Following external radiation the dose-response relationship is consistent with linearity, with excess tumors occurring at doses as low as 10 cGy. The risk of thyroid cancer decreases rapidly with increasing age at exposure and there is little evidence that persons exposed as adults have an excess risk. An elevated risk is observed more than 40 years after initial childhood exposure. Data from the Chernobyl disaster suggest that childhood exposure to radionuclides also increases the incidence of thyroid cancer. Similar to the findings for external radiation, thyroid cancer is not significantly elevated among adult populations receiving medical I-131 therapy or diagnostic procedures.

Hyperparathyroidism, salivary gland tumors, and neural tumors have been linked to radiation in some studies, but the data are insufficient for deriving reasonably precise risk estimates. Radiation appears to induce specific histologic tumor types more frequently than others. Most radiation-induced thyroid cancers are papillary tumors, mucoepidermoid salivary gland tumors have a higher risk than other salivary gland tumors and neurilemomas appear to be more radiosensitive than other neural tumors.

Little is known about the role of radiation in the induction of pituitary tumors because malignant tumors are extremely rare and benign tumors are not routinely reported to most population-based cancer registries. There is no clear evidence for a radiation association with cancers of the pharynx, hypopharynx or larynx. Ionizing radiation clearly can cause cancers in the head and neck, but there are large differences in tissue sensitivity.
THE RELATIONSHIP BETWEEN THE PREVALENCE OF THYROID CANCER AND THYROID NODULES IN THE POPULATION OF THE MARSHALL ISLANDS TO POTENTIAL EXPOSURE FROM NUCLEAR WEAPONS TESTS

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To study the prevalence of thyroid nodules and of thyroid cancer in the population of the Marshall Islands which was alive during the US atomic bomb tests, 1,329 Marshallese residing now in Kwajalein atoll and born before 1964 were investigated using neck palpation, fine needle biopsy and ultrasound imaging of the thyroid. Approximately 55% of the total population at risk on the island of Ebeye was screened. 349 people with thyroid nodules were found, 150 were palpable, 199 could only be diagnosed by ultrasound. In 22 people, the tentative diagnosis of thyroid cancer was made. In addition to the medical examination, an interview was performed which concentrated on the residence history between 1945 and 1964. We will report on the relationship between age and sex specific prevalence of thyroid cancer and thyroid nodules to the Cs¹³⁷ activity from all bomb tests as determined by the Nationwide Radiological Study (as an indicator of potential cumulative exposure to fallout I¹³¹) on the atolls of residence during the period of most intensive A bomb testing 1954-1958.
RECONSTRUCTION OF THYROID DOSES FOR CHILDREN WITH THYROID CANCER IN BELARUS

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Due to the increase of thyroid cancer in children of Belarus after the Chernobyl accident a German-Belorussian project was initiated by GAST (German Committee of radiation research) in order to optimize treatment of the affected children, and to provide assistance for Belorussian colleagues to encounter these consequences of the accident. The reconstruction of the thyroid doses in these children due to I-131 exposure is an important task of the project to demonstrate dose-effect relationships, and for risk analysis and the prediction for the further development of the disease.

A databank containing names, age, sex, location at time of exposition, and time of cancer detection of the affected children was created. It is combined with the deposition patterns of I-131 for the corresponding locations. Due to a different deposition pattern compared to Cs-137, different attempts to reconstruct the deposition of I-131 are applied:

1) the application of a meteorological dispersion model (EURAD) resulting in an I-131 and Cs-137 contamination map due to dry and wet deposition in a 10x10 km raster. The model predictions are cross-checked by measured Cs-137 activity values.
2) the determination of I-129 activities in soil samples at the locations in question in order to recalculate for I-131 deposition assuming a constant ratio I-129/I-131.

The results of the reconstructed I-131 deposition values are used as input parameters into the dynamic radioecological model ECOSYS-87, which was adapted to Belorussian conditions in respect to milk and vegetable consumption, vegetation state etc., in order to estimate age-dependent thyroid doses. Comparisons with the Belorussian estimates based mainly on Cs-deposition information (measurements in soil and vegetation) and direct thyroid measurements are provided.
IS FISH-PAINTING APPROPRIATE FOR DOSE ESTIMATES OF ACCIDENTAL RADIATION OVEREXPOSURE?

Review of cases investigated in France in 1995-1996.

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Human exposure to ionising irradiation can be estimated by analysis of the frequency of structural aberrations in metaphase spreads of peripheral lymphocytes of exposed individuals. In most studies, this has been accomplished by measuring the frequency of unstable chromosome abnormalities (dicentrics and centric rings) and calibrating this against a standard dose-response curve established after analysis of human lymphocytes irradiated in vitro. However, dicentric chromosomes are unstable with time after exposure and a biological dosimetry based on their detection alone present some limitations in the cases of fractionated, protracted or past-overexposure. This is especially problematic when dosimetry is required for occupationally or accidentally exposed individuals because the time between exposure and analysis may be considerable or even unknown. On the other hand, translocations seem to persist for many years after exposure and their scoring might be an indication for past-overexposure. Unfortunately, these stable aberrations are not readily visible with conventional staining, and only scored with difficulty applying chromosome banding techniques. Fluorescence In Situ Hybridisation (F.I.S.H.) has opened new perspectives for the identification and classification of radiation-induced chromosome aberrations. F.I.S.H. technology using whole human chromosome-specific DNA probes, ‘chromosome painting’, provides easy detection of some interchromosomal exchanges (i.e. translocations, insertions). This is generally performed using a cocktail of composite DNA probes specific for the largest chromosomes. The data obtained by the analysis of only a few chromosomes (the painted ones) can be accurately scaled-up to full genomic frequency by assuming a random distribution of break points, and then calibrated against a standard dose-response curve.

Firstly, we present here the generation of a laboratory calibration curve for symmetrical and/or terminal translocations induced in vitro by $^{60}$Co $\gamma$-rays (0.5 Gy/min) in human peripheral lymphocytes. Chromosome analysis was carried out by a tri-colour « F.I.S.H.-painting » using a cocktail of three composite whole human chromosome-specific DNA probes (2, 4 and 12).

Secondly, we compare F.I.S.H. and conventional cytogenetics for dose estimates of human accidental radiation overexposure. During the period of 1995-1996, about ten people suspected of being overexposed to ionising radiation were referred to the Institute for Nuclear Safety and Protection (I.P.S.N) for investigation by chromosome aberrations analysis. These cases were associated with different origins, industrial uses of radiation, institution of research, education or health. Biological estimates of accident overexposure were firstly obtained by the scoring of radio-induced unstable structural chromosome aberrations in peripheral blood lymphocytes. For correlation with a physical dose, the yield of these chromosomal aberrations estimated in 500 metaphases is compared with a laboratory dose-response relationship established in vitro for human blood irradiated with $\gamma$-rays from $^{60}$Co at a dose rate of 0.5 Gy/min. In order to improve the possibilities of DNA damage detection, « F.I.S.H-painting » with the same cocktail of whole human chromosome-specific DNA probes as used for the establishment of the calibration curve was applied to each human blood sample. Then, 2000 metaphases per individual were scored for the presence/absence of reciprocal and terminal translocations. We present here a comparison between the results obtained by the two technologies for each of the cases studied separately. We describe their similarities or differences according to the history of each case (accidental and/or personal) and discuss about the suitability of « chromosome painting » for routine expertise analysis.
THE IN VITRO MICRONUCLEUS-CENTROMERE ASSAY TO DETECT LOW DOSES OF IRRADIATION IN HUMAN LYMPHOCYTES.

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One of the major drawbacks of the in vitro MN assay for human lymphocytes is the reduced sensitivity for the detection of low radiation doses, due to the wide interindividual variation in spontaneous MN incidence. In this paper we studied if an enhancement of the sensitivity of the MN assay could be achieved by analysing spontaneous and radiation induced MN for the presence of centromeres. For this, in situ hybridisation (FISH) with the human centromeric DNA probe, p82H, was used. Our results revealed that a high percentage (73%) of the spontaneous MN contain a centromere. These centromere positive MN are indicative for the presence of a whole chromosome/chromatid. After in vitro irradiation with low doses (0.1-2 Gy) mainly centromere negative MN (93.5-100%) were induced while only a very small number of additional centromere positive MN were formed. This demonstrates that radiation induced MN mainly contain acentric fragments, pointing to the clastogenic action of ionising radiation. Furthermore our data show that the MN-centromere assay allows us to increase the sensitivity for low dose detection by scoring only centromere negative MN.
GLYCOPHORIN A IN LIQUIDATORS FROM CHERNOBYL

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The assessment of radiation exposure of the Chernobyl “liquidators,” or salvage workers, is difficult due to uncertainties in the recorded doses at the time of the nuclear reactor accident, and because of the time that has elapsed. However, this group is of great interest because 600,000 or more people had exposure to ionizing radiation as a result of salvage activities. A small number of these individuals came to Israel as part of the wave of immigration from the former Soviet Union (FSU) during the past five years.

Objective: The objective of this investigation has been the quantitative assessment of human radiation exposure due to the Chernobyl accident. The study has involved the measurement of the incidence of red cells lacking glycophorin A (GPA) antigen, which has been used as a biomarker for radiation exposure.

Principle: Radiation induced mutations in hemopoietic stem cells result in the persistence of clones of circulating red cells which are missing certain antigens. A defect in the MN locus can be detected by the absence of binding of antibodies to GPA antigen on the red cell membrane.

Method: This analysis can be done only on people heterozygous for the MN blood group. Red cells lacking the M antigen, or cells which had duplicated the N antigen, were counted by using fluorescent antibodies bound to red cell M and N GPA antigens. Results were expressed as the number of events per million red cells.

Results: In this preliminary study, we examined a population of 32 liquidators who had immigrated from the FSU. The correct MN blood type was present in 14 subjects, of whom 4 were women and 10 were men. In the male population, there were 4 subjects between 20 and 65 events $10^6$ cells and 3 cases who had 12, 13 and 14 events. The other 3 cases had between 0 to 5. In the female population one subject showed 101 events, 2 cases had 23 and 26 events and one case showed 4 events per $10^6$ cells. We examined 12 female and 9 male control unexposed subjects. Male controls showed an average of 4.3 events per $10^6$ cells and females had an average of 3.3 events per $10^6$ cells. When the results of males and females were analyzed together by the Student T test, the difference between liquidators and controls was highly significant ($p <0.012$).

Conclusions: The results suggests that the GPA assay may be a useful tool to evaluate human radiation exposure, but more work must be done to relate the GPA results to other biomarkers and indices of exposure.
AUTOMATION OF THE DICENTRIC ASSAY: USE OF COLOR-PIGMENT PAINTING, METAPHASE FINDER, AND DIGITAL-IMAGE ANALYSIS


Biodosimetry for accidental radiation exposures is typically performed by the classical metaphase-dicentric chromosome aberration analysis that uses blood lymphocytes of exposed individuals (Bender et al., 1964). Previous efforts to automate the detection of chromosome aberrations involved digital-image recognition of morphological features of chromosome structure. The use of fluorescence in situ hybridization (FISH) technology to detect specific chromosome aberrations has significantly improved the capability to assess radiation injury. Our laboratory has approached automation of the dicentric assay with using non-fluorescence detection methodology; pancentromeric regions are identified using an alternative immunoenzymatic approach. Biotin-labeled human pancentromeric DNA hybridization probes are detected via an avidin/horse radish peroxidase reagent, which is visualized by the conversion of the enzyme substrates H2O2/diaminobenzidine into an insoluble brown or black pigment product. Color-pigmented painted pancentromeric sequences are readily discriminated from Giemsa counterstained chromosomes when using color-video image analysis software algorithms. Samples prepared using Giemsa counterstaining are readily found on slides with an automated metaphase finder, which we have optimized for high throughput analysis. A composite and high-resolution image of metaphase spreads is obtained from serial images captured at incremental steps of the z-axis plane for analysis of chromosome aberrations. In addition, we have incorporated a satellite scoring station concept, where information (postage stamp size image of the metaphase spread and its slide location) obtained from the metaphase finder system can be easily distributed to multiple satellite scoring stations to facilitate high throughput analysis in cases of accidental radiation exposure. Application of this approach for alternative cytogenetic assays (premature chromosome condensation or PCC, etc.) of radiation exposure will also be discussed (Blakely et al. 1995). Use of an automated dicentric analysis system can be of significant benefit in dose assessment for various exposure scenarios. (This research was supported by the Armed Forces Radiobiology Research Institute, under work unit number AFRRI-95-3.)

The aim of this study was to elucidate whether the enhanced skin radiation reaction correlated with enhanced chromosome radiation response. Nine patients of the Department of Radiation Injury Treatment (MRRRC) with late radiation skin ulcers formed after courses of radiation therapy were taken as a group of individuals having an elevated radiosensitivity of skin. Types and doses of therapeutic exposures of the patients are listed in Table 1, together with time intervals (t) between exposure and blood sampling. Five healthy unexposed volunteers made up a control group. Half of the venous blood sample from each donor was irradiated with 2 Gy of 60Co γ rays, then lymphocyte cultures were set up with all the samples by standard technique in Eagle medium supplemented with 15% bovine serum, penicillin and phytohaemagglutinin. The cells were harvested after 51 h incubation (colchicine added 3 h prior the harvest). On the obtained metaphase preparations, all chromosome aberrations needing no karyotype identification were scored and registered as the number (per 100 cells) of aberrant metaphases (AM), total chromosome aberrations (CA), chromosome type aberrations (CsA), including fragments (CsF), and chromatid type aberrations (CtA), including fragments (CtF). Statistical treatment of the results obtained for the healthy donors showed the homogeneity of the data for each of the analysed aberration types both in irradiated and unirradiated cultures, so these data were pooled. Frequency of each aberration type in each patient was compared (by t-test) with the relevant mean healthy donor value. Patients 1, 2, 5, 7 and 9 revealed none difference with controls. The results for the other four patients are given in Table 2 where the first line contains mean healthy donor value. Patients 1, 2, 5, 7 and 9 revealed none difference with controls. The results for the other four patients are given in Table 2 where the first line contains mean healthy donor value. Patients 1, 2, 5, 7 and 9 revealed none difference with controls.

Table 2.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Exposure, Gy</th>
<th>t, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>p 48</td>
<td>1.7</td>
</tr>
<tr>
<td>2</td>
<td>R 20</td>
<td>2.1</td>
</tr>
<tr>
<td>3</td>
<td>R(17+51)</td>
<td>0.4</td>
</tr>
<tr>
<td>4</td>
<td>γ(40+30)</td>
<td>1.4</td>
</tr>
<tr>
<td>5</td>
<td>γ(7+36)</td>
<td>1.6</td>
</tr>
<tr>
<td>6</td>
<td>R(7+4+7)</td>
<td>31</td>
</tr>
<tr>
<td>7</td>
<td>R(30+35)</td>
<td>19</td>
</tr>
<tr>
<td>8</td>
<td>? + R 36;</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>γ (121 + 180)</td>
<td>32</td>
</tr>
</tbody>
</table>

The enhanced chromosome radiation response. Nine patients of the Department of Radiation Injury Treatment (MRRRC) with late radiation skin ulcers formed after courses of radiation therapy were taken as a group of individuals having an elevated radiosensitivity of skin. Types and doses of therapeutic exposures of the patients are listed in Table 1, together with time intervals (t) between exposure and blood sampling. Five healthy unexposed volunteers made up a control group. Half of the venous blood sample from each donor was irradiated with 2 Gy of 60Co γ rays, then lymphocyte cultures were set up with all the samples by standard technique in Eagle medium supplemented with 15% bovine serum, penicillin and phytohaemagglutinin. The cells were harvested after 51 h incubation (colchicine added 3 h prior the harvest). On the obtained metaphase preparations, all chromosome aberrations needing no karyotype identification were scored and registered as the number (per 100 cells) of aberrant metaphases (AM), total chromosome aberrations (CA), chromosome type aberrations (CsA), including fragments (CsF), and chromatid type aberrations (CtA), including fragments (CtF). Statistical treatment of the results obtained for the healthy donors showed the homogeneity of the data for each of the analysed aberration types both in irradiated and unirradiated cultures, so these data were pooled. Frequency of each aberration type in each patient was compared (by t-test) with the relevant mean healthy donor value. Patients 1, 2, 5, 7 and 9 revealed none difference with controls. The results for the other four patients are given in Table 2 where the first line contains mean healthy donor value. Patients 1, 2, 5, 7 and 9 revealed none difference with controls. The results for the other four patients are given in Table 2 where the first line contains mean healthy donor value. Patients 1, 2, 5, 7 and 9 revealed none difference with controls.
HEMPOIEITIC PROGENITOR CELLS IN PATIENTS AFFECTED BY CHERNOBYL ACCIDENT

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Knowledge of the high radiation sensitivity of progenitor cells and information on their ability to accumulate sublethal radiation damage provided the basis for investigating bone marrow patients affected by Chernobyl Accident, in culture. The formation of morphologically identifiable blood cells can be studied in culture because of the development of semisolid system in which committed progenitor cells proliferate to form clones of maturing cells. We used our method of gel diffusion chambers which provides growth of granulocytomonocytic progenitor cells. The aim of this investigation was estimation of indices which describe condition of pool of haematopoietic progenitor cells in 53 patients (48 men and 5 women) irradiated in doses from 0.25 to 3 Sv. In 1986 15 of them worked at the Chernobyl Nuclear Station at the time of the accident. Patients of first group (17 persons) were irradiated in doses from 0.25 to 0.5 Gy, second group (10 persons) from 0.5 to 0.75 Gy, third group - from 0.75 to 1 Gy (9 persons), fourth group - (17 persons) - from 1 to 3 Gy. 25 healthy donors aged 25-56 years were used as a control group. Bone marrow of patients aspirated in sternum puncture. The mononuclear cells were isolated by Ficoll-Hypaque centrifugation (density 1.077 g/ml) and cultivated in original diffusion chambers with medium RPMI, 10 % fetal calf serum, antibiotics and 0.3% agar Difco. Diffusion chambers were inserted in abdominal cavities of mice irradiated in sublethal doses 24 hours before the experiment. We determined efficiency of cloning progenitor cells by quantity colonies - clones on lxl0^5 cultivating cells after 14, 18, 21 and 28 days. We picked up colonies and investigated cytological and cytochemical characteristics in slides after cytospin. Cultivating of progenitor cells 5-10 years after the accident has shown that independently of dose of irradiation in the majority of cases colony forming activity in vivo corresponded to average number of colonies in the control. however, in some patients (8 persons) we observed lowering of the number of colonies in culture in generally accepted term (14-th day), but continuation of the cultivation till 21-th day has shown recovery of cloning efficiency in 5 cases. Mix colonies prevailed. Cytochemical assay (myeliperoxidase) has confirmed cytological data. The fact that the number of cells within the aggregates at the moment of harvesting corresponded to normal in the majority of cases but in some cases (6 patients) the number of cells did not reach 40 (that is the, minimal number of cells in colony) and therefore could be considered as large clusters. However, they turned into colonies at 18-th -20-th day. Disturbance in differentiation of haemopoietic cells in granulomonocytic colonies in two patients from the fourth group was manifested by predominance of early granulocytes (mainly blasts, myelocytes, metomyelocytes). In some patients we determined in culture granulocytic cells with whimsical shape, nuclear fragmentation and great size. Predominance eosinophilic and eosinophilic-neutrophilic colonies in culture of 40 % examined patients was noticed though no eosinophilia in peripheral blood was observed. Presence of large clusters in culture in generally accepted term and recovery of colonies late, predominance of eosinophilic colonies, decrease of colony forming efficiency and disturbance in differentiation of cells in some cases illustrate the need for a high degree of suspicion in making an early diagnosis. Early identification of these patients is important as they are at risk of eventual evolution into more hazardous clinical state. Retrospective analyses of clinical and laboratory data has shown that two cases developed myelodysplastic syndrome and in one case - chronic myeloid sickness.
AGE RESPONSE OF STABLE CHROMOSOME ABERRATION FREQUENCY IN LIMPHOCYTES OF CHERNOBYL VICTIMS AND CONTROL GROUP

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The cytogenetic effect of ionizing radiation in humans used to be studied by routine scoring of dicentrics in cultivated peripheral lymphocytes. These chromosome aberrations though dependent on the radiation dose, disappear with time after irradiation due to genetic imbalance they create in cells. In case of exposure at low doses their frequency, initially not high, could decrease and can not be used directly for retrospective biological dosimetry. The new fluorescent in situ hybridisation technique (FISH) permits registration of radiation induced stable chromosome aberrations (translocations, insertions), which are generally nonlethal for cells, persist through the cell divisions and reflect the dose long after exposure. However, their frequency is known to increase with age in normal population (Tucker et al., 1994).

To estimate the radiation effect in Chernobyl victims two groups were compared. The first one enrolled about 50 persons suffering from the Chernobyl accident (evacuees from contaminated areas and liquidators) in the age range 5-70 years. The second, control group consisted of 30 persons matched with the case one by age. For registration of stable chromosome aberrations in metaphase lymphocytes FISH technique was applied using biotinilated DNA-probes specific to whole human chromosomes 1, 4, and 12.

The data obtained demonstrates that the frequency of stable chromosome aberrations increases with age in both groups compared, being higher in exposed people. Thus, for correct retrospective dosimetry on the base of chromosome painting technique it seems to be important that the normal age response of these events take into account.
PERSISTENCE OF TRANSLOCATIONS IN ACCIDENTALLY EXPOSED RADIATION WORKERS DETECTED BY FISH

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In 8 individuals, the frequency of dicentrics was evaluated shortly after an accidental or occupational radiation exposure. In a second blood sample taken 2 to 11 years later, dicentrics were again scored and symmetrical translocations were evaluated by fluorescence in situ hybridization (FISH). Translocations were determined using biotin-labelled painting DNA probes for chromosomes 2, 4 and 8 and a digoxigenin-labelled α-satellite pacentromeric DNA probe. The frequency of dicentrics from the first blood sample was in agreement with the frequency of translocations from the second sample within statistical variations in 5 individuals. However, in 3 individuals the frequency of translocations was significantly different. The frequency of dicentrics decreased during the time between the two blood samples. The involvement of chromosomes in translocations, regarding the physical length of chromosomes, is as follows: chromosome 2 shows a lower frequency of involvement than expected (35% versus 42%) and chromosome 4 is more often involved than expected (42% versus 33%). The involvement of chromosome 8 in translocations corresponds with the expected value (25%). For transformation of translocation frequencies into doses, a calibration curve for the painted chromosomes 2, 4 and 8 was established by in vitro irradiation.
GENOTOXIC EFFECTS OF PESTICIDES EXAMINED IN LYMPHOCYTES OF OCCUPATIONALLY EXPOSED VINEGROWERS

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A large portion of new synthetic chemicals is widely used in agriculture as pesticides. In order to estimate potential hazardous effects associated with application of pesticides in winegrowing, a group of 27 vinegrowers, mostly tractorists were chosen for cytogenetic examination. They spray a large amount of pesticides, with no use safety covers. Spraying mixture of pesticides usually involve different compounds (diazinon, dithyocarbamide, xylene, cuprum, 2-4-D-dichlorphenoxy acetic acid). The proportion of individual compounds for spraying is changeable, mostly because of resistance evoked in pest and insects, so toxicological characteristic of mixture is usually unknown. The genotoxic effects of pesticides was tested by measuring DNA damage in circulating lymphocytes of vinegrowers, employing chromosomal aberration analysis (CAs), cytochalasin-blocking micronucleus test (MN) and sister-chromatid exchanges (SCEs). The workers examined averaged 37 years and had been employed in agriculture for 15 years. The spraying season usually lasted 3 months. Lymphocytes of exposed workers were cultured during pre-spraying period, a month after starting the spraying and at the end of spraying season. For comparison purposes, the same cytogenetic monitoring program was applied in two control groups: the first control group consisted of 15 teachers from a nearby town, and the second one consisted of 43 volunteers (students and employees of a research institute) 200 km from the vinegrowing area. The results of analysis during pre-spraying period showed slightly elevated level of CAs of vinegrowers (mostly- stable chromosomal aberrations were found), in comparison to controls, with almost no differences in MN and SCEs frequency. A month after spraying, the incidence of CAs, especially excesses acentrics (0.23%) and MN (17.3/1000 binucleated cells) showed significant increase in comparison to results obtained during pre-spraying period in exposed group as well as in both controls. Analysis at the end of season showed increase in CAs (1.18%) as well as in MN frequency (41.25/1000 bi cells), in comparison to both previous examinations. The MN frequency showed the highest increase (almost 2 fold higher than is expected according to obtained chromosomal aberrations): mean value of MN/1000 bi cells was 41.25 (ranged from 21-62) which indicate genotoxic effects regarding both on DNA and mitotic spindle proteins. It could lead to the entire chromosome failing to be incorporated in one of the two daughter nuclei during cell division, and form micronuclei. Significant portion of binucleated cells holding more than 7 micronuclei was noticed. SCE frequency showed no changes. The results of our investigation showed that pesticides used in agriculture are capable of inducing chromosomal aberrations and micronuclei in human lymphocytes of occupationally exposed individuals. It could be due to mixture of pesticides, where the possibility of interactions among them can not be ruled out. Dependent increase of CAs and MN on duration of the exposure was found. Differences relative to controls were significant on the second and third time of examination. The incidence of micronuclei in the first control group was 2-fold increase in comparison to control group 200 km away from the vinegrowing area, only at the end of the spraying season.
STIMULATION OF IMMUNITY AFTER LOW DOSE RADIATION (LDR)

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The regulation of immunity following LDR involves a series of cellular as well as molecular reactions. The cellular reactions occurring in the immune organs after LDR are quite complicated with the activation of the T lymphocytes occupying a pivotal position. It has been confirmed that the following changes occurred after WBI with doses of X- or y-rays of 0.1 Gy: 1) increased reactivity of both the splenic and thymic cells to Con A; 2) potentiation of thymocyte renewal; 3) expression of the TCR/CD3 complex of the thymocytes; 4) increased secretion of CSF by the thymocytes, stimulating the macrophages to produce more IL1 which provides a maturation signal to the helper T cells; 5) enhanced proliferative process in the thymus; 6) increased phagocytic and digestive activity and increased cooperative effect on the T cells of the macrophages; 7) increased secretion of IL2 and IFN-γ by the TH as well as enhanced expression of IL2 receptor on these cells; 8) enhanced PFC reaction in the spleen; 9) stimulated NK and CTL activity.

The mechanism of the stimulatory effect of LDR on the immunologic parameters listed above includes facilitation of signal transduction in T lymphocytes with increased mobilization of [Ca^{2+}]_i and activation of PKC. The coordinated activation of these two second messengers results in increased transcription of the immediate early genes c-fos and c-jun. These molecular changes form the basis of enhanced secretion of IL2 and IFN-γ and increased expression of IL2 receptor on the T cells. The ultimate outcome would consequently be activation and clonal expansion of the T cells.

It has been speculated that LDR would preferentially damage the Ts resulting in a rise in TH/Ts ratio, which would lead to increase of the helper effect within the immune system. We have found that stimulation of immunity by LDR usually occurred with doses below 0.25 Gy, most markedly following WBI with doses within 0.1 Gy. However, flow cytometric analysis of thymic and splenic T subsets in mice exposed to WBI with doses in this range showed no significant changes of TH to TS ratio after irradiation. And it was found that after in vitro irradiation of the separated CD4^+ and CD8^+ T subsets from human peripheral blood with doses ranging from 50 to 100 mGy both the helper function of TH and the suppressor function of TS on the B cell response to LPS were augmented. Therefore, existing experimental data are not in favor of the hypothesis based on the speculation of a rise in TH/Ts ratio due to a preferential structural damage or functional suppression of the TS subset. Another speculation is increased apoptosis of the precursor T cells after LDR leading to increased proliferation of more mature cells. However, the percentage of apoptotic bodies of mouse thymocytes assessed by flow cytometry with doses within 0.2 Gy did not depart from that of the sham-irradiated control or was even lower than that of the control. It is evident that data mentioned above does not give support to the speculation of either the preferential deletion of the TS subset or the facilitation of apoptosis of immature thymocytes as the cellular basis of stimulation of immune functions following WBI with low doses of X- or y-rays. We further probed into the molecular basis of the behavior of apoptosis after different doses of radiation. It was found that Bcl-2/BAX ratio was increased and p53 was lowered after LDR, just opposite to the changes observed after high dose radiation.

At the same time it was found that neuroendocrine factors might be involved in low dose radiation effects. The hypothalamic-pituitary-adrenocortical (HPA) axis normally exerts a tonic suppression on the immune organs, especially the thymus. A decrease in activity of the function of the HPA axis was observed after LDR, expressed as decreased transcription level of POMC in the hypothalamus and lowered plasma level of ACTH and corticosterone in mice exposed to WBI with 75 mGy X-rays. Therefore, in the analysis of the possible mechanistic factors of immunoenhancement following LDR the influence of changes in the microenvironment of the immunocytes as a result of shift in systemic regulation after LDR has to be considered in addition to the direct action of radiation on the cells.

The effectiveness of enhanced immunologic reactivity was then assessed by challenge experiments. It has been found that pre-exposure of mice to LDR suppressed the growth of Lewis lung carcinoma and melanoma cells and markedly reduced their metastasis. Furthermore, pre-exposure of tumor-bearing mice to LDR was found to enhance the tumor-suppressive effect of local high dose radiation to the tumor site and of whole-body chemotherapy via alleviation of the immunosuppression caused by high dose local irradiation and chemotherapeutic agents. We think this is a research field which deserves further exploration.
The cytogenetic studies were carried out at various places in the Altai region which had been subject to past radiation exposure due to 113 atmospheric nuclear explosions which took place between 1949 and 1962. The main contribution to exposure of the population in the Altai region was caused by the first nuclear test. The radiation dose from this test contributed about 50% to the total effective dose which the Altai population received over a long period of time.

The cytogenetic examination of populations in 8 localities in the Altai region was carried out on 256 persons. The group of persons examined included an adult population permanently living on the mentioned territories. The procedure for cytogenetic analysis included the conventional method (i.e., analysis of unstable aberrations) and the method of chromosome painting by FISH (i.e., analysis of symmetrical translocations).

For the 5 examined groups the mean frequencies of cells containing dicentrics and centric rings significantly exceed the control levels (4 - 10 times higher). A statistically significant (p<0.05) exposure effect relationship was confirmed between the frequency of cells with dicentrics and the cumulative dose in the Altai territories.

The frequency of symmetrical translocations in exposed groups was significantly (p<0.05) higher by 5 fold compared to the control level. The application of scoring symmetrical translocations by FISH method to the biological dosimetry of past radiation exposures is considered.
In Chernobyl, with its enormous territory contaminated and millions of people involved, physicians faced not only the problem of radiation-induced disease, but also the problem of the existence of a conceptual danger to between dangerous and safe doses. All the population of the Earth lives in constant contact with ionizing radiation: (as a result of medical investigations, natural environmental background etc). It is necessary to determine the effect of 'low' doses in the limit of 0-1 Gy long term irradiation at low dose rates. Does it lead to an increased chance of developing neoplasms or other harmful effects? The answer can be found only if dosimetry accompanies all radiation effect studies and biological dosimetry particularly relevant (Rad.Protect.Dosim. 42, 33-36, 1992; Brit.J.Hematol 1992, p39). The answer won't be forthcoming if we consider only the oncologic effects of radiation, since the population of humans is not uniform and we know that some families have an especially high frequency of tumors. The iodine-131 dispersed during the Chernobyl accident resulted in an epidemic of children's thyroid cancer which can't be recognized as unexpected or as the 'low dose' effect. In the Chernobyl contaminated regions we have had acute radiation injury of thyroid gland over the background of low dose irradiation of the whole body. Irradiation of the bone marrow was comparatively low and oncogenesis in this organ is questionable. The role of radiation in the etiology of many hemato-oncological diseases is therefore problematic. The 'International Consortium for Research Treatment of Radiation Induced Injury' was created in 1991 for study of the health effects of low dose radiation. According to our present understanding, it is important to point out that negative results obtained in epidemiological search mean nothing except failure of this approach. An interesting finding of Chernobyl studies are the findings of multiabberant cells. In cohorts of liquidators and residents of contaminated regions in the Briansk area, we found multiabberant cells in up to 10% of these population groups. No such large group was studied before. It is necessary to study the genome with different methods and to try to find source of injury. The incorporated alpha-emitting radionuclides can be expected in these subjects. The main problem today is the identification and study of cases of malignancy from Chernobyl contaminated region in association with different methods of biological dosimetry (stable and non-stable chromosome aberrations, ESR of dental enamel etc) to provide answers to questions concerning radiation oncogenesis and as to whether there exists a safe dose of ionizing radiation.
IODINE DEFICIENCY IN BELARUSIAN CHILDREN AS A POSSIBLE FACTOR STIMULATING THE IRRADIATION OF THYROID GLAND DURING THE CHERNOBYL CATASTROPHE

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Ten years after the Chernobyl nuclear plant catastrophe, more than 400 children in Belarus now suffer from thyroid gland cancer. Radioactive contamination with radioactive iodines consequent to that catastrophe seems to be the major cause of so high an incidence of thyroid cancer in children under the age of 15 years (11.7 cases for 100,000 children in the most contaminated areas, and 3.5 cases for the whole of Belarus). There are, however, doubts among scientists as to whether radiation is the only cause of the health situation observed. Thus, it is considered that regional iodine deficiency and high radioactive iodine uptake by the thyroid may also be important factors resulting in the high exposure of the thyroid to internal beta irradiation. Therefore, a countrywide program for investigation of goiter prevalence and iodine deficiency was established in the Republic of Belarus with the assistance of the WHO office for Europe. The program foresees the examination of 11,000 children and adolescents aged 6 to 18 years from 30 schools in urban and rural areas.

The results obtained in the group of 824 children and adolescents (a pilot phase) are presented. Goiter prevalence, as evaluated by palpitation, was found in 66.7% of the children. Within that group, goiter grade IB was observed in 44.2% and in grade II goiter, 20.5%. Iodine concentrations in urine samples were higher than 100 µg/dl only in 24.5 %. Concentrations from 50-100 µg were observed in 48.8%; 20-50 µg/dl in 20.3%; and below 20 µg/dl in 6.4%. These preliminary results are typical for significant iodine deficiency and moderate goiter endemy. It is also clear that the present situation does not completely reflect the situation existing at the time of the Chernobyl catastrophe. However, existing data from epidemiological studies done many years before the catastrophe showed that in the contaminated territories, a high prevalence of goiter was observed. Iodine deficiency at the time of the catastrophe was at least similar to the present one or even more pronounced. Such an assumption may help in the understanding of the pathologies of thyroid glands which were observed.
THE HANFORD THYROID DISEASE STUDY

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The Hanford Thyroid Disease Study (HTDS) was mandated by the USA Congress in 1988 to evaluate the potential health effects of radiiodine emissions which occurred at the Hanford Nuclear Site from 1944-1957. This site was established in 1943 to produce plutonium for nuclear weapons. In 1986, the US Department of Energy released information indicating that in the early years of weapons development, substantial amounts of radionuclides were released to the atmosphere. It has been estimated that 740,000 Ci of I-131, the primary component of the releases, were released during these years. After extensive evaluation of this information by two review panels, two studies were ultimately recommended: The Hanford Environmental Dose Reconstruction (HEDR) Project and the Hanford Thyroid Disease Study.

The objective of the HTDS is to determine whether thyroid disease is increased among persons exposed to atmospheric releases of radioactive iodine from the Hanford site. The study is a retrospective cohort follow-up design with the cohort defined by three criteria: proximity to the Hanford site, time of exposure, and age of exposure. The goal of these criteria is to define a cohort of persons with maximum sensitivity to radiation-induced thyroid disease (young age at exposure) and maximum opportunity to receive both the highest exposures as well as near-zero exposures (proximity to the site, time of exposure).

There are four principal components of the HTDS field work: Tracing, recruitment, thyroid dose estimation, and clinic participation for the assessment of thyroid disease. The status of these components is presented as of September 1, 1996.

- **Tracing.** A total of 5200 people were selected from birth certificates for participation in the study. 4501 (86.6%) were located by the HTDS tracing staff of which 4039 (77.7%) are alive.
- **Recruitment.** Of those people located who are alive, 3907 (96.7%) have been contacted and 3451 (88.3%) have agreed to participate in the HTDS.
- **Dose estimation.** Computer-assisted telephone interviews (CATI) are conducted with the participant’s mother or other close family member to obtain information about childhood residences, diet, and medical history. This information is used to estimate individual thyroid doses, with associated uncertainties, from a model developed by the HEDR Project. Of those agreeing to participate, 2059 (59.7%) have had CATI.
- **Clinics.** Study participants have traveled from almost all 50 states and from outside the US to attend one of several clinics held throughout Washington state. Each participant undergoes a personal interview, a thyroid ultrasound scan, laboratory testing including thyroid function, thyroid antibodies and serum calcium; independent thyroid physical examinations performed by two thyroidologists, and fine needle aspiration biopsies of palpable thyroid nodules. Of those agreeing to participate in the HTDS, 2507 (72.6%) have completed the clinic evaluation. Although the analysis will focus on the clinical outcomes of thyroid neoplasia and hypothyroidism, all thyroid disease outcomes as well as hyperparathyroidism will be assessed. Assuming that 3400 people participate in the clinics, the study will have 92% power to detect an increase of 5% per Gray for thyroid neoplasia. The clinics are scheduled for completion in September, 1997 and results available by late-1998.
POSSIBLE INFLUENCE OF RADIATION EXPOSURE AND IODINE DEFICIENCY ON THE MOLECULAR EVENTS IN THYROID CANCER

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The evaluation of thyroid cancer represents a common and important clinical problem. The distinction among thyroid hyperplastic nodules, adenomas and follicular carcinomas is often difficult. Thyroid carcinoma, which comprises the majority of endocrine malignancies, has a substantial annual morbidity and mortality based on several predisposing factors. One of these factors is radiation. A significant increase in the incidence of thyroid cancer in children was observed following the Chernobyl disaster in Byelorussia, Ukraine and Russia.

We hypothesized that p53 mutations might play a role in the pathogenesis of thyroid cancers arising in Western Russia, since large portions of this region were contaminated with radioactive fallout after the Chernobyl accident in 1986. Moreover, there is iodine deficiency in this area which may contribute to the development of thyroid neoplasia.

Wild-type p53 protein appears to be important in protecting thyroid cells against radiation and carcinogen-induced damage, given the role of this protein in cell cycle control and DNA repair pathways. A series of consecutive thyroid cancers originating from Russia (n=28) were compared against control cases from Albany, NY (n=27). The aim of the present study was to compare p53 levels and iodine levels in thyroid malignant tumors tissue of patients from Western Russia and from Albany, New York.

Nuclear p53 immunoreactivity was assessed using a monoclonal antibody, DO-1, on formalin-fixed paraffin-embedded specimens. Nuclear immunoreactivity for p53 was demonstrated in 30% papillary carcinomas from Russia and in 7% from Albany (p<0.03 Fisher's test).

Iodine concentration was measured using X-ray fluorescent scintigraphy in thyroid malignant tissue from Russia, from Albany and in 10 normal thyroid specimens from Russia (in vitro). Iodine levels were: 206±5.0 mcg/g tissue (Russia), 389±6.0 mcg/g tissue (papillary carcinomas from Russia), 389±6.0 mcg/g tissue (normal specimens from Russia) - p<0.01 - Student's test. Iodine concentration in papillary carcinoma cases from Albany was 102±5.0 mcg/g tissue.

In conclusion, p53 accumulation may play a role in the pathogenesis of a subset of thyroid carcinomas. The higher p53 positivity rate in cases from Russia might result from differences in environmental factors (radiation exposure, iodine deficiency) between Russia and New York. Moreover, our results are consistent with the idea that a decrease in iodine concentration is associated with the stepwise loss of differentiation in thyroid tumors. Further data about DNA content, iRb immunoreactivity and p53 mutations will be needed to assess this issue.
AUTOIMMUNE THYROIDITIS IN CHILDREN AFFECTED BY CHERNOBYL ACCIDENT

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The role of autoimmune thyroiditis in the genesis of various thyroid diseases is well known. It can be suggested that thyroiditis is the earliest effect of any thyroid damaging factors including ionising radiation. Data concerning the connection between thyroiditis and thyroid neoplasia, lymphoproliferative and myeloproliferative processes are also available. Antibodies to thyroid microsomal antigen are the indicator for the majority of thyroiditis.

The content of antibodies to thyroid microsomal antigen was investigated to evaluate the possible appearance of autoimmune thyroiditis. A total of 15771 sera of children who lived in the three districts Kaluga region were investigated (1987-1994). Contamination density in these districts varied from $7 \times 10^{-10}$ to $30 \times 10^{-10}$ Bq km$^{-2}$.

Eight-year dynamics of antimicrosomal antibody detection rate after the accident show that the maximal number of examined children with elevated antibody levels was detected in 1987 (4.8% cases). The number then decreased significantly until 1990 (1.2%), but afterward rose again (1993 - 4.6%).

In May, 1986, direct thyroid gland dosimetry was carried out in children living in the polluted territories of Kaluga region.

There is a significant difference in the frequency of antibody appearance between persons affected by radioactive iodine (2.6 - 7.9%) and those not affected (0.9%). Groups were identical with respect to sex, age and place of residence. Our data is suggested that the elevated rate of autoimmune thyroiditis is one consequence of the Chernobyl accident. (Fig.)

The autoimmune thyroiditis can be a sign of several pathologies of thyroid and gives rise to elevated risk of some haematological disease. We have data concerning the connection between autoimmune thyroiditis and lymphoproliferative neoplasms, cytopenias of unknown origin.

Taking into consideration that the autoimmune thyroiditis can be a sign to elevated risk of other autoimmune diseases, some haematological disease, thyroid neoplasia. The children with recorded autoimmune thyroiditis manifestations should be under continuous observation.
Immune status in children with benign and malignant thyroid tumours

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One of the most grave consequences of radioiodine effect during the course of Chernobyl accident is the increase in the incidence of childhood thyroid cancer. Occurrence of the tumour is reported to be the result of disorders in "surveillance function" of the immune system. It is also known that prognosis of oncologic disease depends, to a large extent, on the state of patient’s immune responsiveness. The aim of our study was to investigate peculiarities of the immunological status in benign and malignant thyroid neoplasms. A total of 112 patients (mean age 12.5 years) were examined. The number of examined children was the following: 20 healthy children (control); 14 patients with thyroid cancer before surgery, 51 patients with thyroid cancer after surgery; 15 children with benign thyroid tumours before surgery; 12 patients after surgery for benign thyroid tumours. In 75% malignant thyroid neoplasms were papillary carcinomas; in 25% - follicular carcinomas.

We studied blood thymulin concentration which is considered to be an integral index of thymic endocrine function, according to the literature data; blood lymphocyte production of humoral factors - mitogen-induced gamma-interferon (γ-IF), interleukin-1 (IL-1) and interleukin-2 (IL-2); blood serum level of circulating immune complexes (CIC) and T-lymphocyte suppressor activity in blood induced by Con A.

A comparative analysis of indices of immunological status in children with benign and malignant thyroid tumours allows the following conclusions:
1. Both in children with benign tumours and thyroid carcinomas all the indices of immunogenesis differ significantly from control before surgery.
2. We have revealed the most considerable manifestations of immunodeficiency (both before and after surgery) in children with thyroid cancer. Preoperatively, thymulin level is more then 3.5 times lower (p<0.001) than in control group. The level of lymphocytic γ-IF is 2 times lower (p<0.05), interleukin-1 and 2 productions significantly suppressed (1.7 times, p<0.05). An increase in T-lymphocyte suppressor activity (for 58%, p<0.05) and CIC concentration (for 31%, P<0.01) was observed. Postoperatively, we noted a further decrease of thymulin and IF contents (5 and 3.2 times, respectively). In 7 patients thymulin levels were not detectable at all. Partial but significant renewal of IL-2, T-suppressors, CIC was observed. We noted more marked changes of the immunological status in children with postoperative hypothyroidisms as compared with euthyroid children.
3. Some indices of the immune status is dependent on the time period following surgery and presence of metastases.
4. Renewal of immunogenesis is more intensive following resection of benign nodules. IL-1, 2, CIC contents, T-suppressor functional activity reach normal values. Thus, the results obtained prove the presence of marked immunodeficiency in children with benign and malignant thyroid neoplasm’s both before and after surgery. Changes in the immune status are more profound in children with thyroid carcinoma. The usage of immunocorrective drugs in combined therapy of children operated on for malignant thyroid tumour is, therefore, advisable.
Among radionuclides released from the destroyed reactor of the Chernobyl NPP the greatest radiation impact on people and related health detriment were provided with radio-iodine nuclides. The most contaminated areas of Russia were formed in Bryansk, Tula, Orel, and Kaluga regions. One hundred and four (104) cases of thyroid cancer in children and teenagers (at the time of accident) were found in these regions during last 5 years. The main problem of risk-analysis of thyroid morbidity among the irradiated population is correct dose reconstruction This problem is the main one considered in the suggested report. Methods of thyroid dose reconstruction used on the contaminated territories of Russia and received dose estimations are discussed in the report.

Dose estimations were based on 19,000 direct measurements of I-131 content in thyroid of inhabitants of Bryansk, Tula and Orel regions performed in May-June of 1986. Most part of the measurements was made with radiometers in non spectrometric regime that created the problem of interpretation of the results of measurement and of subtracting the radiation of Cs-137 distributed in a human body from the radiation of I-131 in the thyroid.

The model of prolonged I-131 intake into a human body during 10-15 days with subsequent decreasing of daily intake with half-time of 5 days (half-time of decreasing radioiodine concentration in milk) was chosen after analysis of all available radioecological and foodstuff data. Stable iodine protection and prohibition of locally produced milk were used in Bryansk region as a protective measure for local population. They were also counted in the dose calculations.

The highest individual thyroid doses, up to 10 Gy, were registered in children of west districts of the Bryansk region. In the Tula region highest individual thyroid doses were up to 4 Gy, in the Orel region, up to 2 Gy. Thyroid dose decreased with age in each settlement, distribution of thyroid dose in each age group was asymmetric, close to lognormal.

Regression analysis results of the relationship between thyroid dose estimated from the direct thyroid measurements and air kerma, radionuclide concentration in milk, soil contamination with long-lived Cs-137 in settlements were used for thyroid dose reconstruction in settlements where measurements of I-131 in inhabitants were not performed in 1986.

Collective thyroid dose were estimated for Bryansk region as 60,000 Person-Gy; Tula region, 60,000 Person-Gy; and Orel region 15,000 Person-Gy. Calculated prognosis of radiation induced thyroid cancer morbidity and thyroid cancer incidence in the most contaminated Bryansk region of Russia are compared in the paper.

Data on thyroid morbidity among the population of six most contaminated districts of the Bryansk region during first four years after the accident were analyzed depending on thyroid dose. Increase of thyroid nodules rate in adults with average thyroid dose higher than 0.5 Gy was found.
ADDITIONAL DOSE-FORMING FACTOR ASSOCIATED WITH THYROID CANCER IN THE BRYANSK REGION AFTER CHERNOBYL

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A rise in thyroid cancer in persons born between 1968 and 1986, i.e. in children and adolescents, can be associated with the effect of radioactive iodine released from the destroyed fourth block reactor at the Chernobyl nuclear power plant. Incidence of disease depends on multiple dose-forming factors, in particular on radioiodine contamination, age and gender of exposed persons, volume of local food consumption, functional condition of thyroid gland, iodine deficiency, and others.

In the Bryansk region, we believe that dwellers failed to take into a most significant factor: that between April and May of 1986, radiation was transferred via the main macadam and railroads, as goods were transported out from the radioactive contaminated zones.

With regard for the "road" factor, 69 thyroid cancers were plotted on Bryansk region map. We observed that a majority of patients with proven thyroid cancer lived and are living in settlements arranged close by highway and railroads. It was not initially expected there would be any dependence between the number of cases and ground contamination by iodine radionuclides and cesium-137. From the data it may be supposed that:

• as a result of intensive transport of goods from the accident zone through contaminated territories and further, the Chernobyl's radionuclides density was higher close to such transport routes.
• dwellers of neighboring settlements use more imported polluted food;
• during the transport, radionuclides accumulated on the ground, plants and buildings more intensively, moving large distances, and through respiratory ways entered the human body;
• cow pastures in the vicinity of main roads led to a greater radioiodine concentration in milk and, accordingly, in large doses delivered in organism; and
• freights carried by rail promoted fast transfer of short-living radioactive iodine isotopes a significant distance from the accident site.

If the above is true, one can expect higher uptake by thyroid gland dose in inhabitants living near the main Chernobyl roads, and therefore there would be a higher incidence of thyroid cancer.

In our view, the comprehensive analysis of radiation along the main roads and neighboring regions in the early months after the accident, is necessary. Analysis should also be done thorough medical examination all of the locations where radioinduced thyroid cancers were found.
ANALYSIS OF THYROID CANCER MORBIDITY IN CHILDREN AND ADOLESCENTS OF RUSSIA DURING THE TEN-YEAR PERIOD AFTER CHERNOBYL

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Bryansk, Kaluga, Orel and Tula regions were areas of Russia most effected by Chernobyl. Activity of iodine-131 in these territories is from 0.1 Ci/km² to 100 Ci/km² and more. In the stated regions, as of December 31, 1995, there were 124 histologically verified thyroid cancers in patients born between the years 1968-1986, i.e. in persons that were children and juveniles at the time of the disaster. The breakdown is as follows: Bryansk region, 69; Kaluga region, 3; Orel region, 35; Tula region, 17. The comparative analysis of expected and observed thyroid cancer morbidity in the above age cohort during the ten years after accident was carried out. To calculate the expected thyroid cancer, we used the age morbidity indexes in Russia in 1991, 1993, and 1994 (conducted by Acsel EM, Dvoyrin VV, Trapesnikov), and population census from 1968-1986 of births in the four regions (based on data of over-all census in 1989). During the ten-year period, there might be 40 expected cases of spontaneous thyroid cancers in the female population. Actually, in the given period, 90 cases were diagnosed, i.e. the number of diseases increased to 2.2 times the expected rate. The highest rate exceeding the expected rate was observed in girls born between 1982 and 1986. In males, expected and observed thyroid cancer was 11.2 and 34 accordingly, i.e. the disease quantity increased to 3 times the expected rate. Boys born between 1982 and 1986 demonstrated more significant morbidity than in the corresponding female group. The highest thyroid cancer increases in boys born between 1984 and 1985 constituted 32 and 29 times correspondingly. With the increase of male and female age at the time of accident the actual expected thyroid cancer morbidity ratio decreases and for persons 1968-1971 years of birth the ratio approximates to one. The analysis of thyroid cancer morbidity from 1986 to 1995 testify to the tendency of thyroid cancer to exceed the expected levels. This was noted in 1991, and was exceedingly high in 1994-1995. In females, the observed excess of actual over expected ratio is as follows: 1986-1982, 7.4; 1981-1977, 5.7; 1976-1972, 2.2; and 1971-1968, 2.7. In analogous male groups, the rate of increase is 36.9, 4.4, 1.9 and 0 accordingly.

Based on this data, we conclude that after the five-year latent period, a progressive rise of thyroid cancer incidence in children and adolescents in the aforementioned regions caused by the Chernobyl accident was observed. Particularly, the risk of additional thyroid cancer appearing in a greater degree defined by the age of the adolescent at the time of the disaster, significantly differs in males and females.
CLINICAL CURRENT OF THYROID CANCER IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS LIVING ON RADIONUCLIDE CONTAMINATED TERRITORIES OF BRYANSK, KALUGA AND TULA REGIONS.


Study introduce the analysis of 26 cases of thyroid cancer in children, adolescents and young adults having been in childhood and teenaging at the moment of Chernobyl accident (1968-1986 years of birth). All of them were hospitalized to diagnostic and treated in MMRC in-patient clinic. At the moment of diagnosis patients distributed as follows: from 7 to 9 years - 2, 10 - 12 years - 11, 13 - 15 years - 7, 16 and older 6 patients. Female - 16, male - 10, female/male ratio 1.6. At the moment of disaster age of these patients was: from 0-4 years - 15, 5-6 years - 5, 7-10 years - 3, from 11 to 15 - 2, and one child borned though 3 years after the accident. Papillary cancer was verified in 23 patients (88.5%) and follicular - in 3 (11.5%). Tumor size varied from 5 to 35 mm, spread on surrounding tissues in two cases. Regional lymph node metastases proved in 13 cases (50%) with two-side involving in six (23%). Lung metastases revealed in three patients (7.7%). Citologically thyroid cancer diagnosed in 20 (77%), in remain - by frozen section or after preparation in paraffin. Hemithyroidectomy performed in ten patients, subtotal in two. Now we advocated hemithyroidectomy in differentiated thyroid carcinoma only in pT1aN0M0 (according to "pTNM" classification, 1992). Thirteen patients were thyroidecomized with lymph node dissection and histologically we saw tumor aggressive trend or/multicentricity. Ten of them had lymph node involving in histological slides. All thirteen undergone radioiodine treatment. Posttreatment whole body scan demonstrated lung uptake in three cases with simultaneous fixing in upper mediastinum in one. All patient are given suppressive doses of L-thyroxine. As result of cumulated experience became the united diagnosis, treatment and follow-up protocol.
THE CORPORATE RESEARCH PROJECT „EFFECTS OF RADIOACTIVE RADIATION ON HEALTH; RISK AND PROJECTION MODELS“
- FIRST RESULTS -

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In 1994 the corporate research project Effects of Radioactive Radiation on Health - Risk and Projection Models has been launched. Two Russian institutes (Institute of Control Sciences, Russian Academy of Sciences, Moscow and Medical Radiological Research Centre, Russian Academy of Medical Sciences, Obninsk) and two German institutes (Department Clinical Social Medicine, University Hospital, Heidelberg and Geomedical Research Unit, Heidelberg Academy for the Humanities and Sciences, Heidelberg) signed an agreement on a long-term collaborative research project. Main objective is to support health policy decision making by reliable forecasts of morbidity and mortality processes in populations living or working in areas where they are exposed to radiation. The scientific kernel of the project is the development of a mathematical, methodological basis for morbidity and mortality models assessing uncertainties in given empirical data as well as in the present scientific knowledge. The general mathematical approach is to model such uncertainties as unobserved or partly observed states in Semi-Markov processes. A general model has been designed and is mathematically described elsewhere.

Here, the results of a first numerical solution of the model are presented which has been realised for estimation of morbidity among Chernobyl liquidators. This specific application of the model tries to assess uncertainties in the data due to the non-regular participation in the annual follow-up health examinations. In other terms: unobserved states in the process of diagnosis registration are modelled to allow morbidity estimates that are stable with regard to random fluctuations in the empirical data. This realisation of the model has been applied to data of the Russian National Medical and Dosimetric Registry. The results of the evaluation of morbidity dynamics among liquidators for the period of 1986-1993 show for 12 major classes of disease groups that estimated incidence rates are lower than those „observed“ in the registry. The figure shows this for the disease group of malignant neoplasms (ICD 140-208). The difference in incidence (per 100,000 population) is explained by „accumulated morbidity“ effects due to missing observations in the follow-up examinations. Whether other uncertainties in the data have similar effects has to be further evaluated. This may have importance not only for health policy decisions making but in other areas as well, e.g. when comparing morbidity rates with a reference (as shown in the figure with regard to the overall Russian population).
MORTALITY, CANCER INCIDENCE AND THYROID PATHOLOGY AMONG ESTONIAN CHERNOBYL CLEANUP WORKERS

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After the reactor accident at the Chernobyl Nuclear Power Station in April of 1986, approximately 5,000 men from Estonia (nearly 2% of the male population aged 20–39) were sent to the Chernobyl area to perform cleanup and reconstruction work. A cohort of these cleanup workers was assembled, based on military and other lists. A questionnaire was mailed to members of the cohort to collect information regarding work history while at Chernobyl, medical and occupational history (for radiation and chemical exposures), and smoking and alcohol use. Completed questionnaires have been obtained from 81% of the workers. The mean documented dose was approximately 11 cGy, and 82% of the men were current or former cigarette smokers. The study population is being followed through linkages with population and death registries. 99% of the population was successfully traced through 1993. A total of 144 deaths were identified during the period 1986–1993. There was a relatively high number of deaths due to accidents, violence and poisonings (also alcohol-related). Nearly 20% of deaths were due to suicide. Deaths due to diseases of the circulatory system also were common. Linkage with the Estonian Cancer Registry revealed 25 incident cancers versus 26 expected. No cases of leukemia were identified. A nonsignificant excess of non-Hodgkin's lymphoma was observed, based on three cases. Thyroid screening examinations, including clinical and ultrasound examinations and fine-needle biopsy, were conducted in spring of 1995, nine years after the accident. The prevalence of thyroid nodules increased with age but was not associated with radiation dose from external sources (as entered in worker records), or other indicators of exposure (date of first duty at Chernobyl, duration of service at Chernobyl, or having helped build the sarcophagus or worked on the roof near the damaged reactor). Two thyroid cancers were identified and these workers were referred for treatment. Estonian cleanup workers do not appear to have experienced an increased risk of thyroid cancer or nodular thyroid disease through the first nine years following the accident. The study provides useful baseline information for reference in future investigations. After about eight years of follow-up, radiation-related diseases appear to be of relatively minor importance when compared with the substantial excess of deaths due to violence and alcohol consumption.
ULTRAMORPHOLOGICAL ABNORMALITIES IN SPERMATOZOA OF SALVAGE WORKERS FOLLOWING DECONTAMINATION WORK AT THE CHERNOBYL NUCLEAR REACTOR AND ITS VICINITY.

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**Aim:** This investigation was conducted to assess effects of radiation on sperm quality, with special emphasis on the ultramorphology of spermatozoa of salvage workers engaged in decontamination procedures at the Chernobyl nuclear reactor accident site or in the adjacent region.

**Methods:** The study population consisted of 30 radiation exposed individuals, employed in exposure control and decontamination work seven years prior to the accident. A population of unexposed Ukrainian males were examined as controls. Semen parameters were assessed by light microscope, biochemical analysis and quantitative Ultramorphological (QUM) analysis by scanning and transmission electron microscopy. Samples were collected in the Ukraine, examined there by routine semen analysis, fixed and transferred to Israel for detailed examinations.

**Results:** Reduction in sperm progressive motility was found in the radiation exposed workers. Ultramorphological defects in the sperm nucleus were noted with high frequency among the exposed workers. Fertility potential was also adversely affected among them and associated with estimated radiation exposure. The adverse changes observed by electron microscopy were more severe in young workers.

**Conclusions:** The radiation exposed population of workers has impaired fertility potential seven years after radiation exposure. The injury was more severe in young workers and was independent of whether the work site was located at the reactor site or in the vicinity thereof. The observed morphological abnormalities are consistent with injury to the sperm chromatin.

The data can form a basis for the development of a radiation response index, which also considers sperm ultramorphological malformations. This index can serve as a tool to improve the accuracy of risk assessment of impaired fertility potential in the absence of information about precise radiation dose.
THE PILOT STUDY OF CLEAN-UP WORKERS FROM LITHUANIA

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This project was developed to study risks of diseases among men who were sent to Chernobyl during 1986-1990. This investigation reflects the joint efforts of research aimed at identifying clean-up workers, evaluating exposures, and identifying malignancies in well defined groups of workers. The radiation exposures received by the Chernobyl workers was recorded for many of the workers, but requires validation. Compared to the neighboring countries, the cohort of clean-up workers in Lithuania was unique in involving a small number of workers at the Ignalina nuclear power station (NPS). This group of professionals has well established dosimetry, which can help in validation of biodosimetry.

The objectives of the pilot study were: to assemble a cohort of Chernobyl clean-up workers from all possible sources, to obtain 600 blood samples for biodosimetry, to administer 600 questionnaires concerning the work experience of clean-up workers at Chernobyl or other possible occupational exposures, to validate documented radiation dosimetry records, to link the cohort with the population registry, to validate vital status, and from the cancer registry records to identify cases of malignancies. A total of 5446 registered Chernobyl clean-up workers was available at the start of the pilot study. The radiation dose was recorded only for 3756 workers. An additional 1706 workers were found during the pilot effort through additional sources. Blood specimens were analyzed at the University of Pittsburgh, applying GPA results. The cohort of registered and identified clean-up workers is estimated to be 7152. It was expected to find a higher proportion of cases from 1986, but the figures indicate an increase of only 18.40%. The ratio of 1986/1987 for clean-up workers from Lithuania (2283/2968) remains relatively low compared to Latvia (3195/1629) and Estonia (2909/1092).

1143 persons were invited for blood drawing and 603 responded. Attendance rate for the Chernobyl clean-up workers was 71.84%. The response rate among Ignalina clean-up workers was only 55.8%. The professionals were more interested in getting information on exact radiation exposure, rather than medical benefits.

Blood samples were processed for the isolation and cryopreservation of viable lymphocytes and a separate aliquot was sent to the University of Pittsburgh for biodosimetric analysis using the glycophorin A (GPA) somatic cell mutation assay. Three groups of subjects were analyzed: population controls (9), cleanup workers (173) and Ignalina NPS staff workers (50). Results indicates a marginally significant difference (p=0.049) between the N/N Vf observed in the controls versus the study subjects (mean±SD; 6.2±4.7 versus 13.6±38.3 and 10.3±13.9). All other pairwise comparisons for both Ø/N and N/N Vf are not significant. Consistent with the biodosimetric results obtained in the Estonian and Latvian cohorts, these data are consistent with the recorded physical dose estimates for these workers. In addition, these results suggest that there is not large subset of workers who received doses substantially above the average physical doses. The studies on health effects in this cohort are ongoing with the focus on thyroid nodularities, thyroid cancer and leukemia.
ON THE THYROID CANCER PROGNOSIS AFTER THE CHERNOBYL ACCIDENT

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The important effect of the Chernobyl Accident was that a great number of children had been exposed to radioiodine. In this connection there is a real possibility of developing thyroid cancer in future. However, the exposure of the thyroid to radioiodine is not the only risk factor of developing cancer. The belonging of the affected territories an also to regions iodine deficiency in the biosphere might also be a reason for a rise in the incidence and changes of the morphological structure of the thyroid malignant tumors. The purpose of this study was to assess the frequency of occurrence of thyroid cancer among children in endemic territories and to analyze its morphological types. A statistical analysis was made of the thyroid cancer incidence among populations in a number of endemic regions of the Saratov district where iodine prevention activities had never been carried out before. In order to specify the morphological peculiarities of thyroid cancer, an analysis was made of 40 case histories of children from the same district, aged between 7 and 14, and operated on for thyroid cancer during the period from 1975 to 1993. There were 7 boys and 33 girls. In all cases thyroid cancer was verified morphologically. When compared with similar data in Russia it was found that the mean (1989-1993) incidence rate among children in the Saratov district is three times as high and constitutes 0.3 par 100,000 children aged between 0 and 14. It was also found that the proportion of thyroid cancer in the structure of solid tumors among children from endemic regions is 4 times as high anal constitutes 7.3%. The incidence of thyroid cancer among children from regions with iodine deficiency in the biosphere reaches 1.6% of the total number of thyroid cancer cases among population which is also higher than in the Russian Federation. Taking into consideration the difficulties of verification and the possibilities of changes in the morphological structure of thyroid cancer under the influence of various ecological Factors, the services of several experts were enlisted for the analysis of post-operative specimen of the thyroid. The papillary carcinoma was identified in 45% of patients; follicular cancer, 20%; follicular-papillary, 22.5%; low-differentiated, 12.5% of children. It should be emphasized that the number of highly malignant forms of cancer in the endemic regions appeared to be 5 times as high as registered in central ontological clinics of Russia. The data presented here is of great importance for the differential diagnosis of biological causes of cancer in the aftermath of the Chernobyl accident.
EPIDEMIOLOGICAL INVESTIGATION OF HEALTH PROBLEM AMONG PARTICIPANTS OF CLEAN UP WORKS FOLLOWING THE CHERNOBYL ACCIDENT (1986-1996)

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Shortly after the Chernobyl accident, the Ministry of Public Health of the USSR made a decision on the setting up of the registry of persons exposed to radiation. The following two basic objectives were persuading in establishing the Registry: information support for health monitoring and rehabilitation of exposed persons as well as long-term radiation and epidemiological follow up aimed to evaluation of the contribution of radiation and non-radiation to the health status.

After the dissolution of the USSR, the Russian National Medical and Domestic Registry has operated at the Medical Radiological Research Center of RAMS (Obninsk). To the January 1, 1996 the database of the Registry consists of data on 435 thousand persons including 152 thousand of liquidators.

Liquidators are the special group in the Registry. Their average age is 43 years old (data on 1996), the mean dose due to external radiation is 0.11 Gy. The basic epidemiological rates, such as: incidence, disability and mortality for the period over 1986-1995 have been analyzed for the cohort of liquidators. The analysis is based on the information of the Registry. The relationship between the above rates and radiation doses as well as a number of other factors, i.e. dates and duration of the work within the 30-km zone neighbored to the Chernobyl NPP has been found.
BLOOD PRESSURE ASSOCIATED WITH EXPOSURES TO CHERNOBYL RADIATION AMONG "LIQUIDATORS" WHO IMMIGRATED TO ISRAEL

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Background: Increased frequency of hypertension has been found among older persons exposed to the Chernobyl explosion and who immigrated to Israel from relatively more polluted areas. It is not possible to distinguish whether the effect is related to radiation or other exposures or to psychosocial stress. This study considers the possible association between hypertension and indicators of exposure among Chernobyl clean-up workers, "liquidators."

Materials And Methods: Data from questionnaires and physical examinations of 87 liquidators are analyzed. Both the history of hypertension and measurements of blood pressure are used as criteria. Exposure gradients (for 75 persons) were determined on the basis of reports by respondents concerning histories of time, duration and types of work in the zone and symptoms of acute exposure. Resulting scores based on arbitrary weights, varied from 1 (low) to 5.5. Statistical methods used were Spearman and Pearson correlation, Chi Square, and Student's "t" test.

Results: Reported prevalence of hypertension prior to 1986 was 6.9%, and current prevalence 42.7%. Of those under 49 in 1985, the rates were 2.8% then compared to 25.8% now, while among the older group the rates were 26.7% then and 56% now. History of hypertension correlated with exposure scores for those up to 48 years, r = 27, p = 0.055. Of the 45 with exposure index <2, 15 (33%) reported onset of hypertension after work at Chernobyl, whereas of the 8 persons with scores of 1-2 none did (p = 0.055). For subjects older than 48, no association of hypertension with scores was found. The association of measured blood pressure with history of hypertension was significant, r = 0.43 for systolic and 0.36 for diastolic. The mean measured blood pressure for those under 49 with scores 1-2 was 111.9 +/- 9.2, compared to 123.8 +/- 13.2 for those with higher scores. For diastolic pressure the gradient was from 70.6 +/- 5.6 and 77.5 +/- 10.7. The differences for males and females were similar, but only the gradients for males were statistically significant. Systolic blood pressure was correlated with year of immigration to Israel, r = 0.32, p = 0.003.

Conclusions: There is a significant association of hypertension, either by history or measurement, with exposure indices for younger persons who worked as liquidators. This analysis can neither prove nor disprove whether the findings are due to radiation or to other conditions, or to their interaction.
Background. Accident of Chernobyl’s Nuclear Power Station (NPS) made a new problem for health professionals in Latvia due to the fact that 6475 inhabitants (mainly healthy and work able men of reproductive age) of Latvia took part in clean-up works in Chernobyl within the period from 1986 till 1991. Most of these people were documented as receivers of ionizing radiation exposure (0.01 - 0.5 Gy). The investigation of Latvian Chernobyl clean-up workers could be of great scientific value due to the fact that they are unique as a group of investigations because they were exposed to the ionizing radiation only for a short time and after that they have been living in places not contaminated with radiation and therefore are different from clean-up workers from Ukraine, Belorussia and Russia who still live in contaminated regions. The aim of work is to investigate and estimate the impact of small dose ionizing radiation to the health of Chernobyl clean-up workers and to work out proper methods for clinical treatment and rehabilitation.

Material and methods. We have worked out system for registration and follow-up of clean-up workers. They are undergoing regular medical check-ups in their places of residency. More detailed and deeper health examinations are done every year in the Center of Occupational and Radiological Medicine of Clinical Hospital of Latvian Medical Academy. We have created Latvia State Register for clean-up workers of Chernobyl NPS accident and their children. At the 01.04.1996, there were registered 5230 Chernobyl clean-up workers, 140 persons evacuated from Chernobyl, 1250 children from the families of clean-up workers (born after the accident). At the moment we have collected the data about time and period of clean-up workers stay in Chernobyl as well as data about the place and kind of work, dose of radiation received, protective measures used, food used, diseases and health status in Chernobyl. There are also data about bad habits (smoking, alcohol abuse and etc.), previous contacts with ionizing radiation and with other harmful occupational exposures and about chronic diseases before the Chernobyl’s accident. There is also huge data set containing results from the clinical examinations and investigations done within the period from 1986 till 1996. Statistical analysis was performed using EPI-INFO and SPSS software. Results. Analysis of dynamic morbidity shows us increased number of diseases connected with nervous system and organs of sense, with organs of digestive system as well as with endocrine and immune systems and metabolic disbalance. During last three years there are also increased number of diseases of musculo - skeletal system. In comparison with Latvian inhabitants clean-up workers have elevated levels of heavy metals (Pb, Zn and etc.) in biosamples (blood, urine, hair). We have determined the connection between the morbidity, duration of stay and place in Chernobyl and dose of radiation received. We have worked out list of diseases that was determined or that turned worse after the clean-up works in Chernobyl and therefore allow us to determine their connection with clean-up works in Chernobyl. 30% of all clean-up workers were registered as disabled persons. 0.3% of them were recognized as disabled persons of 1st group, 65% as 2nd group and 34.7% as 3rd group of disability. We have worked out methods of treatment and rehabilitation for clean-up workers where main attention is paid to normalization of metabolic processes, correction of discirculatory disbalances and adequate psychotherapy. Till the 01.01.96, 3.8% of all registered clean-up workers were dead. Main reasons of their deaths have been - 48% - diseases, 33% - accidents, 12% - suicides, 7% - alcohol intoxication. We have worked out proposals for government to solve medical and social problems of clean-up workers.
THE LATVIAN CHERNOBYL CLEAN-UP WORKERS' COHORT 10 YEARS AFTER THE DISASTER


Up to date a total of 6055 persons are registered who had participated in the Chernobyl Power Station accident clean-up works. Among them 1.4% individuals below 19 years of age, 37.2% - aged 20-29, 46.3% - 30-39 years old. 3346 persons were interviewed, blood samples for biomarker (GPA and Fish) analyses were obtained from 1810 persons.

The first series of GPA Vf were measured in blood samples from 24 control persons and from 281 clean-up workers with reported (documented) radiation doses. The current analyses were unable to distinguish a consistent significant difference between the Vf distributions of exposed workers and controls. The biodosimetry studies of chromosomal translocations in peripheral blood lymphocytes will give an additional information.

A high morbidity rate among the clean-up workers is observed, the main causes: gastrointestinal, nervous system and bone-joint diseases (about 17%-19% each), psychic disorders (11%), cardiovascular (9.5%) and respiratory diseases (7%). The number of endocrine and metabolism disorders (up to 18% in 1995) has increased in 1994-1995, 30% of clean-up workers are disabled. A total of 187 death cases in the clean-up group is registered. Among the main causes - heart diseases (34%), accidents (33%), suicides (12.4%), 5.3% cancer deaths have been observed.

By the end of 1995 48 primary oncological patients were registered, among them 5 leukemia cases, 3 cases of brain cancer, 1 thyroid cancer, two persons have two types of cancer simultaneously.
INTERNAL EXPOSURE OF THE PEOPLE INVOLVED IN 1986 IN REMEDIAL
ACTIONS ON CHERNOBYL NUCLEAR POWER PLANT

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As a result of the Chernobyl Nuclear Power Plant (ChNPP) accident, a great amount of
dispersed nuclear fuel and condensed radioactive vapors was released as aerosol particles
into the atmosphere of the working environment. Inhalation of these aerosols became the
source of internal exposure for ChNPP staff involved in the liquidation of the accident.
The studies showed that aerosol of Nuclear Fuel Particles (NFP) is the unique form of
airborne radioactivity. NFP contain fission products and transuranium radionuclides
strongly bound with the uranium matrix

In 1986 the NFP tracers were found in the bodies of about 750 people, who witnessed
and liquidated the accident at the ChNPP site on 26 to 27 April, 1986. For
reconstruction of individual doses we have chosen out of those accident witnesses a
group of about 400 people, examined with the semiconductor body counter in 1986. The
25 persons of ChNPP staff and fireman who died of acute radiation sickness in 1986
form the second group of accident witnesses for whom the doses of internal exposure
were reconstructed. The results of postmortem studies on the radionuclide distribution in
the organs of members of this group were used for dose reconstruction. The results of
dose reconstructions are presented in the table.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Structure of cohort</th>
<th>(E^\dagger), mSv</th>
<th>(H_L^\ddagger), mSv</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>23 dead witnesses of accident</td>
<td>600*</td>
<td>2400*</td>
</tr>
<tr>
<td>II-A</td>
<td>Alive 125 witnesses of accident, treated in clinical department of IBP in 1986</td>
<td>130</td>
<td>400</td>
</tr>
<tr>
<td>II-B</td>
<td>Alive 250 witnesses of accident, worked at ChNPP in 1986-88</td>
<td>40</td>
<td>120</td>
</tr>
</tbody>
</table>

\(\dagger\) Committed effective dose, \(E\); \(\ddagger\) Committed equivalent dose in lungs, \(H_L\); *to the time of death was realized not more than 6% of that figure.
CYTOGENETIC RADIATION MARKERS IN LIQUIDATORS: WHY ARE WE FINDING THEM LONG AFTER THE ACCIDENT?

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Clean-up workers or liquidators are one of the largest groups of victims of the Chernobyl accident. They were exposed to different types of ionizing radiation. Now they appear to have developed a variety of somatic and psychological diseases. Ten years after the accident we are concerned about oncological diseases in liquidators. Therefore, it is important to know the rate of genetic disturbances in somatic cells of liquidators.

The organizing structure of the All-Russian Centre of Ecological Medicine gave us a unique opportunity to carry out cytogenetic studies on a large group of liquidators exposed to the Chernobyl accident. We used the generally accepted cytogenetic methods. Special medical and social questionnaires were completed for each person. All information obtained was entered into the database of the laboratory.

We have performed cytogenetic investigations in 278 liquidators in a remote period after the accident. The total rate of chromosomal aberrations in liquidators is slightly higher than in control one (2.56±0.15% and 1.69±0.30%, p<0.05%). Nevertheless there are essential differences in aberration spectrum: liquidators show a significant increase in the frequency of chromosomal type aberrations and radiation markers (1.21±0.09% and 0.40±0.10%, p<0.001). Among the total group of liquidators 20.9% persons had dicentric and ring chromosomes; 20.5%, atypical chromosomes; and 15.1%, chromatid type of exchange aberrations. In general, 20% of the liquidators had cytogenetic changes representing mutagenic effects. This frequency did not depend on clinical diagnosis. We found only 9% of persons with such radiation markers in the control.

The presented results demonstrate an increased frequency of radiation markers for a long time period after the accident. According to accepted opinion we should expect the elimination of lymphocytes with chromosomal aberrations caused by the natural lifetime of lymphocytes. The frequency of dicentrics and rings in liquidators is not very high (0.2 per 100 metaphases) but it significantly exceeds the background level (0.06 per 100 metaphases).

We have some suggestions to explain the increased level of radiation markers in liquidators long after the accident: received doses could be higher than officially recorded exposures; "memory" lymphocytes may continue to circulate with a long lifetime; mutations in stem cells; disturbances of DNA reparation system; incorporated radioactive particles. Regardless of the reasons for this phenomena the presence of chromosomal aberrations may be a signal of potential danger for human health. It is known that genome instability is a factor of risk of oncological diseases. Therefore, ARCEM has started to monitor this group including their health and cytogenetical parameters. Long-time observations of the health conditions of people exposed to ionizing radiation is one of real methods of evaluation of medical consequences of Chernobyl and other radiation accidents. We are interested in scientific cooperation with our colleagues in order to study different radiation markers and methods of investigation for our group of liquidators.
HEALTH STATUS OF EMERGENCY WORKERS LIVING IN NORTHWEST RUSSIA

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The Chernobyl explosion produced widespread health effects, because millions received increased radiation doses. Health problems are especially prominent in the cohort of Chernobyl accident emergency workers (EWS). Epidemiological study of such workers is most useful because within the cohort we can identify and compare the experiences of groups subjected to high radiation exposures. We report on the study of 9,071 men who were EWS “liquidators” now living in the northwest Region of Russia. Fifty-six % started EWS work in 1986, and 26% in 1987; 27% had recorded doses > 20cGy and 1% > 25cGy. Morbidity data for them are based on annual examinations at the EWS Registration Center. Health status changes are reported for the period 1990-1994, and exposure status is based on governmental registration.

Results: Diseases of the circulatory system are the most prevalent, and the proportion increases yearly, being 21.6% in 1994. The prevalence of such diseases is greater among the EWS starting work in 1986. The regression ratio for circulatory disease is 33.4; for nervous system disease, 24.9; and musculoskeletal diseases 17.9%. Dispersion analysis comparing those with dose up to 25cGy and those with greater doses shows that time interval between the explosion and starting work and age of participants are about equally important to dose in their effect on initial incidence rates. While the incidence of malignant tumors is greater among workers starting in 1986, it does not exceed the rate for the male population of Russia. Steady increase in the numbers with limited working capacity has been found and was examined by discriminant analysis. Intensity of exposure (more than 20 cGy), age and time of starting work, were the principal variables; cardiovascular and mental disorders were the most prevalent reasons for loss of working capacity. Standard mortality also was greater for the 1986 cohort, compared to other EWS workers, but was not greater than for a comparison group. We feel these results justify more intensive prospective study of risk factors related to radiation and other exposures.
LEUKEMIA AMONG THE LIQUIDATORS: TEN YEARS AFTER CHERNOBYL

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We have collected data and analyzed the incidence rates and 10 years dynamics of different forms of leukemia among liquidators of the Chernobyl nuclear power accident. The initial information on this cohort of the population was obtained from the Belarussian State register of persons who were exposed to radiation due to the Chernobyl nuclear power plant catastrophe. The database of this register contains at present the information on 63,500 liquidators that represents no more than 53 percent of the whole number of Belarussian citizens who took part in the liquidation of the consequences of the Chernobyl catastrophe and had been given the corresponding certificates. In this register the data on the health of liquidators are recorded, including cases of oncohematological morbidity. Since the latter was the subject of the present study that required the special care and the best possible verification of the material, the data obtained from the State register of the exposed persons were compared with the ones from the National Blood Diseases Register that had been put into action at the Hematology and Blood Transfusion Research Institute, and the relevant data from the second register were additionally used in our study.

Thirty-seven cases of acute and chronic leukemia among liquidators were documented. Ten cases (27%) were diagnosed during the first 5 years following the accident (1986-90), the rest during the next 5 years. However, we must be cautious about concluding that incidence rates increase really took place during the latter 5 years period. The point is that state registration of the liquidators as well as assigning them an official status started in Belarus only in 1990-91. So, we cannot exclude the possibility that a certain number of persons who took part in the liquidation of the Chernobyl nuclear power plant consequences fell ill with leukemia and died before this period, and were not, therefore, included in the register of exposed persons. Nevertheless, a comparison of the incidence rates of leukemia among liquidators during the two periods made us possible for us to discover a number of specific features in their characteristics and dynamics. For example, if the ratio of acute leukemia / chronic leukemia incidence rates was 1.5:1, so in the second period it become 1:3. All the acute leukemia cases of the first period were alymphoblastic, while during the second period 2 out of 7 acute leukemia cases were of lymphoid form. The distribution of myeloid and lymphoid forms of chronic leukemia also altered from 0:4 to 1:1.

Thus, we can state that during the years immediately following the exposure, the portion of acute hemopathies was higher than in the next period. It seems apparent, that this magnitude would be still higher if it were possible to include in the study all the persons who took part in the liquidation of the Chernobyl nuclear power plant disaster consequences and who fell ill before 1990-91: it is exactly acute leukemia that, as a rule, rapidly causes the lethal outcomes (60% of all the liquidators, suffered from acute leukemia, died during one year), could be a reason for the mentioned deficiency of information on leukemia incidence rates among the liquidators during the first years following the accident. The dynamics of leukemia incidence rates among the liquidators demonstrates that the peak of morbidity level was in 1991, when 4 cases of acute and 5 cases of chronic leukemia were diagnosed. In 1992-94 one case of acute and 3-6 cases of chronic leukemia were annually diagnosed. The morbidity level of acute leukemia per 100,000 of liquidators reached the magnitude of 6.3 in 1991, of chronic myeloleukemia magnitude, 4.7, and of chronic lympholeukemia, 3.1. These incidence rates of acute leukemia and chronic myeloleukemia (which are potentially radiation-induced diseases) are higher than the incidence rates found in the whole population of Belarus, standardized with the liquidators cohort according to age and sex. However, we must bear in mind that, as it was noted before, almost 50% of the liquidators in the Republic of Belarus have not been as yet included in the State register of the exposed persons as being practically healthy persons who have not yet consulted the specialized medical establishments which provide most of the information to this register. It may be, therefore, that the true incidence rates of leukemia among liquidators are lower by half. However, the observed incidence rates of the chronic myeloleukemia among the liquidators in the last years is sufficiently high to cause concern and requires attention.
INSIGHTS INTO THE MECHANISMS OF RADIATION DAMAGE AND
RADIOPROTECTION THROUGH THEIR MODULATION BY CYTOKINES

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Cytokines, hormone-like proteins that are produced by stimulated cells and tissues, serve as intercellular messengers. The production in pharmacological quantities of an expanding number of recombinant cytokines has permitted assessing the benefit they may provide in preserving and restoring functions of tissues compromised by irradiation. It has been documented that the cytokines Interleukin-1 (IL-1), Tumor Necrosis factor (TNF), Stim Cell Factor (SCF) and IL-12 protect mice from radiation lethality when given prior to radiation, and even in untreated mice these cytokines serve in innate defenses from radiation (1). In contrast, TGF, IL-6 and Interferon (IFN), given before irradiation, sensitize to radiation lethality (2). IL-1 myeloprotection against ionizing radiation depends on the regimen of treatment, and may be related to the temporary patterns of IL-1-induced cytokines and to the resulting changes in the cycling status of the progenitor cells (3). IL-12, through induction and interaction with additional cytokines, has contrasting effects on different tissues, i.e. protecting the bone marrow but sensitizing the gut (4). These studies provided insights into the cellular mechanisms of regulation by cytokines of radiation-induced damage (5). Thus, induction of scavenging enzymes, such as MnSOD in mitochondria, by pro-inflammatory cytokines IL-1 and TNF was shown to contribute to radioprotection. Additional mechanisms of radioprotection may be based on prevention of radiation-induced apoptosis of hematopoietic progenitors and/or induction of primitive hematopoietic progenitors to cycle and to progress to relatively radioresistant S-phase. In contrast, the sensitizing mechanisms may include increased oxidative damage that may occur in the absence of induction of scavengers, or enhanced apoptosis.

References:
MELATONIN AND RADIOPROTECTION FROM GENOTOXICITY: AN IN VIVO-IN VITRO INVESTIGATION IN HUMAN VOLUNTEERS

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Blood samples from four different human volunteers were collected ~10 minutes before, and at 1 and 2 hours after an oral dose of 300 mg melatonin. Immediately after each collection, an aliquot was used to determine the concentration of melatonin in the serum and leukocytes, and duplicate aliquots were exposed in vitro to 1.5 Gy gamma radiation (137Cs, dose rate of 1.087 Gy/minute). The lymphocytes were immediately stimulated with phytohemagglutinin and cultured for 48 hours to determine the extent of genetic damage, assessed by scoring the frequencies of chromosome aberrations. The results indicate a significant increase in the concentration of melatonin in the serum and leukocytes at 1 and 2 hours after the oral dose of melatonin (as compared with the sample collected before the oral dose was taken). Lymphocytes which were collected at 1 and 2 hours after the oral dose of melatonin and exposed in vitro to 1.5 Gy gamma radiation exhibited a significant decrease in the incidence of (a) exchange-type of chromosome aberrations, (b) acentric fragments, and (c) abnormal cells showing chromosome damage (as compared with similarly irradiated lymphocytes which were collected before the oral dose of melatonin). The frequencies were slightly lower in the lymphocytes collected at 2 hours, as compared with those collected at 1 hour after the oral dose of melatonin. The data may have implications for protection of human lymphocytes from the genetic damage induced endogenously or exogenously by free radical producing physical and chemical mutagens and carcinogens.

This research was supported by the Division of Radiation Oncology, The University of Texas Health Science Center, and grants from the United States Air Force Office of Scientific Research (KGAUO-29-035-1-02) and National Institutes of Health (ES07132).
We investigated the radiomodifying effects of taxol, a cell cycle modifying drug. Taxol cytotoxicity is associated with a block in the most radiosensitive G2/M phase of the cell cycle. But in many cases taxol is not a radiosensitizer. Our study refers to the conflicting data on this issue. Murine EMT-6 and J774.2 cells were studied in comparison with human ovarian carcinoma cells (OV-1063) and cultured human skin fibroblasts (HF).

Effects of taxol and radiation were studied by survival assays as well as on the cell cycle level. The cell lines selected had similar radiosensitivity excluding the less radiosensitive HF. However, their sensitivity to 24 hours taxol exposure varied significantly. In EMT-6 and J774.2 cells (IC50~20nM and ~100nM, respectively) taxol showed dose and time dependent radiosensitization; with an increase in G2/M phase and a decrease in the S phase; the groups of possibly apoptotic cells with sub-diploid and subtetraploid DNA content (termed Apo-I and Apo-II, respectively) were significantly elevated. In the taxol-sensitive OV-1063 cells (IC50~3nM) the drug induced most pronounced G2/M block with marginal increase in both Apo-I and Apo-II; but the combination of taxol and radiation resulted in a mere additive effect. In HF (IC50~35nM) the combined treatment yielded a clear sub-additive effect with only a minimal G2/M block and with no change in the S phase. Only Apo-I was elevated significantly. Baccatin III, a less cytotoxic derivative, demonstrated a minimal effect on the cell cycle and only a mere additive effect in combination with radiation. Therefore, taxol induced G2/M block with a depletion in the S-phase seems to be a necessary but not a sufficient condition for radiosensitization.

Of special interest was the sub-additive response to the combination of taxol and radiation observed in HF. Taxol treatment for 6 hours in non-synchronized cells decreased the G1 phase of the cell cycle by ~17% while the S phase increased from ~4% to more than 24%; a sub-additive effect of the combined treatment with radiation was observed. The short exposure of synchronized HF to taxol immediately after the onset of the cell cycle did not change the proportion of the S phase but G2/M phase was elevated; a more additive effect of the combined treatment was then monitored. Taxol treatment at 20-26 hours after synchronization resulted in a twofold increase of the S phase and elevation of the G2/M phase; this resulted in a most pronounced subadditive effect. In all these cell populations 6 hour treatment with taxol did not change significantly the proportion of the presumably apoptotic cells in Apo-I and Apo-II. In conclusion, the clear sub-additive effect of the combination of taxol and radiation observed in slowly proliferating HF seems to be related to taxol mediated redistribution of the cells in the in the more radioresistant phases of the cell cycle, with no apparent role of apoptosis in this effect.
ON THYMUS CARINOGENESIS IN THE MICE AFTER LOW-DOSE IRRADIATION

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It is generally believed that carcinogenesis has an important detrimental effect in man after low-dose irradiation. It has been clearly demonstrated that ionizing radiation has a carcinogenic action in terms of development of thymic lymphoma (TL) after exposure to a relatively high doses (2 or 3 Gy) in mice. In order to investigate the risk of carcinogenesis following low-dose irradiation investigations were carried out in mice considering TL as an end point. The strain of Swiss mice used in the present experiments are refractory to the development of TL as such. However, when a high dose of 2 Gy ($^{60}$Co - gamma rays) administered to 8-10 week old mice, TL developed in about 46% of the mice. A low-dose fraction of 1 cGy, when administered to a similar age group of mice, TL could not be detected during the experimental period up to 260 days. When a fractionated dose was administered at intervals of 24 hours over 5 or 10 days, TL was visible in a small proportion (17% on average) of mice. When mice were exposed to a single dose of 1 cGy 24 hours prior to giving a high dose of 2 Gy, the incidence of TL was reduced to a small extent. When the mice were exposed to 5 or 10 multiple fractions of 1 cGy, before a high dose, the occurrence of TL was decelerated by 30% and 16% compared to the incidence of TL after a high dose. The incidence of TL was very high (76% on average) during the experimental period of 1-4 months following an exposure of high dose of 3 Gy in 8 week old female mice. In female mice a single exposure of 1 cGy 24 hours before a high dose of 3 Gy led to a reduction of about 26% during the same post-irradiation intervals. Single dose of 1 cGy were also found to delay the onset of transplantable tumor (originated from irradiated thymus tumor in our laboratory, by 1 week in 75% of mice against 100% development of tumor in unirradiated control mice within 2 weeks. The growth of transplantable TL was also diminished by about 20%. It may be concluded from these results that a low dose radiation of 1 cGy does not reveal any carcinogenic potential in mice. On the contrary, low doses appear to reduce the risk of carcinogenesis against the definite occurrence of tumor, whether due to exposure of a high dose radiation or by inoculating the mice with cancer tissue cells.
BIOLICAL EFFECT OF HUMIC ACID PRODUCT IN RATS EXPOSED TO 60-Co GAMMA IRRADIATION


Biological effects and complex forming capacity of different extracts of humic acids have been widely studied for many years in early experiments performed in our institute. Decorporation efficacy of natural humic acids product (HA) was studied in rats exposed to 134-Cs or 85-Sr. Natural humic acids were also used to enhance the excretion of inactive toxic metals like Cd and Pb both in rats and human volunteers.

The dose-effects relationship of natural humic acid product on the hematological parameters of rats exposed to 7Gy 60-Co gamma whole body irradiation was studied.

Rats were treated with different doses of HA (90 and 250 mg/day/rat) using pre-, continuous- and post-treatment schedules. Animals were exsanguined 7 days before, 7, 14, 21 and 28 days postirradiation. The number of white blood cells (WBC) and platelets (BP) dropped suddenly 7 days postirradiation in whole body irradiated animals. In these rats hematological parameters were normalized only by the 28th day of the experiment. No changes were found in the number of WBC and BP of rats treated with only HA (90 mg) during the whole period of the experiment.

In irradiated rats treated with HA (90 mg) 7 days pre- and 28 days postirradiation, both the number of WBC and BP increased to the normal level one week after irradiation. Similar tendencies were observed when the treatment with HA was started just after irradiation but there was a two week delay in the normalization of hemopoietic system. A continuous daily treatment with HA in a dose of 250mg had caused no changes in the number of WBC and BP compared to the irradiated group.

It was concluded that this natural humic product could effectively be used in the prevention or lymphocyto- and thrombocytopenia caused by accidental or therapeutical external whole body gamma irradiation and for an increasing normalization of hemopoietic system.
STUDY ON THE POSSIBILITY OF MELANIN APPLICATION FOR PEOPLE PROTECTION AGAINST RADIATION

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Radiocontamination of biosphere results in chronic influence of ionizing radiation in low doses on large groups of living organisms, including human populations. Earlier we have revealed that melanin reduces the percentage of different mutation types induced by acute irradiation and decreases the mutation load accumulated in Drosophila populations as a result of X-ray irradiation for 115 generation. The investigation of melanin possibility to influence chronic irradiation effects was very urgent. The influence of melanin isolated from animal hair on genetic effects of irradiation in mice and human lymphocytes has been studied. Mice were exposed to 1-3 Gy of γ-rays of Cs137 at the dose rate of 0.007Gy/h. The starch gel or melanin suspension in it, in concentrations from 0.3 to 30 mg/kg, were injected into stomach of mice every day. The levels of reciprocal translocations in spermatocytes were analyzed cytologically. Human cells were cultured according to a standard method. Melanin was added to culture media at G1 and G2 stages in the concentrations from 0.1 to 30.0 mg/l. Human cells were exposed to 0.5Gy of γ-rays and were analyzed cytologically.

Melanin in all concentrations was shown to reduce effectively mutagenic action of acute γ-irradiation. The melanin influence on genetic effect of chronic irradiation was even more effective than acute irradiation. It was shown that the pigment at a concentration of 3 mg/kg greatly reduced the percentage of induced mutations at different doses of chronic irradiation. The same effects were shown if melanin was supplied in other concentrations: It was revealed that melanin activity doesn't depend on concentration used.

It is very difficult to compare antimutagenic activity of melanin under acute and chronic irradiation because in the first case one injection of melanin has been used, but in the second case melanin has been injected many times (once a day for 10-20 days). Nevertheless it is possible to draw a conclusion that melanin is no less and even more effective under chronic irradiation than under acute one.

Radioprotective action of this pigment is connected with its high ability to accept and to give back electrons and with anti-radical activity. It is clear that when low-dose irradiation is used, the possibility for melanin to catch free radicals or electrons is better.

The investigations of melanin action have shown, that the aberration frequency in intact cells (control) was ranging from 0.42±0.19% to 1.0±0.3%. These values agree with the literature data. It means that melanin does not increase the control level of aberration and has no mutagenic ability.

The study on radioprotective action of melanin in human lymphocytes has demonstrated, that it in all used concentrations is effective in reducing of aberration frequencies, induced by radiation. Strict concentration effect correlation was not observed either in human cells or in mice. There are some proofs that only small amount of melanin can penetrate into cells, and melanin quantity inside cells doesn't increase with rise in outside melanin concentration, this fact can explain absence of such correlation.

Antimutagenic effect of melanin has been revealed to be the same under irradiation at G2 stage as at G1. These results demonstrate that melanin action does not depend (or little depends) on the repair system. The same conclusion was drawn earlier, when melanin had been investigated in drosophila and mice.

Complete toxicological tests have been conducted. The pigment melanin is not toxic and does not possess a mutagenic activity. Melanin could be used in medicine for people’s protection against genetic consequences of long-term irradiation. We are ready to present this pigment for clinical tests.
STUDIES ON LIVER CHROMATIN STRUCTURE IRRADIATED WITH FAST NEUTRONS

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The growing interest in neutron therapy requires complex studies on the mechanisms of neutron action on biological systems, especially on chromatin (the complex of deoxyribonucleic acid-DNA with proteins in eukaryotic cells).

We extracted the chromatin from a normal tissue-livers of Wistar rats and from a tumoral tissue, Walker tumor maintained on Wistar rats. For chromatin separation, we used a supplementary nuclei's purification through a passage on 1M sucrose and we verified the purity by an absorption test. Suspension of cells: $5 \times 10^6$ cells/ml concentration from Wistar rat livers and from Walker tumors were also isolated. We used irradiation doses from 5 Gy to 100 Gy by fast neutron intense beams produced via d (13.5 MeV) + Be (thick target) reaction at Bucharest U-120 Classical Cyclotron. To study the post-irradiation effects, various methods were employed. So, we pursued the variation in the 260 nm absorbency in chromatin thermal transition (E₀-before and E-after transition). We analysed the chromatin-ethidium bromide complexes fluorescence with $\lambda_{ex}=480$ nm and $\lambda_{em}=600$ nm. To determine chromatin DNA strand breaks a fluorimetric method with cell suspensions as starting material was used. This method requires a partial treatment with alkali, producing three components: T, estimating the total fluorescence of DNA double helix; P, assigning the untwisting rate; and B, the blank, where DNA is completely unfolded. The percentage of DNA double strand-D-, remaining after this treatment, is: $\%D=100 \times (T-B)/(T-B)$. We determined the intrinsic chromatin fluorescence for tyrosine ($\lambda_{ex}=280$ nm, $\lambda_{em}=305$ nm), specific for basic chromatin proteins, and for tryptophane ($\lambda_{ex}=290$ nm, $\lambda_{em}=345$ nm), specific for acid chromatin proteins. The double fluorescent labelling of chromatin was realised with acridine orange for DNA and with dansyl chloride for chromatin proteins. Fluorescence intensity determinations were done with $\lambda_{ex}=505$ nm, $\lambda_{em}=530$ nm for acridine orange and with $\lambda_{ex}=323$ nm, $\lambda_{em}=505$ nm for dansyl chloride.

For normal chromatin, we observed a reduction of the negative fluorescence intensity for chromatin-ethidium bromide complexes with the increasing of the neutron dose (from 0.98 at 5 Gy to 0.85 at 100 Gy). This fact reflects chromatin DNA damage, with the decrease of double helix DNA proportion. Single and double strand breaks are produced under fast neutron action. The quantity of the remaining DNA double strand, determined by fluorimetric analysis of the unwinding DNA, also decrease with the neutron dose. We also observed a reduction of intrinsic fluorescence intensity with the neutron dose (approximately 1.5 times from 5 to 100 Gy), denoting a destruction of chromatin protein structure. The energy transfer efficiency also decreased under neutron action (from 0.224 at 5 Gy to 0.135 at 100 Gy), indicating a more unstable tertiary structure of chromatin.

For tumor chromatin, representing the relative absorbencies (E/E₀) obtained for the thermal transitions of chromatin samples versus increasing fast neutron dose, we observed lower values indicating a damaged chromatin DNA (with a smaller proportion of double helix). The fluorescence intensities of chromatin-ethidium bromide complexes versus increasing fast neutron dose also indicated a reduction, lower values denoting modifications in chromatin DNA structure, so that intercalation of ethidium bromide between pairs of superposed DNA bases takes place to a lesser degree. From intrinsic fluorescence of chromatin tyrosine and of chromatin tryptophane versus increasing fast neutron dose, we observed the reduction of their values indicating a destruction of chromatin proteins.

To study the influence of thiotepa, thyroxine and D₃ vitamin treatments on fast neutron radiolysis in tumor chromatin, we administered, separately or together, to Wistar rats bearing Walker carcinosarcoma 10 mg/kg of anticancer drug thiotepa, 40 μg/kg of the hormonal compound thyroxine and 30,000 IU/kg of D₃ vitamin. We carried out similar studies on chromatin modifications as mentioned below. The results indicate that the association of thiotepa with thyroxine and D₃ vitamin produce a reduction of chromatin lesions induced by cytostatics and, consequently, differences in chromatin fast neutron radiolysis. Such results could constitute an indication for associated chemotherapy-radiotherapy schedules in clinical applications.
CANCEROSTATIC AND RADIOPROTECTIVE EFFECTIVENESS OF THE MIGI-K PREPARATION AND THE POSSIBILITY OF ITS USE IN TUMOR RADIOTHERAPY


We have studied MIGI-K preparation from the meat of mussels produced by the VNIRO Institute. It contains essential and non-essential amino acids, poly- and oligopeptides, polyenolic fatty acids, melanoidine-like substances, some antioxidants, vitamins and macroelements. This preparation is non-toxic, provides a well-pronounced radioprotective effect, is radiotherapeutic as well as radioprophylactic, upon \textit{per os} administration. Especially important is that MIGI-K caused the enhanced level of radioresistance for a long period, about two weeks after the end of its administration. Therefore, this preparation is perspective in the conditions of split-dose irradiation used in cancer radiotherapy. It was therefore important to obtain data on MIGI-K influences on the growth of malignant tumors.

We used Wistar rats with sarcoma-15 and with Walker carcinosarcoma and F1 (CBA x C57bl) mice with the solid form of Erlich ascite carcinoma. MIGI-K was administered with water, 4 ml/kg body weight per day, from the moment of tumor cell inoculation. For tumor radiotherapy we irradiated the area of the tumors in mice with Erlich carcinoma with doses of 10-15 or 30-35 Gy. To evaluate immunomodulative action of MIGI-K we used RBTL-reaction.

It was shown that MIGI-K produces a carcinostatic effect. Tumor growth was slower in animals consuming MIGI-K. For example, sarcoma-45 volume on the 7th day was 2330 mm$^3$ in control animals and only 780 mm$^3$ in MIGI-K-consuming (p<0.01) animals. The difference for Walker carcinosarcoma on the 7th day was 2086 and 575 mm (p<0.01) and for Erlich carcinoma on the 17th day it was 12,630 and 6,060 (p<0.01). We have also shown that MIGI-K potentiates the effect of the radiotherapy. 10-15 Gy X-irradiation of the area of sarcoma-45 causes the diminishing of the tumor size 4-5 fold. MIGI-K use diminishes tumor size a further 1.5 fold. In mice with Erlich carcinoma 30-35 Gy X irradiation of the tumor area on the 7-9th day after tumor cell inoculation causes a short time diminishing of tumor growth and enhancement of the life-time of the tumor-carrying animals. This remission was longer after MIGI-K use and in 20% of mice there was a full curative effect. They were alive and had no tumors 7 weeks after irradiation, when animals from non-irradiated and irradiated with MIGI-K groups died during the 3rd to 4th week. The other 80% of the animals had tumors but lived.

It was proposed that the cancerostatic effect of MIGI-K depends on its immuno-modulative activity. RBTL-reaction study shows that tumor cell inoculation stimulates spontaneous RBTL-reaction of spleen lymphocytes, which ends on the 8-9th day. PHA-stimulated RBTL was close to the control until the 6th day and then was deeply suppressed. MIGI-K modified, as well as spontaneously PHA-stimulated, RBTL-reaction. The data provides evidence for the antigen-specific T-lymphocytes activation under MIGI-K action. All the above-mentioned properties of the MIGI-K, which is allowed by the Minstry of Health of Russia as a food product for prophylactic and curative use, led us to conclude that it can be useful during radiotherapy of tumors.
FEATURES OF RADIATION DAMAGE ACCUMULATION OVER LARGE TIME INTERVALS

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Chernobyl accident and nuclear-related activities have led to the long-term increase of radiation background. It is formed mostly by isotopes with half-lives much shorter than those of natural radionuclides, but comparable with, or exceeding, human lifespan. To determine the maximum permissible dose, it is thus necessary to establish the time over which the existing dose rates should be integrated.

Accumulation of genetic damage is determined by the effects of radiation (DNA damage) and the processes of repair and selection. For time intervals exceeding average lifespan, we showed the process determining the average level of DNA damage to be the natural selection (or any other way of elimination of most damaged lines, such as lower probability of healthy descendants). The characteristic time of this process (around 3 generations) is the approximate time of integration of the dose rate for determination of background. It is formed mostly by isotopes with half-lives much shorter than those of natural radionuclides but may affect next generations. The following equations describe the dynamics of genetic damage:

\[
D_{1} / dt = k_{1} P - \alpha D_{1} - (N_{a} / N) E(D_{1}, D_{2a}, D_{2b}) D_{1} - S(D_{1}, D_{2}) D_{1}
\]

\[
D_{2a} / dt = k_{2a} P - E(D_{1}, D_{2a}, D_{2b}) D_{2a} - S(D_{1}, D_{2}) D_{2a}
\]

\[
D_{2b} / dt = k_{2b} P - (N_{a} / N) E(D_{1}, D_{2a}, D_{2b}) D_{2b} - S(D_{1}, D_{2}) D_{2b}
\]

Here \(P\) – effective dose rate; \(\alpha\) – DNA repair rate; \(k_{1}, k_{2a}, k_{2b}\) – parts of dose rate responsible for the respective types of DNA damage \((D_{1}, D_{2a}, D_{2b})\); \(N, N_{a}\) – respectively, total number of cells in an average organism and the average number of cells with “removable” damage \(D_{2a}\); \(E(D_{1}, D_{2a}, D_{2b})\) – cell replacement rate as a function of its DNA damage (this term and division of \(D_{2a}\) into \(D_{2a}\) and \(D_{2b}\) appear only for multicellular organisms); \(S(D_{1}, D_{2})\) – “selection rate” for affected specimens.

In the simplest case of single cells with “step-like” selection rate after some threshold DNA damage \([S(D_{1}, D_{2}) = \beta]\), the “steady-state” damage is proportional to dose rate but independent of time:

\[
D^{(s)} = D_{1}^{(s)} + D_{2}^{(s)} = P[k_{1} / (\alpha + \beta) + k_{2} / \beta]
\]

DNA repair time \(1/\alpha\) is much shorter than any other characteristic time, thus making the current amount of repairable damage \(D_{1}\) insignificant. Selection rate \(S(D_{1}, D_{2})\) may be assumed proportional to the total damage: \(S(D_{1}, D_{2}) = \gamma(D_{1} + D_{2})\); “selection time” \(1/\gamma(D_{1} + D_{2})\) is about 3 generations for some value of \(D_{1} + D_{2}\), as approximately 50% of mutations manifest themselves within 2 generations. Replacement rate may be assumed “step-like” for specialized cells: \(E(D_{1}, D_{2a}, D_{2b}) = \gamma\) after certain threshold value of \(D_{2a}\).

Cell replacement time \(1/\gamma\) is a small (but not very small) part of lifespan.

The equations (1) were solved numerically: a) for stable dose rate within certain interval, and zero outside this interval; b) for exponentially decreasing dose rate – \(^{137}\)Cs release with \(T_{1/2} = 30\) years (1 generation was assumed 25 years). The results show that, after 3–4 generations under exposure (stable dose rate), the total DNA damage depends on dose rate but is independent of time, similarly to the case of single cells. In the case of exponentially decreasing dose rate, total genetic damage reaches its maximum 33 years after the beginning of exposure, though dose rate at that time falls to 0.45 of the initial value.

Thus, for long-term radiation exposure, the characteristic time of genetic damage accumulation is around 3 generations. To reduce adverse effects on next generations, maximum permissible dose should be established for this characteristic time. For longer exposures, limits should be considered for dose rate.
PREDICTION OF HORMESIS IN RADON CARCINOGENESIS

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We have developed a novel mathematical model to describe general carcinogenesis, and applied it to the induction of human lung cancer in association with radon exposure. In a semi-stochastic way, the model quantitatively describes the probability for malignant cell transformation in a three-stage process, involving mutations of genes, proliferation of pre-malignant cells, and cell killing, both from natural causes and from radon exposure. Essential to the model is the proliferation of cells in the pre-malignant stage, which process may resemble the well-known phenomenon hyperplasia. From this stage, cells may undergo a final transformation to malignancy, which is considered in the model to be equivalent to the induction of cancer.

Pre-malignant cell proliferation, in combination with the possibility of cell killing by alpha-particle hits, may lead to the quantitative prediction of hormesis effects in low-level radon exposure, as have recently been reported in an epidemiological study among the US population (Cohen, Health Physics 1995, 68: 157-174). At the same time, and with the same values of the model parameters, a very good fit results when the model is applied to epidemiological data on radon exposed miners (Lubin et al., J Nat Cancer Inst. 1995, 87: 817-827). Also, when the model is fitted to epidemiological data on human lung cancer as a function of age, excellent results are obtained for all sets of data that have been considered (e.g. UK age-specific incidence data). The numerical values of the model parameters, that these results have been obtained with, all seem to be in agreement with what is known from literature, or with respect to what one reasonably might expect.

As the model makes some very definite predictions (such as the already mentioned hormesis), its validity should be rather easy to test in experimental animals. The results of the model indicate that there need not be an a-priori contradiction between the high lung cancer incidences as found among radon exposed miners, and the hormesis effects that have been reported for domestic exposures. In both situations, the proposed model may provide a theoretical basis for understanding the underlying mechanisms of radon carcinogenesis. In general, it may lead to a completely different approach to the concept of low dose radiation risk.
MENTAL AND PSYCHOSOMATIC DISTRESS OF LATVIAN CHERNOBYL LIQUIDATORS: STRESS-RELATED OR RADIATION-INDUCED?

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Background
Among the health consequences in the aftermath of the Chernobyl catastrophe, mental disorders are of special interest. It is debated whether postdisaster psychopathology is related to the stress of living or working in perceived radioactive accidental release (with possible dose-response effects), or whether mental impacts, as some other pathologies, are caused by radionuclides cellular damages. The Chernobyl clean-up workers have been highly exposed, and are supposed to have their state of health being monitored and registered. Hence, their follow-up represents an important clue to accurately detect and quantify effects of low-dose ionizing radiations on health. The objective of this study is then to identify exposure dose-response effect on mental and psychosomatic distress in the aftermath of the Chernobyl catastrophe and disentangle stress-related from radiation-induced consequences.

Population and methods
On the whole 4664 liquidators have been traced, recorded, and followed-up since 1987 by the State Latvian Chernobyl clean-up workers registry. For all of them, a basic questionnaire on administrative characteristics, and clinical features is filled in during their yearly examination in outpatient clinics. To record data on medical history, and lifestyle, occupational, and environmental risk factors, a sub-sample was prospectively drawn by including the first 1444 liquidators undergoing a medical examination in 1994 who answered a detailed questionnaire. The variables under study are the length of stay in the Chernobyl area, the lengths of works in various places (on the damaged reactor, in the inner zone 0-10 km, in the 10-30 km area...), the number of times the liquidator has worked on the damaged reactor roof, the types of work (construction of the sarcophagus, earth removal, buildings construction or destruction, work in the forest), the use of protective apparatus (gloves, breathing apparatus, protective clothing), the local foods consumption (water, milk, fresh vegetables, fresh fruits, fresh mushrooms, meat), the chemical exposure and the smoking habits. The psychopathology syndroms we focus on in this study are depression (ICD 9 : 300.4 + 309.0), cardiovascular physiological malfunction from mental factors (ICD 9 : 306.2), and disorders of the autonomic nervous system (ICD 9 : 337.9). Comparisons between subgroups of the cohort classified according to exposure type or level are made. Statistical analyses are based on the proportional hazards model, in which the variable of interest is the length of time that elapses before the pathology occurred for the first time. Estimates of relative risks (RR) are adjusted by stratification for age and calendar period.

Results
Work (> 1 time) on the damaged reactor roof (RR = 2.02, 95 % CI 1.00-4.13), and fresh fruits-consumption (≥ 1 time/day) (RR = 2.40, 95 % CI 1.03-5.58) are risk factors for depression. Construction of the sarcophagus (RR = 3.24, 95 % CI 1.42-7.43), and buildings destruction (RR = 1.45, 95 % CI 1.13-1.85) are significantly associated with cardiovascular physiological malfunction from mental factors. Length of work (≥ 28 days) in a 10 km radius from the reactor (RR = 1.38, 95 % CI 1.07-1.78) and work (> 1 time) on the damaged reactor roof (RR = 1.80, 95 % CI 1.16-2.79) are risk factors for disorders of the autonomic nervous system.

Conclusion
The findings confirm that some exposure variables represent risk factors for mental disorders and suggest some radiation induced consequences although surely overweighted by stress-related effects.
TWO-YEAR FOLLOW-UP STUDY OF IMMIGRANTS TO ISRAEL FROM THE CHERNOBYL AREA

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We report on findings from a two year follow-up study of immigrants who originated in the exposed areas around the site of the 1986 Chernobyl accident matched with comparison subjects who immigrated from other Republics in CIS. In the initial study of 709 immigrants, the samples had been matched on age, gender and year of immigration. We assessed two exposure groups - high exposed and low exposed by estimating levels based on levels of ground cesium contamination from the city of emigration from the IAEC maps. We reinterviewed a total of 520 immigrants from the first wave of data collection (a reinterview rate of 73%), 87 from high exposure areas and 217 from low exposure areas and 216 comparison subjects. This study examined the prevalence of Post-Traumatic Stress Disorder (PTSD), its secondary symptoms (depression, somatization, hypochondriasis, anxiety and interpersonal sensitivity) and physical effects (such as high blood pressure and chronic illness). PTSD was measure using the Impact of Events Scale (Horowitz, 1979) and the Scale of Irritability Disorder Arousal (Snaith et al., 1978). Secondary symptoms were assessed by the SCL - 90-R for somatization, anxiety and interpersonal sensitivity (Derogatis, 1967), the CES - D depression scale and the HSIG hypochondriasis scale.

The results obtained in the first wave, conducted 8 years after the accident, showed that the psychological symptoms were significantly higher in the exposed respondents than in the comparison group. In addition, a significant association was found between the symptoms of PTSD, other psychological symptoms and high blood pressure. During the second wave (10 years after the accident) we observed a decline in the prevalence of PTSD and related distress. However, the differences between the three groups were still statistically significant and supported the previous findings. Concerning the physiological effects, in the second wave, the association between exposure and high blood pressure was not found when blood pressure was measured. However, there was a significantly more hypertension reported by the exposed groups. Furthermore, the proportion of those who reported three or more chronic health problems was 48.3% among the high exposure group, 49.3% in the low exposure group, and 30.6% in the comparison group (p=0.0003). The most commonly reported problems were heart disease, problems with vision or hearing, migraine headaches, problems with the lymphatic system, and arthritis.

Based on the results, it was concluded that the Chernobyl accident was a powerful stressor, having a strong impact on both mental and physical health. Since all of the respondents were engaged in the process of acculturation and accommodation to a new country following emigration, it is encouraging that this study shows that levels of psychological distress are waning as the new immigrants are absorbed into Israeli society. However, there still remains some independent effect on health associated with the experience of the Chernobyl accident.
RF FIELD EXPOSURE AND CANCER: WHAT DO THE LABORATORY STUDIES SUGGEST?

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Concern has been expressed that exposure to RF fields may be associated with an increased incidence of cancer. While there is no convincing evidence of RF-induced DNA breaks or increases in chromosomal aberration frequency when temperatures are maintained within normal physiological limits (WHO 1993), two recent, unconfirmed rodent studies suggest RF fields may affect DNA directly (Sarkar et al 1994, Lai and Singh 1995).

Szmigielski et al (1982) and Szudzinski et al (1982) report that chronic exposure of mice to RF accelerated the development of: sarcoma colonies in the lung following subcutaneous injection of sarcoma cells; mammary tumours in mice having a normally high incidence of these tumours; and skin tumours in mice that were chemically induced by painting the skin with the carcinogen 3,4-benzopyrene. Szmigielski et al (1988) also reported that exposure to RF fields increased the number of chemically induced hepatomas and sarcomas and increased the number of skin tumour in mice given a subcarcinogenic dose of benzopyrene.

In contrast to these reports, Salford et al (1994) report no effect on the progression of tumours cells injected into rat brain following exposure to continuous or pulsed 915 Mhz RF fields and Santini et al (1988) found that the progression of subcutaneously implanted melanoma cells in mice was unaffected by daily exposure to pulsed or cw exposure to RF fields. Further Wu et al (1994) also report no effect of RF exposure on chemically induced colon cancer in mice. No single type of malignant tumour was enhanced by RF exposure of rats in a lifetime study (Chou et al 1992). However, the incidence of primary malignancies in the exposed group was significantly higher than the controls but was similar to the levels of primary malignancies reported elsewhere in this strain of rat.

While there are conflicting results from the few studies conducted so far, only a few studies have been conducted and there is a clear need for more good, long-term studies on laboratory animals to provide confidence about conclusions of RF-induced carcinogenesis. This paper provides a review of the laboratory studies to date and suggests what further research is needed.

References:

BIOLOGICAL EFFECTS IN ANIMALS EXPOSED TO EXTREMELY LOW FREQUENCY (ELF) ELECTRIC AND MAGNETIC FIELDS

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There is now convincing evidence from a large number of laboratories that exposure to extremely low frequency (ELF) electric and magnetic fields produces biological responses in animals. Many of the observed effects appear to be directly or indirectly associated with the neural or neuroendocrine systems. Such effects include increased neuronal excitability, altered behavioral responses, some of which are related to sensing the presence of the field, chemical and hormonal changes in the neuroendocrine system, and changes in endogenous biological rhythms. Many additional indices of general physiological status appear relatively unaffected by exposure, although effects have occasionally been described in bone growth and fracture repair, reproduction and developments, and immune system function. More recently, an enhanced effort has been focused on the question of cancer and exposure to ELF magnetic fields. Although most of the reported studies do not support an association between cancer and ELF field exposure, there are recent publications suggesting that 50 Hz magnetic field exposure increases the incidence of mammary tumors in rats. These results are being investigated in several ongoing replicate studies.

Three major challenges exist for ongoing research, including: 1) knowledge about the mechanisms underlying observed bioeffects is incomplete, 2) the exact physical aspects of exposure that produce biological responses is not understood and 3) health consequences resulting from exposure to ELF fields are not clearly and reproducibly demonstrated in humans or animals. Although no animal studies firmly establish deleterious effects of ELF fields, several are suggestive of potential health impacts. The need to define basic mechanism and investigate health consequences of ELF exposure has been enhanced because of emerging epidemiologic information on possible field association with cancer and immune system impairment.

From the perspective of laboratory animals studies, this paper will discuss biological responses to ELF electric and/or magnetic field exposures. Possible implications for human health will also be reviewed.
Public and occupational exposures to microwave radiation occurred in two distinctive eras. That connected with military, industrial uses and to some extent broadcast exposures were in the first era, and it is from this period that the data to be cited are drawn. The current widespread use of the cellular telephone dominates the exposures in the second era.

Four types of effects have been reported: (1) Increased spontaneous abortion; (2) shifts in red and white blood cell counts, including reports of polycythemia vera (3) increased somatic mutation rates in lymphocytes, and (4) increased childhood and other cancers. Assumptions and limitations of reasonable uses of the data are the next step toward basing health protection on the data. For some of the findings, experimental validation could well be done simultaneously.

As a transitional strategy prior to any drastic changes in existing standards, a program of epidemiological monitoring is recommended, especially among cellular phone users, using reproductive outcomes and shifts in blood counts as outputs. At the same time, prudent avoidance of unneeded exposures is indicated. In particular more extensive use of shielding for hand held phones and for broadcast facilities would be a desirable step.
Epidemiologic Research On Magnetic Fields And Cancer. Ahlbom A. Division Of Epidemiology, Institute Of Environmental Medicine, Karolinska Institute, Box 210, 171 77 Stockholm, Sweden

During the last two decades the hypothesis that exposure to weak extremely low frequency magnetic fields increases the risk of cancer has attracted a growing interest among epidemiologists, toxicologists, biologists, physicists, and others. Since epidemiologists rather consistently have found associations between magnetic fields and cancer in their studies epidemiology has to some extent been driving this research. One consequence of this has been an increasing interest for epidemiology among scientists in other disciplines. This has also affected the discussion about results from epidemiologic studies and scientists without epidemiologic training and with limited experience from epidemiologic research has participated in this discussion. As a result certain issues have received more attention than is usually the case in discussions regarding epidemiologic studies while other issues have received less attention. To some extent it appears as if scientists outside epidemiology perceive epidemiology differently than epidemiologists themselves. This seems to hold for the basic issues of what type of question that is addressed through epidemiologic research and what type of answer that is received. It also appears as if evaluation of studies and assessments of limitations and strengths in epidemiologic research are done differently by epidemiologists and others.

The aim of the present paper is to present some fundamentals of epidemiologic theory and methods and while doing so emphasizing certain issues that have been raised in discussions regarding studies on magnetic fields and cancer. The issues addressed include evaluation of confounding, effect of exposure misclassification, possibility of chance findings, multiple comparisons and post hoc analyses, and overall evaluation of epidemiologic findings.
For centuries, underground metal miners in the Erz Mountains of eastern Europe in the 16th century experienced remarkably high occurrence of respiratory diseases. The miners were subsequently shown to have unusually high rates of lung cancer and, early in this century, radon-222 was hypothesized to be the cause. The findings of epidemiologic studies of additional groups of radon-exposed underground miners in the 1950s and 1960s led to the acceptance of the hypothesis and radon is now classified as a human carcinogen by the International Agency for Research on Cancer. While there is still concern about the impact of radon exposure on workers, we have now recognized that this respiratory carcinogen contaminates the air of homes and other buildings.

For the purpose of public health protection, there have been numerous assessments of the risks posed by chronic exposure to radon progeny and models have been developed based either on the dosimetric approach or on the epidemiologic approach. This presentation will review the approaches used in the two risk assessments conducted by Biological Effects of Ionizing Radiation (BEIR) committees of the National Research Council the first in 1988 (BEIR IV); the second is currently in progress and will be published in 1997 (BEIR VI). Data from studies of miners have been central and informative in developing these risk models. The pooled analysis of four cohorts performed by the BEIR IV committee included data on 360 lung-cancer deaths among 22,190 miners. The BEIR VI committee had access to the results of a pooled analysis of data from 11 studies of underground miners published by Lubin and colleagues as a U.S. Department of Health and Human Services monograph (NIH Publication No. 94-3644). The more recent pooled data set includes over 2,700 lung-cancer deaths among 68,000 miners followed for nearly 1.2 million person-years. Both committees used regression analysis to model the relationship between exposure to radon progeny and lung cancer risk. The BEIR VI committee is using the expanded data set and thereby gaining statistical power to characterize lung cancer risk and its determinants in the miners.

The BEIR VI committee began its work approximately 6 years following the publication of BEIR IV. In addition to the availability of a larger data set, new experimental and epidemiologic evidence of an effect of exposure rate on -particle carcinogenesis, new evidence from the studies of miners that the interaction of smoking and radon might be less than multiplicative, further information relevant to the dosimetry of radon in mines, and new evidence of the potential importance of other factors in mine atmospheres, such as the presence of arsenic in Chinese tin mines and silica in underground uranium mines, were examples of factors which were cited by a scoping committee in 1994 as reasons why it should be feasible and appropriate for a BEIR VI committee to reassess the health effects of exposure to radon (Health Effects of Exposure to Radon: Time for Reassessment?, National Research Council, 1994). The resulting BEIR VI committee identified six issues deemed critical in characterizing the risk of exposure to radon. Those issues, which are points of uncertainty in formulating a risk model, will be reviewed as will the overall committee approach. Radon progeny represent a chronic exposure, both for workers and for the general population. The BEIR committees have developed an approach to characterizing the resulting risk that draws to the fullest extent possible on relevant experimental and observational data.
LACK OF ASSOCIATION OF INDOOR RESIDENTIAL RADON EXPOSURE
AND RISK OF CHILDHOOD ACUTE MYELOID LEUKEMIA (AML)

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Radon in indoor air has been estimated to be responsible for a substantial number of cases of lung cancer
in nonsmokers. Ecologic studies have linked residential radon exposure with risk of leukemia and other
cancers, and reports have suggested that effects may be more pronounced for AML. The Childrens Cancer
Group (CCG) and NIEHS evaluated the risk associated with residential radon in a large case-control study
designed to assess the role of environmental risk factors in the etiology of childhood AML. The cases
were identified between January 1, 1989 and March 31, 1993 through CCG institutions. The study included 525
cases under age 18 with a diagnosis of AML as defined by the French-American-British (FAB)
classification, and 619 age- and race-matched regional population controls. Information was collected
through telephone interviews with parents on known and suspected risk factors, including pesticides, solvents
and petroleum products, and maternal marijuana use.

Study subjects were eligible for the radon component if they lived in their current residence at least 5 years
up to the time of leukemia diagnosis (or their entire life for those under 5 years of age). A total of 238
cases and 298 controls met the eligibility criteria; 194 case and 255 control families participated in the radon
study. The study involved completing a supplemental residential questionnaire and the placement of 2-3
alpha-track radon detectors in designated areas of the home for a period of one year. The first monitor was
placed in the index child's bedroom, and the second monitor was placed in a room in the lowest living level
where the index child spent a substantial amount of time during the day. A third detector was placed next
to one of the others in 8% of homes for quality control purposes. Another quality control measure included
blind reading of spiked and blank detectors.

Unconditional logistic regression analysis was conducted to evaluate leukemia risk associated with radon
exposure adjusted for socioeconomic status variables, including maternal race, maternal education, and
family income. The mean radon level (average of detectors 1 and 2) in the current residence was 1.44
pCi/L in cases and 1.60 pCi/L in controls. No increased risk was observed in relation to the radon value
as a categorical variable (<2, 2-3.99, 4+ pCi/L). Cumulative lifetime radon exposure was estimated by
assigning to unmeasured previous residences since conception for cases and controls the mean measured
radon value for controls. Cumulative exposure was also not related to leukemia risk. No associations
emerged after further characterization of radon exposure by maternal smoking status, level of detectors
(above ground, at ground, below ground), or by taking into account the proportion of time the index child
spent in various levels of the home and away from home.

Further analyses focusing on a subset of 126 cases and 176 controls where the family lived in the same
residence since the birth of the index child were performed to evaluate the degree of bias introduced by
potential misclassification of exposure in the overall analysis. The risk of AML was unrelated to radon
exposure. These results do not support the hypothesis that indoor radon exposure increases the risk of
childhood AML.
LEUKAEMIA IN THE PROXIMITY OF A GERMAN BOILING WATER NUCLEAR REACTOR: EVIDENCE OF POPULATION EXPOSURE BY CHROMOSOME STUDIES AND ENVIRONMENTAL RADIOACTIVITY

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The detection of an exceptional cluster of leukaemia in children 5 years after the start-up of the nuclear power plant Krümmel in 1984, accompanied by a significant increase of leukaemia cases in adults gave rise to investigations of radioactive contamination in the environment. The rate of dicentric chromosomes in peripheral lymphocytes of 6 parents of leukaemia children and 20 other inhabitants in the proximity of the plant was significantly elevated and showed decreasing but repeated exposure over the years of operation, indicating chronic leakages by the plant. This was confirmed by elevated concentrations of the fission product tritium measured in trees as well as several findings about long-lived artificial radioactivity in air, rain water, soil, and vegetation registered by the regular monitoring programme. Calculations of the corresponding source terms of radioactivity show that the originating emissions must have been well above authorized limits. These contaminations are interpreted as relics from releases of predominantly short-lived nuclides. The bone marrow dose is thought to be originated mainly by ingestion of β-aerosols as Sr 89 (50 d). Overdispersion and multiaberrant cells in the chromosome studies suggest, moreover, the incorporation of bone-seeking α-emitters.
FEASIBILITY ASSESSMENT FOR EPIDEMIOLOGIC STUDIES OF COMMUNITIES NEAR NUCLEAR WEAPONS FACILITIES IN THE UNITED STATES.

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In response to the health concerns of people living in communities near United States Department of Energy (DOE) nuclear weapons development and production facilities, the Centers for Disease Control and Prevention (CDC) systematically assesses environmental radiation exposures and possible adverse health effects in those communities. For one facility, the former Feed Materials Production Center, near Fernald, Ohio, a radiation dose reconstruction and an epidemiologic feasibility assessment will be completed in August 1996. The Fernald facility, which was operated as a metal foundry from 1952-1988, produced highly refined uranium metal that was used in operations at other DOE nuclear facilities. The dose reconstruction conducted for this facility determined the radionuclides (uranium, radon, thorium, and others) and the amount of radiation released to the environment as a result of the facility’s operations. Results of the dose reconstruction were also used in a computer model for estimating radiation doses (and the uncertainties in the dose estimates) received by representative persons at various places within a 10-kilometer radius of the facility, which we call the assessment domain. To assess whether an epidemiologic study is possible, we obtained information on the estimated size and mobility of the population within the assessment domain, on data sources useful for identifying and locating residents, and on data sources for morbidity and mortality.

We are also estimating the sample size required to conduct an epidemiologic study with acceptable statistical power. Using a life table approach that combines data from the U.S. Census and U.S. Geologic Survey, we have developed a method to estimate the size and dynamics of a potential study population. This approach, used with representative per person dose estimates obtained from the dose reconstruction, provides possible distributions of person-years at risk for given dose levels. To determine if it is possible to identify past residents of the assessment domain, we are reviewing records available through local government offices, such as tax assessors and voter registrars, and through local utility providers. As a preliminary assessment of the health experience for the population of the assessment domain, we are examining the geographic distribution of deaths from bone and lung cancer. After collecting the above information, we will then compute the required study size, and the impact that uncertainty in the dose estimates has on that size. The result of the feasibility assessment will be options for potential analytic studies and public health surveillance programs. These options, and guidelines for decision making, will be discussed with a community advisory committee composed of local area residents, scientists, and physicians. Similar approaches are planned for other communities with U.S. Department of Energy nuclear facilities.
CURVILINEARITY IN THE DOSE-RESPONSE CURVE FOR CANCER IN THE JAPANESE A-BOMB SURVIVORS

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The recently released data on cancer incidence in the Japanese atomic bomb survivors are analysed using a variety of relative risk models which take account of errors in estimates of dose to assess the dose-response at low doses. For all solid cancers analysed together there is a significant positive dose-response (at the one-sided 2.5% significance level) if all survivors who received 0.5 Sv or less are considered, but the significance vanishes if doses of 0.2 Sv or less are considered. If a relative risk model with a threshold (the dose-response being assumed linear above the threshold) is fitted to the solid cancer data, a threshold of more than about 0.2 Sv is inconsistent with the data, whereas these data are consistent with there being no threshold. Linear-quadratic models with and without an exponential cell-sterilisation term provide no better fit than the linear model. If solid cancer subtypes are considered separately, only for non-melanoma skin cancer is there evidence that incorporation of a dose threshold significantly improves the fit of a linear-quadratic model.

For the three main radiation-inducible leukaemia subtypes analysed together (acute lymphatic leukaemia, acute myeloid leukaemia and chronic myeloid leukaemia) there is a significant positive dose-response (at the one-sided 2.5% significance level) if all survivors who received 0.5 Sv or less are considered, but the significance again vanishes if doses of 0.2 Sv or less are considered. If a relative risk model with a threshold (the dose-response being assumed linear above the threshold) is fitted to the leukaemia data, a threshold of more than about 0.3 Sv is inconsistent with the data. In contrast to the solid cancer data, the best estimate for the threshold level in the leukaemia data is significantly different from zero, even when allowance is made for a possible quadratic term in the dose-response, albeit at borderline levels of statistical significance (p = 0.04). There is little evidence for curvature in the leukaemia dose-response from 0.2 Sv upwards. However, the possible underestimation of the errors in the estimates of the dose threshold as a result of confounding and uncertainties not taken into account in the analysis, together with the lack of biological plausibility of a threshold, makes the interpretation of this finding questionable.
DELAYED HEALTH EFFECTS OF EXPOSURE TO THE 1957 KYSHTYM NUCLEAR ACCIDENT: EXPOSED PERSONS AND THEIR OFFSPRING

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The 1957 Kyshtym accident spread radioactive contamination among rural villages in the Kamensk district and the Lenisnsky Borough (L-B) of Kamensk-Uralsky City. In 1992 a case referent study of L-B residents, matched by sex, age and socio-occupational status with less radiation exposed residents of Oktyabrsky-Borough residents (O-B) was undertaken. Measurements were made of health status, including hematologic, immunological, and biochemical indices, and comparison was based on computerized pattern recognition methods. In 1993 another sample of O-B women not employed in industry were matched with those living in the Chkalovsky borough (ChB). Lead and other toxic metals were high in O-B compared to ChB, but neither had a history of radioactive contamination. Similar evaluations of health status were used, and we were able to identify differences of health status between populations with exposures to radioactive materials, heavy metals, and those less polluted ones. Children living now in LB with parents or grandparents who had been exposed here to maximum radiation in 1957-1962 as well as children living in rural villages outside radioactivity contaminated areas where their parents had been resettled in 1957-1959 from those most densely contaminated with radioactivity also showed poorer health status on the tests used, including laboratory, clinical and health history criteria. Children with several exposed parents or grandparents showed greater effects than those with lesser numbers of such forebears.

We conclude that our method allows us to discriminate between the effects of radiation, and of the general pollution with metals, from populations living in non-polluted conditions, and that radiation exposure of populations, even at the periphery of vast territories contaminated due to similar accidents, can affect future generations.
Atmospheric nuclear tests conducted at the Semipalatinsk Test Site from 1949 till 1962 produced a harmful effect on the Altai Region population. A dire medical situation in the early 1990s required complex measures for the rehabilitation of the exposed population. In 1996, a few scientific groups developed a concept on the exposed population rehabilitation taking into consideration the following Altai case peculiarities:

- radioactive products exposure;
- mostly the acute character of exposure;
- questions on the population rehabilitation were raised more than 40 years after the first nuclear test when there were no effective radiation protection measures;
- initial biological effects must have occurred at that time. Long-term consequences are revealed by a growing incidence of stochastic effects;
- approximately a half of radiogenic cancers was predicted to occur before 1995, with the other half in the next 20-30 years if no appropriate direct measures were taken.

To arrange radiation protection measures 2 levels were set:
1. Significant risk level that is the minimal risk value in the cohort (equal to 5% of the incidence of spontaneous cancers during the cohort life span).
2. High risk level that is the high cancer realization probability in the cohort (equal to 15% of the life span risk value conditioned by radiogenic and spontaneous cancers of a definite type).

The protection measures management system leans on the radiative-epidemiological register containing:
1. persons with ailments that are presumed to be caused by the nuclear tests;
2. exposed persons to
   • the effective dose of more than 50 mSv;
   • the overall body dose of 10 mGy and more during the intrauterine development period;
   • the thyroid dose of 0.5 Gy and more at the age of 18 and older when exposed;
   • the thyroid dose of 0.2 Gy and more at the age of less than 18 when exposed.
3. persons born after the tests to parents who were exposed to an effective dose of more than 50 mSv.

To manage direct rehabilitation measures a 4-part medico-radiological subregister has been assigned, including:
1. cohorts for which the stochastic effect additional relative risk realization is stated significant;
2. cohorts for which the stochastic effect realization probability is stated to exceed the high risk level;
3. persons with the stochastic effects conditioned by exposure and those whose death was caused by determined effects;
4. descendants of the exposed people with the effective dose of more than 50 mSv.

Based on the principles of selectivity and directness, timely decision making on medical issues implies differential use of rehabilitation measures directly to risk bearers to identify, prevent or soothe the consequences. Taking a decision is based on the following:
- the detailed radiation risk prognosis in relation to the dose, the sex, the age at the time of the test, the time gap after the test, local medico-demographic conditions etc.;
- results of direct medical observations and studies.

Conducting optimal protection measures for the risk group can result in a reduction of full risk, less or equal to the forecast value in the control regions.
MORTALITY FROM MALIGNANT TUMOUR AMONG THE MEN EXPOSED TO THE NUCLEAR TEST OF AUGUST 29, 1949, AT THE SEMIPALATINSK TEST SITE

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This report covers the results of the study of mortality from malignant tumour among 4,776 men exposed to the nuclear test of August 29, 1949, at the Semipalatinsk Test Site with effective doses from 50 mSv to more than 2000 mSv. The exposed cohort with the effective dose 50-249 mSv included 1028 subjects; 250-499 mSv, 1651 subjects; and more than 500 mSv, 1615 subjects. We drew two control groups. The first group consisted of 2025 immigrant men born before 1950 who had moved in the exposed areas after August 29, 1949. The second comprised 1433 male residents of unexposed districts.

We found a higher mortality level from malignant tumour during 44 years among the exposed men as compared to the men of the control cohorts. The most significant difference was revealed during the 20 to 34 years after exposure. Relative risk of cumulative mortality among the men exposed to the dose 50-249 mSv at that time was 1.63; 250-499 mSv, 1.64; 500-999 mSv, 2.16; and more than 2000 mSv, 2.98. In 44 years after the test the mortality rate among the men with effective dose less than 500 mSv did not differ from that of the control groups, whereas among the exposed with the dose 500-999 mSv it was 1.40, and with the dose of more than 2000 mSv, 1.69.

Based on mortality from all malignant tumors, we found that dose for lung and stomach cancer exists only among the men exposed when less than 44-years-old. For 1 Sv exposure, excess relative risk of mortality from lung cancer in 24 years after the exposure equaled 1.54, and from stomach cancer, 2.71.
CYTOGENETIC INVESTIGATION IN THE POPULATION OF ALTI REGION SUBJECTED TO THE ACTION OF IONIZING RADIATION

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The cytogenetic investigations were carried out at some places of Altai regions subjected to radiation as a result of 113 atmospheric nuclear explosions which have taken place between 1949 and 1962. The main contribution to exposure for the Altai region population was caused by the first nuclear test. The radiation dose from this test consisted of about 80% to the total effective dose which the Altai population got over a long period of time.

The cytogenetic examination of population in 8 localities of Altai region was performed (256 persons examined). The group of examined persons included an adult population permanently living in the mentioned territories. The procedure of cytogenetic analysis included the conventional method (i.e. analysis of unstable aberrations) and the method of chromosome painting by FISH (i.e. analysis of symmetrical translocations).

For five examined groups the mean frequencies of cells contains dicentrics and centric rings significantly exceeded the control level (4-10 times higher). The statistically significant (p<0.05) exposure effects relationship was confirmed between the frequency of cells with dicentrics and centric rings and the cumulative dose in the Altai territories.

The frequency of symmetrical translocations in exposed groups was significantly (p<0.05) higher (5-fold) compared to our control level. The application of scoring symmetrical translocations by FISH method for biological dosimetry of past radiation exposures was considered.
THE DELETERIOUS EFFECTS OF CHRONIC RADIATION EXPOSURE FOR INHABITANTS OF THE AREA NEAR SEMIPALATINSK NUCLEAR TEST GROUND

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In the Semipalatinsk Region, North-West part of Kazakhstan Republic, 459 nuclear tests were performed by former USSR military from 1949 to 1989, among them 89 atmospheric, 26 ground and 346 underground. Total yield of explosions was 60 megaton of TNT. Accumulated dose equivalent of chronic radiation exposure for residents of 15 villages near the Nuclear Test Ground (NTG) exceeded 1,000 mSv, for example in Karakorik village - 5,024 mSv and in Dolon village - 4,474 mSv. In total, about 47,600 residents were exposed to a dose equivalent higher than 350 mSv. Their collective equivalent dose is 52,116 person-Sv. About 99.2% of the total collective equivalent dose inhabitants of the area received at the first four years after the beginning of exposure to ionizing radiation - from 1949 to 1953.

Study cohort of these heavily exposed residents was formed in 1957. In our Institute we are continuing an epidemiological survey on them untill now. The total number of investigated persons during the study period 1957-1993 is 40,333; among them 24,374 were investigated repeatedly. The matched control cohort included 12,000 persons. It was calculated that in the structure of excess mortality among those heavily exposed in the Semipalatinsk area only 48.1% attributed to malignant tumours, 31.1% - to circulatory diseases, 18.1% to infectious diseases. Deleterious effects of chronic radiation exposure included: 2,085 cases of fatal cancer, 417 cases of non-fatal cancer, 2,250 fatal non-malignant disorders and 417 cases of serious heritable effects.

Relative risk (RR) of infant mortality among babies from heavily exposed mothers depended on the time after receiving main part of the total dose. At the study period 5-18 years after beginning of radiation exposure it was: because of congenital deformities and malformations (mainly microcephalia) - 2.03, because of endogenous infections (pneumonia and septicaemia) - 1.74, and because of exogenous infections - 1.57, among them RR=1.80 for tuberculosis, RR=1.60 for influenzae and measles, RR=2.22 for diphtheria and scarlett fever, and RR=1.20 for other types of acute infectious diseases. At the next study period, 21-44 years after the beginning of radiation exposure in the Semipalatinsk area, RR of infant mortality in the same heavily exposed cohort because of congenital deformities and malformations was 2.13 (p<0.01), but statistically not significant for infectious diseases. During the whole 36-year period of observation it was statistically significant prevalence of microcephaly and deformities of the scalp in babies from heavily exposed mothers - 1.76 times higher, than among non-exposed control (p<0.001). Contrarily, skeletal deformities, mainly syndactily, polydactily, phokomely, brachydactyly and some others) occured more frequently in the control group. There were no statistically significant differences between the parameters for other types of congenital anomalies and deformities, such as those of the cardiovascular system and genito-urinary tract, but in newborns of the heavily exposed cohort there was a tendency for the prevalence of other deformities of the brain to be high, especially during the first 14-year study period; among the deformities of the brain, more than 70% accounted for hydrocephaly.

The incidence of Down's syndrom during the period of underground nuclear tests was 0.058% in the heavily exposed area in comparison with 0.032% in the control area (difference a 1.8-fold), but the cytogenetic study showed no difference in the incidence of the additional 21st chromosome, about 70% in both compared cohorts. There were also no data on the prevalence of monogenetically inherited diseases in both cohorts during the period of underground nuclear tests (1965-1989) and later.

Chromosomal aberrations were encountered in 64% of residents, exposed to a dose equivalent 2,000 mSv, 53.3% of the population aged below 30 years and 80% of these aged more than 30 years had chromosome aberrations. The percentage of aberrant cells ranged from 2 to 8%. In the appropriate control group, only 15.5% had chromosomal abnormalities and that too in less than 2% of their cells. The frequency of chromosomal aberrations as well as the number of aberrant cells per individual was significantly higher in the exposed group as compared to the control (p<0.01). Similarly, the number of pair fragments, rings and dicentrics was significantly higher in the exposed group (p<0.01). The average number of aberrations per cell was also higher in the exposed as compared to the control (p<0.01).
PATHOGENESIS OF PSYCHO-NEUROLOGIC DISORDERS ASSOCIATED WITH CHRONIC RADIATION EXPOSURE.


Since 1987 we have carried out follow-up observations on survivors of the Chernobyl accident. These studies have included clean-up workers ('liquidators'), especially those who have been working in the Chernobyl exclusion zone since 1986-87 for 5 or more years, as well as persons who have been living illegally in the Chernobyl exclusion zone (so called 'self-residents'). The health assessment was carried out for 1,000 liquidators (total dose 0.05-3.00 Sv) and 200 'self residents' (0.06-0.82 Sv, thyroid doses 0.28-2.36 Sv). Ionizing radiations cause both genetic abnormalities and cellular metabolic disorders. The primary radiochemical reactions include direct and indirect damage of important cellular biochemical reactions. The results are disorders of the function of neuro-humoral centers, with resultant disorders of the hypothalamo-pituitary-adrenal system, the autonomic nervous system, immune system, metabolic activity and the blood coagulation system. Unfavorable ecological factors of the Chernobyl exclusion zone, together with alcohol abuse and psychogenic stress, contribute further to the overall effect. The psycho-neurological disorders associated with chronic irradiation could be caused by both direct and indirect effects of ionizing radiation. The threshold dose TD50 of the dysadaptation syndrome associated with chronic internal and external radiation is 0.12 ± 0.06 Sv. The pathophysiologic basis of brain function disorders during chronic radiation involves microcirculatory and metabolic disorders of cortical neuron activity and dysfunctions of the diencephalic-limbic-reticular complex, brainstem reticular function and thalamic structures which are related to absorbed dose. The physiopathological effects of chronic irradiation have a persistent and progressive character which are the basis of the observed disorders. Therefore among the health effects of the persons who have been living and/or working in the Chernobyl exclusion zone since 1986-87, it is necessary to consider the organic CNS syndrome and psychosomatic disorders as signs of chronic radiation disease.
PSYCHOSOCIAL STATUS AND PSYCHOSOMATIC HEALTH OF ADOLESCENT VICTIMS OF THE CHERNOBYL DISASTER

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The Chernobyl disaster had associated with it a complex of damaging factors, including ionizing radiation, emotional stress, psychological and social problems. The present study examined the psychosocial status and psychosomatic health of adolescent victims of the disaster.

The first stage was to match the psychosocial status of adolescents from evacuated from Chernobyl and adolescents living continuously in Kiev, and to make observations one year and eight years after the disaster. The psychosocial states of evacuated adolescents were different in 1987 and 1995. In 1987, evacuated adolescents were distinguished from their non-evacuated counterparts by their targeted responses and by their highly conflictual relations to family and mother. There was a predisposition toward adaptational difficulties for females who were unable to secure employment appropriate to their educational achievements as a result of evacuation. Nearly all the evacuated adolescents (97%) were afraid of health effects, mainly cancer. Many of them (78%) had a sensation of “predestination” (fatalism).

The evacuated adolescents observed in 1995 are more similar to their non-evacuated counterparts. The aforementioned conflicts with mothers are not found. Only a small portion (12%) of them had a fatalistic orientation. Twenty percent had suffering connected with the accident, and most did not remember evacuation (72%). Adolescents in 1987 emphasized their role as Chernobyl victims in expecting social privileges. The adolescents in 1995 hid their identities as victims. They feared discrimination in further education, work and marriage.

The second stage of the study was evaluating the risk of vegetative distonia and the sum of factors accompanying Chernobyl. Vegetative distonia as determined with clinical tests, ECG, cardiointervalography and defined by ECD9 337.9 was considered as an outcome because vegetative distonia occupies first place among psychosomatic diseases. From another standpoint, the imbalance of the two parts of the vegetative nervous system is connected with damage to the thyroid gland by radioactive Iodine during the first month before evacuation.

The design strategy included three types of epidemiological studies: cohort, cross-sectional and nested case-control, analyzing EpiInfo-6 with confidence interval 95%. Observation included the period from 1987 to 1995. The measure of exposure was estimated by risk ratios and risk differences. To control cofounding variables, the following variables were matched: sex, height, sex ripening, hereditary vegetative distonia, hypertension, obesity and results of psychological observation.

The strength of the association between the whole complex of factors connected with the Chernobyl disaster and vegetative distonia increased with age and time after the disaster. The risk ratio increased from 2.6 in 1990 to 3.8 in 1995, the risk difference from 16 to 24, population attributable risk from 11 to 17 and population attributable risk fraction percent from 50 to 62.

Doses of ionizing radiation above 3 sZv during the 36 hours before evacuation in nested case-control studies were considered as exposure. Controls were chosen from the same group, adolescents evacuated from Chernobyl. The odds ratio in the case-control study = 3.4.

Only doses of ionizing radiation above 3 sZv resulted in a significant association with vegetative distonia. The vegetative distonia manifests more frequently in situations of psychosocial strain. In addition, its pre-morbid conditions occur within a more restricted time frame than occur without the psychosocial strain.
POST-TRAUMATIC STRESS DISORDER IN THE POPULATION LIVING IN THE CONTAMINATED REGION AFTER THE CHERNOBYL ACCIDENT

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The purpose of this study was to ascertain how widespread PTSD symptoms are among populations affected by the 1986 Chernobyl accident. A representative group of 632 patients (37% - men, 63% - women, aged 19-64) living in the region polluted by the accident (Novozybkov) was studied. The average radiation dose received by members of this group during the 9 year post-accident period was about 4.5 mSv. Participants were examined by a psychiatrist and filled in the SCL-50 Symptom Check List, a list of stress sources, and the Impact Event Scale by Horowitz (IES, 1979). The results are as follows: all the patients characterized the Chernobyl disaster and its consequences as a highly traumatic event breaking the bounds of usual human experience. Predominant among 50 percent of the patients were avoidance reaction and symptoms of high arousal and somatoform disorder that had not been present before the accident and had been taking place for not less than 12 months. Only the relationship of high level intrusion IES subscale and different levels of the avoidance IES subscale permits us to qualify the pathology of the involved population (15%) in the range of chronic PTSD and to define therapeutic models for the disease.
MENTAL DISORDERS RELATED TO THE CHERNOBYL DISASTER

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The worst disaster in the history of nuclear power occurred at Chernobyl on April 26, 1986, producing the most serious environmental contamination ever recorded. The explosion at the Chernobyl reactor was an unprecedented disaster that has put the health of millions of people at risk. Many millions have suffered and continue to suffer from consequences of the accident.

The task of cleaning up a 30-km zone around the accident site has been left to some 800,000 workers ("liquidators") brought in from different regions of the former Soviet Union. Most of them were exposed to radiation for an average of 2 months, often without proper safety equipment and dosimetry badges.

At present, many people who were involved in combating the Chernobyl disaster's effects have been diagnosed as having non-psychotic mental disorders. We evaluated both clinically and psychologically 250 patients who were exposed to low doses of radiation resulting from the Chernobyl disaster. We used a special questionnaire and psychological tests to obtain the information.

We saw the early beginning of illness among patients who received higher levels of radiation. The doses of our patients depended on the time of the beginning of their work in the contaminated area, and how long they worked there. The first signs of disorders appeared at the end of 1986 among 55% of the patients. It took about 1.5 to 2 years for disorders to evolve.

Most of our patients had the same multiple complaints: headache, dizziness, fatigue or chronic tiredness, poor concentration and lack of attention, memory loss, irritability, sometimes anger, mood swings, anxiety, exhaustion of physical and mental activity, high blood pressure, autonomic and vascular ton dysregulation, feelings of hopelessness, and lack of libido. They had a high sensitivity to loud noises, bright light, and high temperature. At the same time, most of our patients had different somatic diseases.

The overall symptoms of this syndrome were so alike that we called it post-Chernobyl cerebrasthenic syndrome. In some cases, the cerebrasthenic syndrome evolved into encephalopathic syndrome.

The results of psychological research indicated poor attention, lack of concentration, memory loss, exhaustion of mental activity, inability and instability of attention. Seventy percent of patients had high levels of anxiety. More than 80% had changes of character and 90% of patients had low levels of self-esteem and self-evaluation.

We diagnosed asthenia, depression, panic attacks, pseudoneurosis, anxiety and somatoform disorders, and different stages of organic mental disorders among our patients, too.

Clinical and psychological findings allowed us to describe specific post-Chernobyl cerebrasthenic syndrome as a first stage of organic mental disorder. Cerebrasthenic syndrome is one of the typical problems which appeared after the Chernobyl disaster.
PSYCHOLOGICAL PECULIARITIES OF CHERNOBYL ACCIDENT
“LIQUIDATORS” AND CAUSES OF DISADAPTATION

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A screening study of 507 clean-up workers of Chernobyl accident was conducted with a specially designed questionnaire which provided data on social-demographic characteristics, radiation impact assessments and beliefs about radiation threat. Included were several scales used to estimate the reaction to stress and the severity and structure of mental disease (according to DSM-III-R). The cohort under study included citizens of Moscow, regional centers and different areas of Russia who were not professionals in the atomic power industry. The average absorbed dose of radiation in that cohort was 16.5 Gy. A wide prevalence of mental disorders of neurotic level was revealed in 84% of the examined cohort of liquidators, that was 1.5 more than in the inhabitants of radiation contaminated areas of Russia and twice that of the inhabitants of clean territories. In contrast to the population of the contaminated territories that have mostly preclinical manifestations of mental disorder, liquidators suffer from severe mental diseases. Symptoms of somatization prevail in the picture of mental illness. But depression was most significant in the group of liquidators with severe mental disorders. The evolution of mental disadaptation in many cases involves depression that consequently increases the risk of suicidal behaviour. The frequency of neurotic disorder, especially of severe mental problems, increased with dose. Analysis of possible causes of stress related diseases revealed that 70-80% of the examined cohort, who participated involuntarily in the decontamination, did not trust the official information about doses, did not have sufficient information and knowledge about radiation protection, and had expectations of indefinite future damage.
HEALTH CONDITION AND ABILITY TO CONTINUE PROFESSIONAL WORK IN PATIENTS WHO SUFFERED ACUTE RADIATION SYNDROME AS A RESULT OF THE CHERNOBYL ACCIDENT

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People who suffered acute radiation syndrome (ARS) as a result of the Chernobyl accident can be divided into three main groups: military persons, employees, and builders. As detailed analysis of medical documentation has shown, prior to the accident the first two cohorts had medical examinations every year in Ministry of Internal Affairs and NPP special medical departments, and were healthy persons. The population of the last cohort was in general healthy. The Karnofsky score of these groups was 99.8% on average and their professional working ability was 100%.

After the irradiation, the patients' health condition was characterized by increased frequency of digestive and circulatory diseases and its chronic flow, decreased physical and mental capacity, and the transformation of neurovegetative and psychoneurological disorders into organic neurovascular pathology (hypertensive disease, dyscirculatory encephalopathy, psychoorganic syndrome). Steady changes of brain functional status with non-linear "dose-effect" correlation were revealed.

The organic and functional pathology changed the Karnofsky performance score from 88.5% in 1987 to 73.6% in 1996 in the group of patients who suffered ARS of 1 degree. In groups of patients after ARS of 2 or 3 degrees these data were 90.2% in 1987 and 79.5% in 1996, and 67.5% in 1987 and 53.1% in 1996, respectively.

After the irradiation, workers of Chernobyl NPP lost any possibility of continuing their work at any NPP. Most of the military persons were not able to serve and others were weakened and could not do their professional work for 100% of the time. This situation was reflected in disablement that was established for these patients. At the end of 1995, 58.3% of patients after ARS of 2-3 degrees and 39% after ARS of 1 degree had a second degree of disablement in our national scale and 20% of patients after ARS of 2-3 degrees and 22% after ARS of 1 degree had a third degree of disablement.

All persons who suffered ARS are under physical and social rehabilitation based on the results of annual clinical observation and health status.
In September 1987, the removal of the rotating assembly of the shielding head of a Teletherapy unit and the dismantling of the capsule containing 50.9 TBq (1375 Ci) of Cs-137 gave rise to the most serious radiological accident to have occurred to date. It resulted in the injury by radiation of many people, four of them fatally, and in a widespread contamination of the central sector of Goiania, a Brazilian City of one million inhabitants. This radiological accident was singular, because it happened in an urban zone, and the center of the town. The accident presents lessons that cover the pre-accident phase, the emergency phase and the post-accident phase up to the present (9 years later) and, in each of them, can be found both mistakes and correct actions by individuals and organizations. Today, Goiania, besides being the site of medical treatment to the patients (groups) under observation, is also the site for the final Goiania Radwaste Repository to store 3,500 cubic meters of waste, a project that involves social, economic, deliberation, and psychological emotion, especially among the population in the neighborhood of the site, Abadia de Goias, 20 km from the town. This radiological accident, in view of its uniqueness in the world, brought to light several adverse indicators not observed in publications concerning emergency planning and preparedness. We learned in Goiania, dealing with all classes of the regional society, that not only social, political, economic and technical problems had to be dealt with, but also that there was apprehensive psychological aspects, such as fear and depression of the population and stigmatization and discrimination against the victims and the main products of the city. This paper alerts national and international organizations, especially those devoted to the progress of developing countries, such as IAEA and WHO, for such psychosocial conflict in the past and, to date, still in Goiania, and gives emphasis to the fact that the lessons from this radiological accident, until now were not yet enough discussed and learned. The paper also considers how public and professional perception psychologically affects the population, due to conflicts of information, distortion and misunderstanding. Finally we mention several psychological questions in the early phase of the accident which were not foreseeable, and which have not been addressed in the literature, but suddenly come to the fore through unexpected situations or questions that we never thought about and which must continuously be analyzed in terms of Safety Culture Problems Identification and Safety Culture and Human Behavior. I have no doubt that if another scenario like Goiania happens anywhere in developing country, it is likely that authorities, organizations, and the media, will again repeat the same mistakes, and this will not be good for the progress of nuclear energy. For developing countries, no major program of power reactors, specially those ones in the process of establishing or improving the national radiation safety infrastructure, the accident in Goiania, at every step, is the greatest laboratory to learn how to deal with emergencies involving the sentiment of the population.
PSYCHOSOCIAL ASSISTANCE IN THE AFTERMATH OF ENVIRONMENTAL ACCIDENTS: SOME POLICY CONSIDERATIONS AND AN AGENDA FOR THE FUTURE

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There is now a substantial body of literature on the psychosocial impacts of radiological and chemical accidents, dealing primarily with clinical issues such as diagnosis and treatment. Less attention has been focused on program and policy issues connected with efforts to plan and provide psychosocial assistance. With large-scale environmental accidents likely to occur in the future, and with psychosocial services certain to be a crucial part of the public health response, it is important that such policy and program issues be more fully considered.

One issue concerns the potential for psychosocial assistance efforts to become objects of conflict. With debates over the causation of illness usually at the center of environmental episodes, every statement or action by service providers has the potential to affect how the accident situation is defined. In the context of the intense and heated controversy often associated with nuclear or chemical accidents, psychosocial assistance efforts may themselves become objects of social contention.

Other related program and policy matters which may warrant consideration include the issue of balancing individual and community-level assistance efforts; deciding how to facilitate stakeholder participation in shaping service provision; and choosing how to interface with citizen self-help and other voluntary groups. Finally, several proposals are offered that may help smooth the path for psychosocial assistance programs in future environmental emergencies.
PROBLEMS OF EXPOSURE ASSESSMENT IN RADIOFREQUENCY EPIDEMIOLOGY RESEARCH


The widespread use of certain radiofrequency devices has focused attention on possible health impacts of longer term exposure at low intensities to high frequency sources. Beginning with the categories of occupational exposure to EMF developed by Milham (1982), later revised by Lin, epidemiologic studies of cancer continue to utilize the occupational categories regardless of the fact that both ELF and RF exposures to electromagnetic fields are included and undistinguished in these schemes. Job categories with opportunity for exposure to RF fields, such as communications engineers, electronics workers, and television repairman, include little information on exposures to power frequency fields and other exposures such as chemicals. This situation prompted a systematic analysis of exposure assessment methods in epidemiologic studies of potential longterm RF exposures.

Only 8 studies of cancer were located in which exposure assessment specified opportunity for RF exposure. Most of these were cohort epidemiologic studies in which RF exposure to workers was assumed because of the location of a RF source in the workplace. No study included either individual exposure or area measurements of RF. Few studies offered even as much exposure information as a recent case-control study (Siemiatycki 1991) of 11 types of cancer, in which each subject was interviewed to determine lifetime occupational history, and exposures to RF on the job were rated by industrial hygienists. Studies of reproductive outcome, mostly of physiotherapists, include more specific information, such as frequency, on the RF source in the workplace. However, individual exposure in studies has based on self-reported use of the equipment, as established by questionnaire.

More complete characterization of RF emissions from devices and potential exposures in the work area can be found in the literature, for example for police radar devices, cellular telephones, and heat sealing devices. Epidemiologic studies have not yet integrated this information with health data. The value of obtaining RF exposure assessments specific to work environments and likely worker exposure lies in the ability to plan epidemiologic studies at various frequencies (and intensity levels) to augment the data anticipated from cellular telephone studies.
FREQUENCY OF MICRONUCLEI IN THE PERIPHERAL BLOOD AND BONE MARROW OF CANCER-PRONE MICE CHRONICALLY EXPOSED TO 2450-MHZ RADIOFREQUENCY RADIATION

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Mammary tumor-prone (C3H/HeJ) mice were exposed to continuous wave 2450-MHz radiofrequency radiation (RFR) in circularly polarized waveguides at a whole body average specific absorption rate of 0.3 W/kg, for a period of 18 months (20 hours/day, 7 days/week). Sham-exposed mice were used as controls. At the end of the exposure period, all mice (58 mice in the control group and 62 mice in the RFR exposed group) were necropsied for detailed pathological examination. From each animal, peripheral blood and bone marrow smears were made, and from each of these tissues, 2000 polychromatic erythrocytes (PCEs) were analyzed for the incidence of micronuclei as an indicator of genotoxicity. There were no significant differences in the incidence of micronuclei in the peripheral blood between control (average 8.0±1.12 SD/2000 PCEs) and RFR-exposed mice (average 9.0±1.23 SD/2000 PCEs). The frequencies of micronuclei in the bone marrow were also similar in control (average 11.4±1.60 SD/2000 PCEs) and RFR-exposed mice (average 12.2±1.78 SD/2000 PCEs). In contrast, within 24 hours, the positive control mice (7 mice of the same age) which had been injected with mitomycin C (1 mg/kg) showed a significant increase in the incidence of micronuclei in both peripheral blood (average 101.8±6.18 SD/2000 PCEs) and bone marrow (average 110.4±4.65 SD/2000 PCEs). These observations indicate that long-term, low level exposures of mammary tumor-prone mice to 2450-MHz RFR are not genotoxic.

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EFFECTS OF ELECTRIC FIELDS ON DROSOPHILA: PHYSICAL MODEL, PHYSIOLOGICAL ACTION AND GENETIC CONSEQUENCES

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At present artificial electromagnetic fields become an important environmental factor. There are unfavourable physiological effects caused by power lines and radars. These effects lead to stress influencing man's health and animal's behaviour. Insects are a good model object for studying physiological activity of low frequency non-ionizing radiation. We described the influence of extremely low frequency (ELF) electric fields on the behaviour of the fruit fly Drosophila melanogaster.

Our experiments show that the effect depends on the frequency of electric fields and is different for a solitary drosophila and an insects' group. To explain these two effects, we developed a physical model. The model is based on the assumption that the chitin-containing exoskeleton of an insect can play a role of a capacitor within which the electric fields concentrate. In the case of a solitary fly, the exoskeleton charge at low frequencies (10 - 50 Hz) is quite sufficient to immobilize the insect by uncoordinated vibration of its chitin elements (so called "electro-mechanical effect"). When studying the whole group, the value of the individuals' discharging against each other increases with the rise of the electric field frequency. As a result, the drosophila mobility increases linearly up to frequency about 1 kHz. Peculiarity of physiological reception of electric fields is important to explain the effects observed at higher frequencies. The insect nervous cell excitability is characterized by such a parameter as the refractory period. This leads to decrease of the biological effects in accordance with the dependence $1/(f - 1/\tau)$, where $f$ is field frequency, and $\tau$ is absolute refractory period (about 3 msec).

Thus, a simple model gives the possibility to account for physical and physiological mechanisms of some behaviour effects of ELF electric fields in Drosophila melanogaster. It can be important to elaborate methods of insects' behaviour control.

We studied ELF electric field effects on genetic apparatus of drosophila, too. When investigating recessive and dominant lethal mutations, we have not found mutagenic effect. However, there was double increase in epigenetic changes (morphoses) at field intensity higher than 100 kV/m. It shows an influence of electric fields on cell genetic system, i.e. modification of gene expression.

The proposed model gives us the possibility to pass from physiological effects to genetic ones. According to the model, the stress, caused by 100 Hz - 10 kHz electric fields with intensity about 400 - 800 kV/m, leads to gene expression modification in insects. The similar effects can exist in other living organisms, particularly in man. It is possible that such a modification of gene expression leads to change of cell aging rate, increase in development disorder probability and rise in cancer disease frequency.
EFFECT OF ULTRAVIOLET RADIATION ON BONE'S ELECTRON STRUCTURE

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Electron structure of a bone's surface is strictly important to control electron/ion exchanges between the bone and its environment. Destroying of these processes provokes diseases (osteoporosis, for instance). These variations may be occurred under external factors, electromagnetic irradiation being among them.

Ultraviolet light (UV), an energy of photons being about 6 eV, affected the bovine bone, taken from an adult animal. Duration of excitation was chosen to maximise the influence of UV on the bone. To test its changes, the method of exoelectron spectroscopy (ES) [1] was used.

This technique is based on electron emission measurements, when the specimen is heated with a constant rate and simultaneously irradiated by photons. This mode provides relaxation processes manifested by dependence of an emitted electrons current (I) on temperature (T) (EE spectra). Such regularities have a maximum of I reflecting the greatest rate of relaxation.

Irradiated specimens have similar features at T=100°C, in contradiction with non-irradiated bones. This is typical for bone tissue, affected by UV, [2] and accords with appearance of electron states.

Electron distribution vs. energy, measured from the vacuum level, is shown in Fig.1. Four main centres are clearly displayed. The centres C1 and C3 explicitly exist at initial T, but C2 and C4 are imaged only due to heating. The intensity of C1, C2, C4 is rising till T=100°C, but for C3 it remains constant. The maximum of the C1, C2, C4 intensity occurs at T, corresponding to the greatest I. The irradiated specimens differ from the initials with greater intensity for all of the above centres.

![Figure 1](image)

Figure 2. Electron distributions by energy at different temperatures: a - non-irradiated specimen, b - irradiated specimen.

In conclusion, one may assume, UV indeed changes electron structure of the bone surface. This may be related with breakage of atom and molecular couples. UV does not insert new centres, in comparing with the initial bone. By this reason EE spectra of the bone are related with variation of the above centres' concentration.

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Non-infectious morbidity of adults (12,000 persons) living near radar installations was studied. Statistically significant increases of general morbidity was observed (in comparison with control) for respiratory diseases, malfunctions of cardiovascular system and CNS, allergic diseases, and dermatological infections. The two last groups of diseases were observed among women 2 times more often than among men.

The data obtained permit us to infer a decrease of immune resistance associated with EMF over 3000 MHz to 30 GHz as well as greater risk of occurrence of disease in working age women. The influence of EMF generated by radar on the health of the population was established. A correlation between the level of EMF and the population morbidity was observed. Mathematical models of this dependence can be used to forecast the health effects from EMF.
DISTINCT SENSITIVITY OF NORMAL AND MALIGNANT CELLS TO ULTRASOUND *IN-VITRO*

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The effect of ultrasonic irradiation on the viability of human normal and tumor cell lines was studied. Cells were grown and subjected to ultrasonic irradiation with a frequency of 2 MHz and intensity of 0.33 W/cm² for variable periods of time. Several parameters were tested to determine the effects on cell viability and cellular function. Normal cell lines were relatively resistant to the ultrasonic irradiation, however cells derived from melanoma or breast carcinoma were highly sensitive to the irradiation. Maximum damage occurred at 4 min after exposure of the malignant cells to the irradiation. Cellular DNA and protein synthesis were clearly affected as a function of time of irradiation in malignant cells as compared to their normal counterparts. Similar results were obtained using cloning efficiency technique in liquid media, as a measurement of the cell ability to multiply. In order to generalize the consistency of the ultrasonic effect, studies on other normal and malignant human cells of distinct origin are under way to test their sensitivity to ultrasonic irradiation. The applicability of ultrasonic irradiation as an anti-tumor agent may be important in the development of a new methodology in the treatment of malignancy.
APPLICATION OF RF REGULATION -
THE GENERAL POLICY IN THE I.D.F.

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In every modern armed force, as well as in the Israel Defence Forces (I.D.F.), a wide variety of equipment is used, with sources of electromagnetic radiation - communications, detection (such as radar), control, E.M.C. and also commercial equipment (welding equipment, sealing equipment, heaters, etc). This equipment radiates over the entire radio frequency spectrum as well as in the E.L.F. and V.L.F. bands.

The wide variety of applications requires a comprehensive policy of protective measures, which will ensure the occupational health of the personnel, exposed to the radiating sources. In the state of Israel, there are no mandatory standards, regarding the protective measures for RF radiation hazards, although there are recommendations of the Ministry of the Environment.

The I.D.F. does apply regulations in this area (since 1988). The regulations are mandatory throughout the armed forces. The regulations were based on the IRPA occupational limits, which neglect various relevant parameters such as measurement methods, partial body exposure, whole-body (vertical) averaging and personal health aspects (periodic examination and examination on overexposure). Hence, to improve the protection measures, new regulations have been developed, based on the following factors:

a) Adapting IRPA and ANSI standards, both occupational and general public standards.
b) Relaxing the requirements of the general public standards, since military personnel are generally young, healthy and controlled. The basic guideline was to base on the IRPA standards, because of the well-defined chronic effects due to RF radiation, referenced by this standards; for those points for which the ANSI standards were more restricting, the latter were applied.

c) Permitting the relaxation of requirements for partial body exposure and applying whole body averaging, as required by the ANSI standards; the IRPA standards recommends applying this method, but does not describe the necessary procedure.

The new regulations detail the measurement procedure (since the measurement results depend strongly on the method applied). The procedure includes:

a) Definition of measurement type.
b) Time interval between measurements.
c) Measurement equipment requirements.
d) Calibration.
e) Transmitter scanning.
f) Vertical weighting averaging procedure over the body and relaxing limits for partial body exposure.

The necessity for medical examination is not clear yet, with the exception of the case of over-exposure.

Thus, our approach is to restrict exposure by applying comprehensive protective measures.
BEHAVIORAL EFFECTS CAUSED BY MICROWAVE EXPOSURE

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One of the most informative approaches to the study of reactions of the central nervous system (CNS) to modulated electromagnetic fields (EMF) from radar is to evaluate the reaction of its different integrative levels. In order to estimate the behavioral characteristics of the animals under EMF the following studies were done.

Methods: We used the conditioned defense reflexes of active avoidance with the purpose of the next parameters registration: the general latent period of all reactions, the number of conditioned reactions, work capacity, the number of intersignal reactions. The duration of one behavior test composed 75 trials. The animals (white random bred rats) were exposed to 10 cm EMF of 1500, 1000, 500 μW/cm$^2$ power densities (frequency repetition, 375 Hz; observation period, 10 seconds) during 4 months, 12 hours daily in the anechoic chamber.

Results: Five hundred μW/cm$^2$ EMF caused the changes in conditioned reflex activity during all periods of exposure. A statistically significant ($P<0.05$) increase of latent period after the third month of exposure was observed. This process of inhibition was not constant but variable during the period of after exposure of activation. Decrease of latent period during all period registration (75 trials), increase in the number of conditional reactions (25 trials and of work capacity (75 trials) were the main features of the conditioned reflex activity in rats. Nearly the same shifts in behavioral activity of rats exposed to 1000 μW/cm$^2$ EMF were noticed. The slight activation was presented after stopping the exposure. But the changes were only registered during the first 25 trials.

One thousand and five hundred μW/cm$^2$ EMF led to the increase of latent period of conditioned reactions during 50 trials after the first and second months of exposure. There were no statistically significant changes in the period of after exposure in this group of animals.

Discussion: The experimental results show that 10 cm EMF affected the behavioral reactions of the animals. The weakest field with 500 μW/cm$^2$ power density had the strongest effects on the activation process of CNS in the period after exposure, whereas the strongest field (1000 to 1500 μW/cm$^2$) caused lower levels of activation. The study has also indicated a dependence of this level of CNS functions upon the level of the intensity of exposure.
RADIOFREQUENCY EXPOSURE NEAR HIGH VOLTAGE LINES

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Aim: This work intends to show that some of the epidemiological studies which have shown an increased incidence of leukemia in people residing near high voltage lines, have to be re-examined in order to ascertain the presence of a confounding factor that has been ignored up to now.

Method: Many high voltage lines have been monitored in Italy, and one in Sweden, by means of coil, which were tuned at variable frequencies, and capable of detecting both the 50 Hz magnetic field and the radio frequency magnetic fields.

Results: Radio frequency magnetic fields in the range from 112 kHz to 370 kHz have been detected under many Italian high voltage lines and under one Swedish high voltage line in Stockholm. The intensity of these fields is very low, if compared to the intensity of the 50 Hz magnetic field emitted from the same lines. However, as long as we remain in doubt about the real nature of the interaction between magnetic fields and human body, we have to consider that this interaction may be related to the electric currents induced in the human body, not only to the primary agent (the magnetic field). From this point of view, we have to remember that the induced current density in human body generally increases with increasing frequency. This means that lower and lower values of magnetic fields are necessary to produce the same density current while increasing the frequency.

Conclusion: The presence of these radio frequency magnetic fields cannot be ignored, in as much as their frequency and their intensity are such that they may have played a role in determining the threshold of 0.2 - 0.3 μT over which, according to some epidemiological studies, an increased incidence of leukemia occurs. Investigations are foreseen in order to identify the origin of these radio frequencies.
The Ukrainian/American Chernobyl Ocular Study (UACOS) Group has been established to provide an infrastructure to monitor the effects of occupationally conditioned ionizing radiation and considering the other confounding factors on ocular tissues, with particular emphasis on the lens.

The studies, which are overseen in Ukraine by the Ministry of Health and The Academy of Medical Sciences of Ukraine, and in the United States by several agencies, are organized in conjunction with seven centers throughout Ukraine and three institutes in Kiev.

The longitudinal Scheimpflug slit-imaging of the eyes now in its third year, has, to date, enrolled over 400 patients ranging in age from 26 to 60 (ATE) with doses spanning 0.76 to 250 cGy. Analyses of light-scatter from the lenses as a function of dose and/or age reveal that, if the entire lens is considered, age has a more potent negative effect on transparency than does dose. However, when corrected for age (and, more importantly, the lenticular region being considered), a trend towards a dose-dependent loss of posterior subcapsular (PSC) transparency becomes apparent. It is critical to note that, characteristically, radiation cataracts first appear in the PSC region of the lens.

Now, planned the organizing period of start-up work in seven sites of Ukraine for such works:

1. Develop the epidemiological questionnaire in Ukrainian with an English translation to be used for the Liquidators recruited in the study.
2. Identify and screen the professional staff which will examine the Liquidators at the seven examination sites selected for data acquisition. For each site at least one trained ophthalmologist, with an assistant will be brought into the study and his/her suitability to meet the necessary compliance aspects of the study must be ascertained.
3. Develop, in Ukrainian (with English translation), the examination protocol, with appropriate cross-references to the criteria required on the proposed examination forms.
4. Select the potential candidates for inclusion in the study, initiate contacts with those selected and determine their level of willingness to comply with the requirements of the study.
5. Begin the site certification process. Each site must be visited to assess the facilities and the space to be made available for the conduct of the study. Provide the examiner at each site with the rationale and particulars of the overall project and detail the expectations of his/her contribution.
6. Initiate the relevance of the eye database period which is to be eventually integrated into the overall Chernobyl dosimetry and registration database.
It was believed that one of the health effects of the Chernobyl accident radiation exposure would be the increase of hemoblastoses (leukemia and lymphoma) incidence rates among the population of Belarus: the Republic of Belarus is the country mostly affected by the Chernobyl disaster consequences in terms of the portion of population living in radiation-contaminated territories, of the real content of $^{137}$Cs in tissues and $^{90}$Sr in bones of inhabitants etc. and also in terms of the estimated long life bone marrow doses in the inhabitants. Therefore, epidemiological studies of post Chernobyl hemoblastoses incidence rates are vitally important in terms of obtaining more precise knowledge of the mechanisms of the effects of chronic exposure of population to the so-called "small doses" of ionizing radiation.

One of the main obstacles of such studies in Belarus was the lack of the pre-Chernobyl verified data, and our team created the National Blood Diseases Register both retrospectively and by following up the current morbidity data. As the present the Register includes the data on 10,128 pre-Chernobyl (1979-85) hemoblastoses cases (14.7 per 100,000 of population) and on 12,994 (18.2 per 100,000) post Chernobyl (1986-94) cases among the population of the Republic of Belarus of more than 10 mln of people.

We fulfilled the register-based study referring to the above periods. The comparative analysis of childhood leukemia before and after the Chernobyl accident did not demonstrate an increase of the incidence rates (4.34 cases per 100,000 of child population in 1979-85 and 4.45 per 100,000 in 1986-92). In 1993 and 1994 the incidence rates were even lower (3.28 and 3.02). (In the below table these data are plotted featuring absolute numbers/relative magnitudes per 100,000 of children.)

We discovered the statistically significant increase of the incidence rates of all the forms of leukemia among adults. If in 1989-90 the increase was of only the chronic forms of leukemia, after the nine years long exposure to the Chernobyl radionuclides the incidence rates of all the forms of leukemia were discovered. The specific features of the leukemia incidence rates among adults determined in this study correspond to those for radiation-and-chemical cancerogenesis action in children.

We conclude, therefore, that an utmost important measure of prophylactics of cancerogenous action of the small doses of ionizing radiation is the reduction of the chemical contamination of the environment. It is very much possible that, without the chemical exposure, the small doses of radiation themselves could not make any sufficient impact in additional mortality caused by the ionizing radiation.
PRINCIPLES OF COLLECTION AND ANALYSIS OF HEALTH DATA FROM BELARUSIAN CHILDREN WHO WERE EXPOSED TO RADIATION AS A RESULT OF THE CHERNOBYL ACCIDENT

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In order to follow-up the health status and incidence of disease in the population exposed to radiation in 1986, the State Registry of Individuals Irradiated as a Result of the Chernobyl Accident (Chernobyl Registry) was initiated soon after the disaster to provide a comprehensive registration and follow-up system.

Four groups of subjects were identified for whom registration and follow-up was mandatory: (1) participants in the 'liquidation' of the consequences of the Chernobyl accident, i.e. the so called 'liquidators' or clean-up workers; (2) subjects evacuated from the most contaminated territories (>40 Ci/sq km); (3) persons living in the contaminated areas (>15 Ci/sq km); and (4) children of subjects in groups 1 and 3. The personal files contain the following data: demographic variables, information on location and behavior at the time of the accident (food and milk consumption, time spent in contaminated areas), work in the Chernobyl area, dosimetric information (when available) and medical information was updated periodically to include all diagnoses and treatments. Methods for data collection and analysis were developed, together with ways of expressing output which make it possible to group information according to various parameters, such geographic area, level of radiation exposure, sex, age and other personal information. These data are collected in child health care facilities on the rayon level, then transmitted to oblast registries, and finally sent to the Central Chernobyl Registry which is situated in the Belarussian Center for Medical Technologies (BelCMT) in Minsk.

Since 1986, about 66,900 children from high exposure areas have been registered in the Chernobyl Registry database. Some of them became adults and at present there is information on 33,522 children from 0-14 years of age. Most of them (56%) live in the Gomel region and in the high contamination regions (>15 Ci/sq km Cs-137). According to the register, they are distributed as follows: those evacuated from the 30 km zone - 6%, children residing in or resettled from areas where Cs-137 contamination is greater than 15 Ci/sq km - 69%, children born after the accident from parents who were exposed - 25%. Measures of I-131 uptake by the thyroid gland were obtained in 21,976 children.

During 1987-1995, among children exposed to radiation as a result of the Chernobyl accident, the number with chronic diseases has increased. According to annual medical examinations, the number of apparently healthy children decreased from 61% in 1987 to 20% in 1994, whereas the number of children with chronic diseases increased from 11 to 19%. This may be explained in part by more extensive medical examinations in the highly contaminated areas, in comparison to the less exposed regions.

Within the period that has elapsed since 1987, an overall increase in the incidence of disease was registered for the children followed up by the registry. In particular, there has been an overall increase in the incidence of thyroid cancer and thyroid endocrine disease in this group of children.
THE IMMUNE STATE OF CHILDREN LIVING IN LARGE CITIES OF THE UKRAINE SEVEN YEARS AFTER THE CHERNOBYL ACCIDENT

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The immunological investigations of 7-10 year-old Ukrainian children was undertaken 7 years after the Chernobyl accident. These children live in 4 large industrial centers: Kiev, Dniepropetrovsk, Dnieprodzerzhinsk and Cherkassy. Among these cities only Kiev suffered from the Chernobyl catastrophe.

Investigations were undertaken in 3 zones with different levels of environmental contamination with chemicals in every city. Children with varying developed immunodeficiencies as a risk groups but without chronic pathology were investigated.

It has been shown that the most profound changes of immunological indices in comparison with standard (presented in literature) were observed in children from Kiev. The comparative analysis of immunological indices in children living in the most polluted regions of examined cities allowed us to establish the significant decrease of total lymphocytes amount, accounting T-cells, the increase of neutrophils quantity, and the lowering of IgG and IgM levels in the blood serum of Kiev's children.

The obtained data demonstrated that combined effect of chemical and radiological factors provides more impairment in organism's immune system than isolated influences of xenobiotics. We determined that the more significant changes in cellular and humoral immunity in the child population was a factor of living in the most chemically polluted regions of Kiev.
The work presents the results of descriptive analysis of development of oncoepidemiological situation in six the most polluted regions owing to the Chernobyl accident in 1981—1994. The increase in risk of development of malignancies is one of the most probable effects of ionizing radiation on populations living on radioactively polluted territories. In the Russian Federation the most polluted by radionuclides owing to the Chernobyl accident are the territories of the Bryansk (BR), Kaluga(KR), Orel(OR), Tula(TR), Ryazan(RR), Kursk (KuR) regions to be urgent.

Base of research were materials of official oncological statistics and data personal cancer registers.

There is the steady growth of the malignant neoplasm incidence (MNI) in the population of these regions as well as in whole Russia. However, since 1987, the MNI in the 6 above mentioned regions has become higher than in Russia. In 1994 the rates of the general oncological incidence were: in BR —333.2, KR — 294.3, OR—313.3, TR—339.3, RR—357.1, KuR—300.0, whereas the average rate in Russia was 278.0 per 100,000 of population. Along with it the rate incidence increments in 1994, as compared to 1981, were: in BR —38.6%, KR — 29.6%, OR—40.1%, TR—21.4%, whereas an increment of the average rate in Russia was 19.1%. The analysis of the sex- and age-standardized rates evidences high incidence rates in males of the BR and the RR. In 1994 the incidence rates in the male population of these regions were 304.9. and 305.2, respectively (in Russia — 272.4). High rates of the incidence, which tend to grow, are in the junior group (0—29) of male population of the BR. Over the scrutinised period the incidence rates in female population of the BR and RR were higher than in whole Russia and in 1994 they were in BR —178.2, KR—145.5, OR—171.5, TR—163.4, KuR—148.3, RR—180.2, whole Russia —169.2. Afterwards the accident the structure of the MNI did not significantly change. In order of prevalence rates everywhere over the territories, excluding the BR, the first place goes to lung, trachea, and bronchus cancers, the second place — to stomach cancer. In the BR, first goes stomach cancer, whereas cancer of the respiratory organs goes behind. The contribution of the stomach, hemopoietic and lymphatic tissue, thyroid, pharynx malignant neoplasms to the total incidence of cancer in the BR is more than in Russia. As for the OR the contribution of thyroid cancer to the total incidence of cancer in this region is significantly more than Russia. Dynamics of the incidence of lung, trachea, bronchus cancers in the population of the investigated territories has a positive trend, the highest rates being for the KR, TR, RR. However, the damaged territories were characterised by the highest incidence rate of stomach cancer than in whole Russia as before the accident as after it along with decreasing indices. In 1994 the BR occupied the second and third places in the incidence rate of stomach cancer in males and in women, respectively. The incidence rate of hemopoietic and lymphatic tissue malignant neoplasms in the BR, TR, and RR is higher than in whole Russia. In 1994 the highest incidence rates were registered in the RR: for males — 18.0, for females — 13.5. The growth of thyroid malignant neoplasms incident rate appears to be everywhere over the damaged territories and its increment is significantly higher than in whole Russia and the highest ones in Russia were registered in 1994 in the BR, OR, RR and they were 7.8, 7.7, 7.7 per 100,000 of population, respectively. In 1994 the BR was marked highest in the Russian Federation for a level of malignancy incidence in children. The standardized rates for boys and girls made up 21.8 and 24.2, respectively. Appropriate parameters for the Russian Federation were 10.9 and 9.0. Formation of the current rates of malignant neoplasms incidence, its structure and the trends of its dynamics (except TC) can be traced to the complex of factors that had been established before the accident. Unfavourable trends in development of the oncoepidemiological situation appear to be for the BR and the RR. To monitor the incidence one must to use population cancer registers.
Resolving problems of medical and social help organizing for population in Israel repatriated from zones of radiation pollution, must be based upon objective estimation of its quantity differentiated according to the dose of absorbed radiation.

In connection with this we have undertaken a medical - demographic study of the radiation influence on this part of population.

543,544 people came to Israel in 1989-1994 with the "Alya-90." From this number 378,709 people came from republics directly exposed to radiation because of the Tchernobyl catastrophe.

From this population 56,125 (adults and children) are from the radiated area having -1 km² and need medical control and special social and economical status.

The evaluation of the radiation dose in this population after the study accomplished permits asserting those 93% of people coming to Israel from the Tchernobyl zone have absorbed a radiation dose that can not be harmful for their health and the health of their descendants. (less than 5 REM). The late result of radiation in this number of repatriates will be minimal and hardly differentiated from spontaneous oncologic and genetic diseases.

At the same time there is a risk group of 16,000 of children and 2,000 adults who need preventing measures of the thyroid gland.
Radiation induced cerebral meningioma is a well known entity. It is related to low doses of radiation, less than 1000 cGy for localized disease of scalp (Tinea capitis, nevi) or to higher dose radiation for intracranial tumor. The published world experience with intracranial meningioma after low dose irradiation comes mainly from studies in Israel.

During the first twelve years of mass immigration to Israel (1949-1960), nearly 17,000 children were irradiated for Tinea capitis.

Several publications reported a fourfold increase in the incidence of meningioma in irradiated patients when compared with control groups. The mean latency period reported was up to 38 years. Histological characteristics, locations, recurrent rates, incidence of multiple meningiomas and malignancy were reported.

The current study analyzed post irradiation meningioma in comparison to the total number of meningioma diagnosed in Soroka Medical Center in two time periods, 1976-1986 and 1990-1996.

Between 1976 and 1986, 15 cases of total 77 meningiomas were post irradiation (19.5%). In the second time period, 1990-1996, 28 cases of a total of 150 meningioma were post irradiation (18.6%). The mean latency period for the last 6 years was 43 years. The radiological presentation and biological behavior in our series are presented.

We conclude that the mean latency period has not yet been reached as we continue to see a high incidence of post irradiation meningioma in the cohort of irradiated early immigrants.
SYNERGISTIC INTERACTION OF IONIZING RADIATION WITH OTHER HARMFUL AGENTS AND ENVIRONMENTAL HEALTH CRITERIA

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At present there are various sources of antropogenic contamination in the environmental including ionizing and non-ionizing radiations, different chemical pollutions, etc., which can interact in a synergistic manner with each other. In this report, regularities of synergistic interaction of damages induced by various agents are analysed using our own experimental data and results published by others. Theoretical prognosis of the extreme synergistic effects and their comparison with experimental findings are also presented. The used mathematical model is based on the suggestion that synergism is expected from the additional lethal damages arising from an interaction of sublesions induced by both agents. The model predicts the highest value of the synergistic effect, and also suggests the conditions under which it can be achieved. The practical significance of this data may be expected in the area of improving the analysis of ecological/environmental impacts of combinations of harmful agents. The main conclusion pertained to this aspect of the model is that under simultaneous action the less intensity of one from two agents applied, the less intensity of another factor have to be used to obtained the highest value of synergism. This conclusion was verified in experiments with various cell systems for simultaneous theromradiation as well as UV-light and heat treatment. The correlation between dose rate (or fluence rate) and exposure temperature which provide the highest synergistic interaction was observed. It follows that the temperature, at which radiation is delivered should be decreased to obtain maximum synergistic effect with decreasing dose rate (or fluence rate). Hence, the synergistic interaction, in principle, can take place between existing background of ionizing radiation, microwaves, ambient temperature, natural UV-radiation and chemical pollution and thereby to strengthen their harmful action. This fact should be taken into account under developing the environmental health criteria.
MORPHOFUNCTIONAL STATUS OF UPPER SECTIONS OF DIGESTIVE TRACT OF CHILDREN FROM REGIONS SUBJECTED TO RADIONUCLIDE CONTAMINATION

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Taking into account anamnesis and a number of screening tests, the morphofunctional status of the digestive tract of the upper sections was analyzed for 125 children from 3 to 14 years old. Esophagoduoenoscopy with biopsy of stomach and duodenum mucous membrane (histological study of biopsies and estimates of their cell composition and spectrum of immunocompetent cells) and ultrasonic investigation of abdominal cavity organs were performed. Acid-forming function of stomach and exacrinous activity of pancreas were estimated. Changes of stomach and duodenum mucous membrane were identified for all the children with clinically manifested forms of pathology and for 84.4% of the children displaying no typical signs of digestive system lesion. For all the patients, combined lesion of stomach and duodenum mucous membrane was established during endoscopy, which manifested itself by thickened, hyperemic folds, pronounced hyperplasia in the form of different-sized protrusions of the stomach, bulb and postbulb sections of the duodenum, multiple lymphangioectasia, whitish patches or thick white deposit on its walls. Terminal esophagitis was diagnosed for 12 children. Changes of mucous membrane in the lower third of the esophagus were represented by focal hyperemia, edematic folds in the precardial region, single erosions. Duodenogastral reflex was detected for 38.5% of the children, while the gastroesophageal one, for 33.3%. Histomorphological investigation of biops confirmed the combined character of stomach and duodenum changes for 61.5% of the children. At that 68.7% of the children had gastritis of a diffuse character and 31.3%, of a superficial one. The duodenum biopsy displayed chronic diffuse duodenitis for the majority of children. An increased number of lymphocytes and fibroblasts, as compared with a decreased number of plasma cells was found in the stomach and duodenum mucous membrane. Local production of Ig of all the three classes was also increased with simultaneous decrease of the number of cell synthesizing SIgA, accompanied by an increase of the number of cells producing IgG. During the morphometric analysis, atrophic changes of epithelium and villi were detected. Accumulations of Helicobacter pylori were found in parietel and pit mucus of stomach antral section for 67.5% of the children. The ultrasonic investigation of abdominal cavity organs revealed changes of gallbladder structure in the form of strangulations and flexures for 38.4% of the children, flocculent precipitate was found in the gallbladder for 12.8% of the children, increase of the liver size was confirmed for 6.5% of the children. Reactive pancreatitis was diagnosed for 23% of the children. The presented results of examining the children make the foundation for forming the clinical data base that will allow rehabilitation actions to be implemented more effectively hereinafter, taking into account specific features of the body status.
Informative computer complex was developed for carrying out computer analysis of effect of different therapeutical strategies and also for prognosticating effect of immuno-modulating means at the treatment of acute leucoses and myelodysplastic syndrome. The complex will used at the treatment of patients of increased radiation risk - liquidators of Chernobyl accident, suffering from some forms of preleucose conditions and hemoblastoses. Created complex includes the methods and means of modelling and optimal control of some links of hematopoiesis regulation system; data base for illness history keeping on preleucose conditions and hematoblastoses patients of increased radiation risk, the division of processing graphical images of cell structures, obtained with the use of electronic microscopy. Complex allows to User to solve following problems: a) investigation of influence biologically active substances on the reserve possibilities of immune system; b) specification of regimes of immunomodulator's introduction for correction of immune system during a treatment; c) operative saving, processing and handling over of big arrays of information and timely finding out conditions of hematopoiesis regulation system.

Computerised analysis of standard subject cards, containing clinical and immunological indices of pre-leucoses and hemotoblastoses was carried out. The results of retrospective estimation of leucoses frequency among participants of Chernobyl accident consequences elimination show, that one of the important manifestation of preleucoses, that precedes the tumour rise development, is mie-lodysplastic syndrome (MS). The correlation analysis of indices of peripheral blood, marrow bone and other clinical parameters for determination of additional criteria of different forms of MS prediagnostic was carry out on the base of mathematical models. The results, that were obtained show that most important for prediagnostic parameters are the hemopoesis signs, the number of blast elements and obvious dishematopoiesis in marrow bone and peripheral blood.

The problem of determination of reserve possibilities of control mechanisms of humoral and cellular links of immune system under different levels of radiation doses was also investigated. The dynamical models were used for these parameters dynamic and radiation effect on immune system determination. The contribution of beta-cells and immunoglobulines in development of immune system pathology was estimated. Modelling influence of low doses of radiation on immune response was in interval from 0 to 0.5 Gy. They were compared with more significant doses, lying in diapason from 1 to 4 Gy. One have shown, that even on interval of low doses gradual decreasing level of antibodies takes place, when antigen level is beginning to increase. It testifies about weakening reserve possibilities of humor link of immune response.

The following problems of optimal control of immune response at different doses of radiation were examined: (1) directional effect immunocorrectors on the interaction between antigen, effectors and supresors cells; (2) determination of dynamics of changing levels interleukin-2, and also activating, proliferating and producing interleukin-2 T-helpers. Carrying out investigation permitted to determine optimal change of above mentioned control parameters, that maximize the reserve of defensive functions. Time diapasons, on which the character of control is principally changing, were determined for different doses of radiation.
STUDY OF REMOTE CONSEQUENCES OF CHERNOBYL ACCIDENT AND ITS PREVENTION BY USING ANTIOXIDANT PREPARATIONS

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The accident at Chernobyl Nuclear Station has had tremendous consequences not only in Byelorussia, Russia, and Ukraine, but also in such a distant country as Armenia. We have conducted dynamic observations of 2,000 persons who participated in the clean-up of the Chernobyl accident (liquidators) during the years 1986 to 1996.

Observation has demonstrated that the major contribution to morbidity rate takes the nervous system pathology, which has increased during the last years. At the same time there has been a gradual increase in of cardiovascular, lung, and gastroenteric diseases. This process is characterized by gradual transition from functional pathology to organic one. There is an indication of damage in the immune status and decrease in resistance to infection. In addition to these changes we have observed increase of level of chromosome aberrations, spermatogenesis and clastogenic factor alterations.

To treat and prevent the remote alterations we widely use antioxidant (AO) preparations, including well-known tocopherol, tanakan, AOB, and home-made Loshtak (Brionia alba). Comparative analysis of these preparations operation shows that they have different degrees of positive antioxidant and anticlastogenic effect. Therefore it is expedient to use them widely to help prevent development of the remote consequences of radiation damage.
BIOLOGICAL ANTIOXIDANTS OF THE DEAD SEA FOR THE TREATMENT OF LOCAL RADIATION LESIONS

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The "LENOM" Clinics have a lot of preparations that are being created on the base of biological antioxidants in the form of ointment, fomentation, gargles, irrigation, capsules for local and general use. The feature of these preparations is their derivation of natural agents of the Dead Sea, the absence of toxicity, presence of natural vitamins, antioxidants, and other biologically active agents, which has a direct influence on pathological body cells. By a high penetrating activity of biologic agents the direct influence is being realized on the genetic system of the cell. A clinical trial of preparations took place in 45 patients with local radiation lesions secondary to a complex treatment (radiation therapy + treatment) of mammary gland tumor, carcinoma of laryngopharynx, and lung cancer.

During the treatment of radiation skin lesions of degree I and II (12 patients) there were a relief of anxious pruritus, painful tissue tension, the reduce of healing time and in the degree III (moist erythroderma) - only a subjective amelioration.

A positive effect has being seen after the treatment of the late radiation skin fibroses (14 patients) manifested by fibrous changed tissues softening and relief of hyperpigmentation.

In patients with radiation ulcers (7 patients) it has being noted reduces of pains, intensification of exudation, cleansing of ulcer surfaces with subsequent development of granulation.

In 12 patients with late radiation pneumofibrosis it has being noted subjective and objective amelioration on X-rays and during spirometric studies.

The treatment with biological antioxidants (BAO) is tolerated by patients and has no side effects.

The uses of BAO in the Dead Sea preparations considerably enlarge the number of medical methods in preventing and treatment of radiation lesions.
The systems of rehabilitation of patients with radiation pathology have not been worked out yet; neither available are scientifically based systems of spa treatment for such patients. Insufficient attention is paid to the spa treatment of conventional diseases of patients which had a contact with ionising irradiation in the past. The present research provides an overview of the first ever experience in using unique climatological and balneological factors in the spa treatment & recuperation programs for the participants in the elimination of the aftermath of Chernobyl disaster at medical clinics located near the city of Arad and the Dead Sea. Among 96 Chernobyl victims which took spa treatment courses in Israel there were 40 patients whose diagnosis included irradiation as etiological factor of the disease: consequences of acute and chronic irradiation disease, astheno-neurotic syndrome, dis-circulatory encephalopathy, subatrophic laryngopharyngitis, obstructive bronchitis. Among conventional diseases which have direct indication for treatment in the special environment of Arad and the Dead Sea, there were 88 patients with problems of locomotor system, respiratory system diseases and skin problems. The course of treatment included the Dead Sea water baths, mud applications, sun baths, climatotherapy, different kinds of phisiotherapy, massage, bioenergy therapy, inhalations, moisturizing creams etc. Summing up the results of the spa treatment programs, we can observe a significant improvement with the disappearance of the leading symptoms with 82% of the patients; 13% of the patients showed improvement with significant decrease of the symptoms; 5% of the patients had no visible results.
The NASA Space Radiation Health Program is a research program intended to establish the scientific basis for radiation protection of humans living and working in space, and journeying to other planetary bodies. The population at risk is small, and consists of exceptionally healthy men and women, subject to the stresses of space travel. The major radiation hazards beyond the Earth's magnetosphere are due to protons from solar energetic particle (SEP) events and to galactic cosmic rays. The latter consist of protons and highly charged, energetic nuclei of the elements ("HZE particles"). As a consequence of their high energy, the range of these particles is comparable with their nuclear mean free path. Thus, a substantial number of nuclear interaction products will be produced in shielding and tissues in the path of the radiation. Data on the interaction of HZE particles with matter are sparse and methods to calculate radiation transport in shielding have had only limited validation. The likely biological effectiveness of space radiation is poorly understood. Most of our knowledge of the biological effects of radiation is based on x-rays or gamma rays; however, the biological damage induced by charged particles occurs with greater probability, greater intensity, or both, than comparable effects of x-rays. Thus, space radiation constitutes a very different radiation hazard from that posed by conventional sources on Earth. Assessment of the radiation risks associated with space travel requires predictions of health effects in order to establish appropriate exposure limits. Reliable estimates of the uncertainties associated with these predictions are required for cost-effective design of spacecraft and space habitats. Risk management requires the development of countermeasures when prescribed levels of radiation may be exceeded. Such countermeasures include evasion strategies and shielding design. Given the rapid pace of progress in biology and medicine, they may eventually include prevention and pharmacological or clinical intervention. Evidently, exposure to space radiation requires the resolution of many fundamental problems in physics and radiation biology. The current status and some of the accomplishments obtained by the NASA Space Radiation Health Program in pursuit of its goals will be reviewed.
Joint cancer risks among workers having silica, smoking, and radon exposures must be examined. David E. Goldsmith (Western Consortium for Public Health, Berkeley, CA 94704) John R. Goldsmith (Ben Gurion University of the Negev, Beer Sheva, Israel)

Because silica is now considered a probable human carcinogen by the International Agency for Research on Cancer (IARC) and other environmental health agencies, it is necessary to understand the occupational cancer risks among quartz-exposed uranium miners who also smoke. Most epidemiological research and human health hazard assessment have focused on the lung cancer risks among several cohorts of uranium miners having smoking histories with their work files. The Biological Effects of Ionizing Radiation (BIER IV) Committee of the National Academy of Sciences developed a multivariable model of lung cancer risk among uranium miners that assumes smoking and radon progeny act in a greater than additive (i.e., synergistic) fashion. However, the model does not currently address the biological effects of exposure to crystalline silica. One consideration is to evaluate the evidence for pairwise relationships from extant studies of radon and smoking (uranium miners, nuclear processing workers), and silica and smoking (gold miners, diatomaceous earth workers, and silicotics), examine the resulting models and uncertainties, and then search for data sets for testing critical aspects of plausible three-way models. Particle concentration levels, freshness of fracture, radon emissions, adsorbence of radioactive decay products onto particulate surfaces, and changes in mining and processing technologies are relevant to silica and radon hazard levels and are all likely to affect lung (and perhaps other sites) cancer risk models. Once agreement on models to be tested is reached, then they can be examined with cohorts having the best possible measurements of smoking, exposures, and disease. Because the current BIER equation has been used to determine acceptable occupational levels for the U.S. Occupational Safety and Health Administration and Department of Energy, and is the basis for permissible indoor radon levels by U.S. EPA, these policies must be re-examined to account for the role silica plays in a reconfigured cancer risk model.
A STUDY OF DETERMINISTIC HEALTH EFFECTS OF RADIATION EXPOSURE IN CHELYABINSK-65 NUCLEAR WORKERS

Niel Wald, University of Pittsburgh, for the Research Team Members* of Project 2.3 of the Joint Coordinating Committee for Radiation Effects Research of the U.S. and the Russian Federation

Most of our current knowledge about deterministic or nonstochastic effects of ionizing radiation overexposure in humans has been derived from extrapolations from experimental studies of various animals; studies of the Japanese populations exposed to atomic bombs at extremely high dose rates; data about medical side effects arising in radiation therapy patients given in fractionated, localized doses, or published data about the relatively rare accidentally exposed radiation workers, predominantly male, as well as of some members of the public, who developed deterministic effects.

Although all of these experiences have provided extremely useful radiobiological data, they are limited for the purpose of our general objective, to identify the best clinical and laboratory correlates for medical prognostication and management of human radiation injury. The radiation workers group is of particular value despite its relatively small number, because workers are generally in good health at the time of exposure and the medical management of any mishaps usually includes detailed dose reconstruction as well as close clinical observation.

During the past 50 years, defense-related activities in the Russian Federation and in the United States resulted in occasional accidental occupational radiation exposures of nuclear workers as well as in some population exposures. Information has now become available for scientific study about activities of the first Russian nuclear weapon production facilities, the Mayak Production Association at Chelyabinsk-65 (now Ozersk) in the South Urals. Several thousands of workers, about 30% female, were exposed to relatively high levels of external gamma radiation and, in many cases, to internal alpha radiation from inhaled plutonium as well. Annual average gamma doses at the radiochemical plant in its first 5 years (1949-1953) were 31-113 cSv. A number of workers developed health impairments that were considered to be forms of radiation injury. More than 1,800 cases of occupational diseases were diagnosed by 1960 and chronic radiation sickness was identified as a major contributor to the total. This syndrome was described by A.K. Guskova and G.D. Baisogolov in 1971. In a recent review N. D. Okladnikova also described early deterministic effects including cases of the acute radiation syndromes, local radiation injuries, and lens cataracts as well as pulmonary pneumosclerosis following large plutonium inhalations.

Systematic medical observations have been carried out by Branch 1 of the Institute of Biophysics (FIB-1) of the Russian Ministry of Health on all workers as part of the radiation protection program that began with the start-up of the Mayak facilities. For 48 years these unique data have been collected, now allowing the study of a wide range of deterministic effects, including those involving the hematopoietic, immune, nervous, cardiovascular, and visual systems, as well as the key organs of plutonium deposition, i.e., liver, lungs and skeleton. Over the same time period the dosimetric data developed by the Mayak Radiation Protection Department on each employee, using methodology recently described by A. F. Lyzlov, have also been maintained.

In February, 1996, we began a collaborative feasibility study supported by the U.S. Department of Energy and the Russian Federation Ministry of Health, Institute of Biophysics, with the help of E. Lyubchansky, Director of FIB-1, and the research team members*: N. Okladnikova, V. Pesternikova, M. Sumina, M. Azizova, V. Telnov and A. Fevralev of FIB-1; A. F. Lyzlov of the Mayak Production Association; B. Boecker and B. Scott of the Inhalation Toxicology Research Institute (ITRI); and R. Day, S. Shekhter-Levin, I. Linkov (now at Harvard University) and N. Wald of the University of Pittsburgh. An important long term objective is to make a significant addition to the available cases of various deterministic effects for analysis and if suitable, for possible inclusion in the DOE/REAC/TS Registries and the International Computer Database for Radiation Exposure Case Histories developed by T. M. Fliedner and A. E. Baranov. The design and progress of the feasibility study will be described.
A cohort of 4800 male Estonians who participated in the cleanup activities of the Chernobyl accident in the years following the accident in 1986 was assembled using four sources. The main activities of these workers at Chernobyl were determined using a questionnaire survey with an 85% rate of response. The official radiation doses of the workers have been assembled. The doses were validated using the glycophorin A (GPA) somatic cell mutation assay based on blood samples obtained from two-thirds of the workers. The results indicate that the workers' radiation exposure did not greatly exceed the physical dose estimates of 10 to 20 cGy, the minimum level at which radiation effects are likely to be detectable by the GPA assay. Moreover, there was not a substantial subset of the workers who received doses above this level.
CANCER INCIDENCE IN IMMIGRANTS TO ISRAEL FROM THE FORMER

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174,668 young immigrants from the former Soviet Union (SU) who arrived in Israel
at age 0-24 years during the period 1989 to 1994 were passively followed until
January 1, 1995, (~586,000 persons-years). Jews born in Israel were selected as
controls (1930 incident-cases, ~9.8 millions persons-years). The Israel Cancer
Registry registered 132 malignant neoplasms among immigrants from the former
Soviet Union. Nineteen cases (15%) diagnosed during the first two months
immediately after their arrival were excluded as representing the 'sick migrant effect'.
Relative risk (RR) of the remaining 113 subjects compared to Israel-born controls was
1.06 (CL 95%: 0.88, 1.23). For leukemia, the RR was 1.69 (CL 95%: 0.72, 2.67)
with a preponderance of subjects whose last residence was in the Russian Federation.
The RR for tumours of the central nervous system was 1.19 (CL 95%: 0.75, 1.62),
the highest incidence being observed in Ukrainian immigrants. Two cases of thyroid
cancer registered during the study period came from Gomel (Byelorutus) and Moscow,
respectively. From the reported incidence of thyroid cancer in the city of Gomel (8.5
per 100,000 person-years), it is expected that among the 3,000 young immigrants to
Israel from that city there will be one case every four years in the next 20 years. The
policy we advocated in 1990 of passive follow up through the Cancer Registry and
appropriate alertness on the part of primary care physicians is still recommended. No
excess in total malignancy incidence in young immigrants arriving from the greater
Chernobyl area has thus far been recognized, but comprehensive passive follow up
through the Cancer Registry should continue.
UACOS - THE UKRAINIAN/AMERICAN CHERNOBYL OCULAR STUDY

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In the early morning of April 26, 1986, Reactor Number 4 of the Chernobyl Nuclear Power Complex underwent a power excursion resulting in a steam explosion which spewed solid and gaseous radioactive materials into the environment. In all, 600,000 people were exposed to, what has been described as, "significant" levels of radiation. A joint Ukrainian/American Chernobyl Ocular Study (UACOS) Group was instituted to provide an infrastructure to monitor the effects of radiation on ocular tissues, with particular emphasis on the lens. This consortium has been focusing on the subset of the over 250,000 individuals who were assigned clean-up and maintenance duties after the accident; the so-called "Liquidators". The planned 30 year study has three main thrusts; (1) an extensive cohort study of cataract incidence in relation to dose and other factors, (2) a quantitative, longitudinal, non-subjective assessment utilizing Scheimpflug image acquisition and, finally (3) the establishment of a tissue repository for capsulotomy fragments or "tags" to be made available for investigational use. The last arm of the effort currently involves calibration of the micronucleus test in lens epithelia against known doses of radiation. The studies, which are overseen in Ukraine by the Ministry of Health and The National Academy of Sciences, and in the United States by several agencies, are organized in conjunction with six centers throughout Ukraine and three institutes in Kiev.

The longitudinal Scheimpflug slit-imaging of the eyes currently in its third year, has, to date, enrolled approximately 350 workers ranging in age from 26 to 60 (ATE) with doses spanning 2 to 240 cGy. Analyses of light-scatter from the lenses as a function of dose and/or age reveal that, if the entire lens is considered, age has a more potent negative effect on transparency than does dose. However, when corrected for age (and, more importantly, the lenticular region being considered), a trend towards a dose-dependent loss of posterior subcapsular (PSC) transparency becomes apparent on an inter-subject basis. It is critical to note that, characteristically, radiation cataracts first appear in the PSC region of the lens. Approximately 50 of the workers have been assessed a second time with an inter-observational interval of 18 - 24 months. The results show a strong tendency for increased light scatter in the PSC region of the lenses of the same individuals with. When fully analyzed following a third evaluation we believe that the positive slopes will be highly correlated to the dose received. In addition to the observations on the effect of dose on lenticular transparency, there is a measurable effect of the radiation on the dimensions of the antero-posterior axis of the lens. Heretofore only anecdotal evidence has been available regarding radiation effects on lens size. Once adequately quantified over time and as a function of dose, the geometric changes in the lens may provide an additional endpoint for assessing radiation exposure to human populations.

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LESSONS LEARNED IN THE STUDY OF IMMIGRANTS TO ISRAEL FROM AREAS OF RUSSIA, BELARUS AND THE UKRAINE CONTAMINATED BY THE CHERNOBYL ACCIDENT


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During the past 6 years, large scale immigration to Israel of 700,000 persons from the former Soviet Union (FSU) included the arrival of about 140,000 immigrants who came from regions of Belarus, Ukraine and Russia near Chernobyl. In Beer Sheva, a major center for immigrant absorption in Israel, our first objective was to create a clinic for the benefit of the new immigrants and to evaluate their health status.

Measurement of Cs-137 in the immigrants was carried out with a portable whole body counter lent by the Canadian Dept of Health. In a study of 1228 men women and children, Cs-137 levels were found to be lower than that reported by the IAEA, and there was a clear correlation between whole body counts, extrapolated back to the time of leaving the FSU, and the degree of Cs-137 ground contamination in previous regions of residence. The exposed population could be divided into two groups with greater and lesser exposures, depending on the degree of ground contamination.

The thyroid status of 309 local immigrant children was evaluated due to (a) iodine deficiency in regions of origin, (b) high consumption of milk containing I-131, and (c) the reported increases of childhood thyroid cancer in these regions. Comparative group: subjects from less contaminated areas, based on IAEA soil Cs-137 maps. Lab tests: thyroid hormones including TSH, thyroglobulin, and antithyroid antibodies. Thyroid morphology was evaluated by palpation and ultrasound. Enlarged thyroids were found in about 40% of both groups. One 12 year old Gomel girl had a malignant papillary carcinoma. No changes in autoimmune status were found. TSH levels were significantly increased (p=0.023) for girls from high exposure regions, though within normal limits.

Salvage workers (liquidators): Assessment of past dose is being carried out by several forms of biological dosimetry, including the measurement of clastogenic factor (CF) and glycoporphin A (GP-A). Significant increases in GP-A and CF were found.

Psychosocial studies: Our colleagues Drs. Cwikel, Abdelgani and Yevelson of the social work department of the Ben Gurion University have carried out collaborative studies on over 700 people from the radiocontaminated areas and control subjects from unaffected regions of the FSU. Evidence for post-traumatic shock disorder was found in a subgroup of the persons interviewed. These findings are reported elsewhere in this conference.

In conclusion, whole body counting of immigrants showed that radio-cesium body burden is dependent on the degree of ground contamination, and that the exposed population can be divided into groups who came from regions of higher or lower radiocesium content. Using this way of establishing comparison groups, we have compared thyroid hormone levels in children and found shifts to higher (though normal) TSH levels in girls who came from the regions of higher ground radiocontamination. We hypothesize this to be a homeostatic response of the thyroid-pituitary axis to sub-clinical thyroid damage caused by the uptake of iodine-131 and short lived radioiodines. Psychosocial studies demonstrate a comparative increase in post-traumatic stress disorder in immigrants who came from areas of higher exposure nearer to Chernobyl. Liquidator studies show measurable elevations of clastogenic factor in serum and of glycoporphin-A antigen mutation in red cells.
RISK ASSESSMENT OF RADIATION EFFECT ON IMMUNE AND ENDOCRINE SYSTEM

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One of the important stages of restoration of thyroid gland function at hypothyroidism is the normalizing level of thyroid hormones - triiodothyronine and thyroxine. There is a problem of determination of an optimal strategy of therapeutic influences, which should allow to optimize the effect of specific preparations, normalizing the level of thyroid hormones. It will permit to estimate contribution of different metabolite chains to the formation of some kinds of thyroid system pathology and increase therapy effect due to investigating mechanisms of acting some therapeutic preparations to synchronize different regulation links, responding for co-ordinate function of nervous, endocrine and immune systems. The problem can be solved by the methods of optimal control theory.

Informative computer complex was created to investigate disturbances of neuroimmunoendocrine regulation mechanisms at the action of radioactive iodine on thyroid gland and for working out optimal therapy directed on the restoration of thyroid gland functions due to synchronization of different regulation links, responding for co-ordinate function of endocrine and immune systems of persons suffering as result of Chernobyl accident.

The complex includes the mathematical models of regulation of neurohormone activity of thyroid gland and metabolite regulation of synthesis of thyroid hormones; methods and means of modelling optimal control of balancing processes of synthesis and consumption of energy; software for solving problems of modelling and optimization of the restoration of thyroid gland function and investigating mechanisms of disturbances of neuroimmunoendocrine regulation, data base for illness history keeping on thyroid gland pathologies.

Computerised analysis of these data base, containing clinical and immunological indices, obtained under action of various dose of radiation was carry out. The models of some correlations between immune and endocrine systems were used for comparative analysis of contributions of metabolite and thyroid factors to disturbance of feedback system, realizing metabolite regulation in norm and at the some diseases of thyroid system: hypothyroidism, T3-thyrotoxicosis, T4-thyrotoxicosis and hyperthyroidism.

Preliminary results shown, that primary disturbances of regulation mechanisms of thyroid system, passing on the level of metabolite regulation due to changing intensity of calcium currents and energy synthesis, bring at hypothyroidism the most disbalance in processes of synthesis and consumption of energy in a cell (inhibition of energy synthesis due to reducing levels of triiodothyronine and thyroxine and activation of energy consumption connected with increasing of calcium influx to cell). The disturbance of the balance leads to metabolite shifts (changing level of cAMP and prostaglandines), which may carry compensative character, limiting negative changes in correlations of thyroid hormones. Obtained results allow to determine the dynamics of intensity of oxidative phosphorylation, calcium influx to cell and iodine level in blood, that minimize damage to thyroid system from radiation.

The problem of determination of influence of radiation on immune system was also investigated by elaborated model. It was shown that risk of negative consequences for immune and endocrine systems after radiation action may be decreased by metabolite changes which normalize the balance between processes of synthesis and consumption of energy in antagonistic populations of cells.
RECONSTRUCTION OF THE DOSE ACCUMULATED IN INHABITANTS OF RUSSIAN REGIONS CONTAMINATED WITH RADIONUCLIDES AS A RESULT OF THE CHERNOBYL ACCIDENT

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The population of nineteen regions of Russia along with the population of Belarus and Ukraine are affected by long-term external and internal irradiation from radionuclides released ten years ago as a result of the Chernobyl accident. Reconstruction of the dose received by the people during this period has the following practical aims: (1) substantiation of the special medical aid to population; (2) substantiation of measures of social protection for population; (3) informing the public and the authorities; (4) ensuring epidemiological investigations.

Input data for the dose reconstruction are data bases of measurement results performed during ten years. These data include results of exposure dose rate measurements in different inhabited areas, analysis of soil and other environmental samples contamination, analysis of radionuclide content in drinking water and in food products of agricultural and natural origin both vegetable and animal. Of particular importance for the reconstruction of individual and group doses are results of personal monitoring: 1-131 content in human thyroid; Cs-134,-137 content in the whole body; external dose measured usually with termoluminescent dosimeters (TLD). The number of the validated personal measurements performed in Russia, mainly in the most contaminated Bryansk, Kaluga, Tula and Orel regions, is about 50, 300 and 10 thousands, respectively. Analyses of Sr-90 and plutonium radionuclides content were performed in several tens of autopsy samples of human tissues collected in the Bryansk region.

In the case of 1-131 thyroid measurement its result is directly connected with the thyroid dose. For the reconstruction of the long-term internal exposure with caesium radionuclides early whole body measurements performed in summer-autumn 1986 are especially important because in many regions of the former USSR main intake in the population occurred namely at this early stage. Late whole body measurements, autopsy samples and TLD-measurements are mainly used for validation of internal and external dose reconstruction models.

The paper presents models of dose reconstruction developed and used in Russia for the population of contaminated regions. The average accumulated effective doses are calculated for inhabitants of 1700 localities of the Bryansk region. For the reconstruction of the dose in particular age-sex, social and professional population groups the system of correcting factors is used based on the results of personal monitoring both of external and internal dose. For individual dose reconstruction the person is interviewed on its way and conditions of life and on its food habits. According to the interview results individual doses of external and internal exposure are estimated. Numerical results of the dose reconstruction for different social and professional groups of the inhabitants of some contaminated localities of the Bryansk and Tula regions are presented in the paper.
INCOMPATIBILITY OF INDIVIDUAL AND POPULATION RISK ESTIMATIONS FOR RADIATION

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As a result of the known exposure to such an event as the Chernobyl disaster, the most natural interest of exposed persons is how the experience is likely to affect their lives and health; the individual risk estimate (IRE). The sources of relevant information are virtually all based on population risk estimates (PRE), of which the most common is the proportional increase in background cancer rates, over a lifetime. Much fear, and misapplied medical resources and public expenditure can be traced to the failure to realize that these PREs are not compatible with IREs. The basic premise of a correctly derived (PRE) is that it reflects the absolute or relative increase in disease or mortality which would occur in a defined population over a specified period as a consequence of exposure to the risk factor, in our case assumed to be radiation. PRE's are always derived and not based on experiment; experimental exposure and long-term follow-up are neither ethical nor practical. In their customary form, PREs are always probabilities, and low ones at that. For example, of 135,000 evacuees from the 30 km zone around Chernobyl with an estimated average exposure of 10 mSv, 65 cases of leukemia would be expected in 10 years of which 5 additional cases (0.004%) may be predicted as a result of this averaged irradiation. (According to an IAEA paper not to be quoted or referenced.) For expression of an individual's risk this cannot be distinguished from 0, and even when looked for epidemiologically, has not been found. The first source of incompatibility are the inappropriate assumptions which lead to PREs, for example uniform exposures and homogeneity of population susceptibility. The second basis for incompatibility is the tiny numerical values of PREs with respect to the concern of an individual, which often as well makes them unmeasurable. The third major source of incompatibility is the dependence on cancer incidence or mortality as a source of PRE. In fact, most exposed persons are much more likely, in our experience, to be affected by excess cardio-vascular, respiratory, emotional or socio-economic distress, and for these types of effects, PREs provide no information. The fourth is that PREs as presently estimated and reported simply do no recognize, measure or reflect the types of risks most likely to be occurring. It is as though the health scientists responsible for protection against radiation risks have never listened to a victim of the risk! There are ways out of this incompatibility, based on listening to the victims. It is then possible to set up health status monitoring for relevant outcomes and look for gradients in health status, associated with proximity, or dose estimation. The monitoring may involve biological indicators, health behaviors (for example avoidance of contaminated types of food, or use of check-ups), or it may be restricted to abstracted data on health events such as hospitalization, complaints, survival, or to work or school productivity.
The cumulative experience of accidental situations of different types and caused medical consequences in persons participated in these situations including that experience accumulated for 162 situations within 10 to 45 years of observation gives an opportunity to develop principles of the health consequences analysis and to reveal main sources of errors done for decisions for expertise and treatment.

Basic postulate consists in the recognition of strict correspondence of type of accident, main accidental radiation and non-radiation factors with structure and occurrence rate of injuries in individuals involved. The specificity of spatial-temporal distribution of exposure dose remains to be important for occurrence of early and late consequences of radiation action.

Basic types of accidents and adequate assessments of their health consequences and decisions relating to health status at early periods after the accident will be shown in the report.

For minor accidents the low number of participants is specific as well as the combination of severe local injuries and total body damage with significant variability of findings and outcomes in some participants of the accident. The exposure from external radiation sources in minor accidents (gamma, gamma-neutron) was predominated together with sufficient nonuniformity of dose distribution in body segments.

Large-scale accidents similar to that happened in Chernobyl in April 26, 1986 were frequently prone to environment release of gamma-beta emitters. The accident of such type have the specific features as follows:

- involvement of large number of people into the situation together with low percentage (5-10%) of individuals undergone to significant overexposure and consequently with lower number of severely injured patients (134 verified cases of Acute Radiation Disease (ARD) and 28 lethal cases caused by Chernobyl accident).

The importance of internal exposure was usually negligible excluding Chernobyl Nuclear Power Plant personnel employed at "iodine" period and children lived in areas contaminated by radioiodines release in April-May, 1986. The quantitative estimates of doses in these children have a number of limitations, which aggravate the interpretation of health status assessments.

The assessment of early health effects occurred after the accident in employees engaged in accident consequences elimination ("liquidators") and in population provides the well substantiated opportunity to obey their direct correlation to the radiation exposure and to analyze these effects on the background of unfavorable social-psychological factor actions. No any confident increase of morbidity rate of leukemia and solid tumors was found in contaminated area population within 10 years passed after the accident.

The data accumulated to assess stochastic health effects in "liquidators" are not singular and increase of surveillance period is required for detailed epidemiological analysis.

The unique experience gathered in Clinical Department of the Institute of Biophysics and its affiliated branches for investigation and treatment in radiation accident victims covers the information for approximately 1000 individuals involved in the situations and more than 450 persons suffered from acute whole body damage and from local radiation injuries predominantly.

Each of such cases were assessed by experts at different periods, when the presence and severity of radiation injury or its consequences were estimated as well as the degree of workability limitations for general employment and specific jobs, which assessment served to be the basis for corresponded social decisions.

The decisions dealing with early deterministic health effects (different forms of acute and chronical radiation disease) are best elaborated and included into Manuals and instruction recommendations on the legislative basis.

Medical expertise and social decisions in people involved in the accidental situations but without clear signs of threshold deterministic health effects are more complicated and multifactorial, which complications are also shown for expertise worldwide.

The emphasis should be done on separation of specific role of radiation factors in polyethiological syndromes and diseases at late periods after irradiation.

The information on working experience of Expert Council of Clinical Department will be given together with examples of approaches formed by this body for the decision making process to discuss these approaches with international scientific community.

Specific ascent will be provided to the sources of errors occurred at the assessment of correlation between health status changes and radiation exposure caused by different accidents and incidents.
Modern approaches to implementing radiation protection measures for people residing in the contaminated areas of the Republic of Belarus

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Despite the fact that it has been 10 years since the accident at the Chernobyl NPP happened, elaboration and implementation of adequate measures to further minimize its medical and biological consequences are still urgent.

Proceeding from the foregoing, in April 1995 the National Commission on Radiation Protection approved "Concept of protective measures at the rehabilitation stage for people residing in the territory of the Republic of Belarus contaminated as a result of the Chernobyl NPP accident" which was ratified as a state one in November 1995.

Fundamental points of the Concept are based upon the following:

- Statement that the Republic of Belarus is at the rehabilitation stage of elimination of the consequences of the ChNPP accident.

- Proposition that mechanisms of a combined impact on sanogenesis rendered by a complex of unfavourable factors, which directly or indirectly accrued from the ChNPP accident, are the basis of the observed health deformation in people residing in the contaminated areas and receiving an additional dose of accidental radiation.

Major propositions of the Concept can be summarized as follows:

- An analysis of a present radiological situation testifies to the fact that the republic is at the rehabilitation stage of minimization of the consequences of the ChNPP accident. On this basis all public protection measures should be elaborated. Doing so, the NCRP of the Republic of Belarus confirms its devotion to international radiation protection principles as it proceeds from the fact that recognition of the republic's transition to the rehabilitation stage does not envisage grounded (optimized) public radiation protection measures to be loosened, nor to be abolished. This recognition highlights only a need in strengthening measures of a rehabilitation virtue which aim at the gradual, stage-by-stage restoration of full-scale economic activities in the affected territories (including excluded ones) and a people's return to a usual (pre-accidental) way of life;

- It is defined that main objectives of radiation protection are to further lower a probability of developing stochastic effects in this generation and ones to come. The aforementioned is to be achieved by the undeviating reduction of individual and collective doses of accidental radiation;

- The major criterion for decision-making and implementing protective measures as well as for defining their nature and scope is average annual effective dose (AED) received by inhabitants of a settlement;

- Implementation of radiation protection activities should be based upon the strict compliance with an "optimization principle", that is to say that one must not accept measures bringing more harm than benefit. Doing so, priority of implementing protective measures should, as a rule, be defined according to the "averted collective dose" criterion;

- To implement basic measures of radiation protection in practice, to define expediency, sequence, nature and scale of protective measures the Concept assumes the threefold gradation of settlements and their habitats according to the value of annual effective dose of accidental radiation. These are:

1. Settlements where AED does not exceed 1mSv. In these settlements and adjacent territories life and economic activities are not limited according to radiation factor. The above dose is proposed to be reckoned as an permissible one. In such territories we suggest conducting the radiation monitoring the environment,
foodstuffs and drinking water in order to assess radiation doses and to implement, if necessary, local protective measures based on the ALARA principle;

2. Settlements where AED falls into the range from 1 mSv to 5 mSv. Here and in adjacent territories grounded (optimized) radiation protection measures are carried out side by side with the monitoring the environment, agricultural production and drinking water.

3. Settlements where inhabitants can receive AED higher than 5 mSv. Here residence is not recommended, and economic activity is limited. It should be noted that defining this dose limit to be impermissible is not based upon modern theory and practice of radiobiology. It marks only a public protection level which has been actually achieved in the republic.

- The Concept suggests that while assessing a possible influence on the population’s health through accidental radiation doses one should obligatory take into consideration the danger extent of an impact on its indices rendered by a complex of various unfavourable factors;

- It is emphasized that it is important and necessary to draw more attention to conducting activities aimed at medical & biological rehabilitation of people residing in the contaminated territories. Doing so, the Concept foresees a possibility of continuing to implement such measures in settlements where a radiation dose does not exceed 1mSv as well. The set forth below are considered to be an important component of prophylaxis of negative medical & biological manifestations:
  - a high level of health care services;
  - a large-scale recuperation of the population;
  - a provision of high quality food products;
  - and other attributes forming a “healthy way of life” notion.

- The Concept focuses attention on a necessity of solving a number of scientific and practical problems which are bound up with rehabilitation of the contaminated territories and a gradual people’s return to excluded lands restoring full-scale activities there.
Panic speculations about the "terrible" consequences of the Chernobyl accident irreparable for many generations of mankind have not been the work of journalists alone, but mainly of medical people ignorant in the sphere of radiobiology and radiation medicine and submitting pseudoscientific data to the mass media. Even medical journals and special monographs sometimes published reports of this kind. Hence, an improvement in training physicians in radiation medicine becomes a priority task; specifically, objective scientific information should be made available for medical people. This function has been important goal of our Journal "Medical Radiology and Radiation Safety" during the decade that passed since the accident.

During this decade our Journal took a steady position to distinguish between the radiation consequences proper and the psychosomatic morbidity of an origin other than radiation, using data of the numerous studies of the leading radiation biologists as well as practical experience. Besides individual papers, the Journal organizes special discussions and publish annually three-four Supplements devoted mainly to the most interesting scientific conferences.

The report will give examples of the actual radiation consequences of the accident and present a critical analysis of the Chernobyl myths.
ANTIOXIDANT (UBIQUINONE-9) PROTECTION OF IMMUNE SYSTEM AND CNS UNDER CHRONIC LOW-DOSE IRRADIATION


Although many substances have been studied in order to reduce chronic radiation effects, many synthetic protectors used in acute radiation disease treatment cannot be utilized for a long period due to their high toxicity. In this aspect, in the present study we had used as a dietary supplement coenzyme Q-9, natural nontoxic antioxidant. The problem of action of chronic low level ionizing radiation on the functional state of immune and nervous systems is an actual problem nowadays, because there are many instances of ionizing radiation in our environment. The data from human epidemiology alone cannot provide the detailed dose-effect relationships. More adequate are the experiments performed with animals where it is possible to provide accurate dose rates and times of exposure as well as modifying agents for protection from ionizing radiation.

Methods. Rats were exposed for 3 months to chronic γ-rays (\(^{137}\)Cs) with 0.43 and 3.0 cGy/day dose rates. Cumulative doses were 11, 23 and 35 cGy (dose rate 0.43 cGy/day) and 50, 150 and 200 cGy (dose rate 3.0 cGy/day). Half of the exposed rats were given eight mg of ubiquinone Q-9 per kg of body weight per day with food. Spontaneous and Con A-stimulated \(^3\)H-thymidine in vitro incorporation in splenic T lymphocytes, T cell viability and animals behavior (exploratory activity and sensory attention to the different modality stimuli) were measured.

Results. The enhance rate of T cell spontaneous \(^3\)H-TdR incorporation was demonstrated after exposure with dose rate 0.43 cGy/day, but not 3.0 cGy/day. The increase of T cell proliferation was most pronounced after 23 and 35 cGy cumulative doses. In contrast, the Con A-induced T cell proliferation was decreased after treatment with both dose rates. Immunosuppression induced by chronic exposure with dose rates of 0.43 and 3.0 cGy/day had no functional correlation with significant loss of splenic lymphocyte number. We had demonstrated significant protective effect of ubiquinone treatment on proliferative responses of both stimulated and unstimulated lymphocytes. Radiation-induced disturbances of the exploratory activity and animal inattention, as well as suppression of immune function, were partially eliminated by ubiquinone diet.

Significance. The level of ubiquinone is altered considerably in connection with various physiological and pathophysiological conditions. It has been noticed that the oral administration of coenzyme Q in human improved exercise performance both in patients with ischemic heart disease and in normal individuals (Beyer R.E., et al., 1984; Folcers K., 1981, 1985). Bliznakov first reported about the role of CoQ-10 as an immunomodulating agent (Bliznakov at al., 1970, 1981). The data presented here suggest the radioprotective potency of ubiquinone.
Hyperthermia is currently broadly applied in oncology practice. High temperature causes tumor cytotoxicity and significantly sensitizes tumor cells to ionizing irradiation. Local tumor heating is accompanied by changes in microcirculation and metabolism, including increased lactate level and ATP hydrolysis, oxidative phosphorylation impairment (Kelleher D.K., et al., 1995). Mechanisms of heat toxicity were elucidated (Engin K., 1994). Hyperthermia in vivo was supposed to result in reoxygenation, that may be a reason for thermic radiosensitization (Oleson J.R., 1995). The mechanisms of blood oxygen transport are poorly studied, particularly a change of hemoglobin-oxygen affinity (HOA) which is the important determinant of adequate tissue oxygenation. Direct effects of temperature upon HOA in vitro are well-known (Colleta M., et al., 1992), but were not investigated during whole body hyperthermia (Uchingaski S., et al., 1995). Therefore the present work was designed to study the state of HOA and its main modulators under hyperthermia.

Experiments were performed on male rabbits (weight 2.5-3.2kg) with a rise of body temperature to 42°C and maintained at this level for 60 minutes. Blood sampling was performed from the right atrium cavity through the right external jugular vein at the end of the heat treatment and at one and four hours after it. HOA was assessed as p50 (oxygen pressure, corresponding to 50% hemoglobin saturation) by a "mixing" technique in modification (Scheid P., Meyer M., 1978). Bohr effect was determined by titration of blood sample with oxyhemoglobin saturation near 50% by 0.1 N HCl in 0.9% NaCl. Blood gas and acid-base balance parameters were measured by micro gas analyzer ABL-330 "Radiometer." 2,3-diphosphoglycerate (2,3-DPG) concentrations were determined by spectrophotometric method (Dyce B.J., Bessman S.P., 1973). Results obtained were treated by statistical methods of software package “Statgraphics” on PC.

Real oxyhemoglobin dissociation curve was shifted to right compared with baseline (p50 = 42.7 ±0.77, P < 0.01 vs. initial p50 = 39.1± 0.64 mm Hg). System of HOA regulation inside erythrocytes is relatively autonomic and largely provides an adaptive change of blood oxygen-binding properties. In this system 2,3-DPG has a function of allosteric glycolysis regulation triggering and is a device for coordination of metabolism with functional demands. This organic phosphate is known to exert essential influence on HOA. At the end of heating we observed the lowing of 2,3-DPG concentration from 6.31 ± 0.69 to 4.13 ± 0.69 mM (P< 0.01), which also remained significant during the next four hours. This is obviously due to lowing of pH and activation of 2,3-DPG phosphatase in red blood cell glycolysis (Chiba H. et al. 1977). Experimental investigation of Bohr effect had shown its enlargement from 0.446 ± 0.017 to 0.538 ± 0.01 ( P< 0.01) at the end of heating which remained significant during the next four hours. The oxyhemoglobin dissociation curve shifted up leftwards because lowered 2,3-DPG synthesis does not improve oxygen unloading to tissues. O2 delivery in such case is provided by rise of temperature and Bohr effect rather than by metabolic modification of hemoglobin properties in red cells. Further change of blood-carrying properties at normal temperature lowers its ability to deoxygenation and does not facilitate restoration of oxygen deficiency appearing during hyperthermia.

Therefore, HOA is substantially changed during hyperthermia and hence influences oxygen fluxes to tissues. HOA must be taken in to account for treatment of oncology diseases by hyperthermia.
RADIATION ACCELERATES THE TERMINAL DIFFERENTIATION OF SENESCENT HUMAN AND MOUSE FIBROBLASTS


Normal physiological cellular aging is the result of various processes, leading to the irreversible cessation of proliferative potential and eventual death. In many cell systems one of these processes is a terminal differentiation. Fibroblasts have served for more than three decades as a model of cellular senescence. Normal senescent (nontransformed) human and mouse fibroblasts differentiate along a 7-stage irreversible terminal sequence, that is accompanied by loss of the proliferative potential, changes in cellular form, DNA content and polypeptide pattern (Bayreuther et al., 1991). In this cell system three mitotic fibroblasts (MF) differentiate along a sequence MF I - MF II - MF III, and three postmitotic fibroblasts (PMF) proceed along a sequence PMF IV - PMF V - PMF VI. PMF VI is the terminally differentiated cell. After a period of metabolic activity, PMF VI either dies (PMF VIa) or transforms (PMF VIb), which shows the coupling between differentiation and cellular senescence, death and carcinogenesis. The goal of the present study was to investigate the influence of radiation on the rate of differentiation process in cell populations of human cultured fibroblasts (irradiation in vitro) and fibroblasts of mouse lung tissue (irradiation in vivo). Human fibroblasts cell cultures were established from the 8-12 weeks embryo by the cultivating cells in appropriate culture medium. Cell suspension in plastic tubes were irradiated with gamma-rays ($^{137}$Cs, 0.5 - 10.0 Gy) and seeded at a low density. In the experiments of the first type after 20 days of growing, clonal cultures were fixed and stained. The number of clones, colony size (number of cells in the clone, the largest clones consisted of about 40,000 cells) and the proportion of mitotic fibroblasts MF I (small spindleshaped cells) were counted in microscopic fields. In the experiments of the second type, cells were cultivated in the hermetically sealed glass vessels and after different periods of growth were analyzed with the aid of an inverted microscope. The numbers of mitotic and postmitotic fibroblasts of different cell types (according to Bayreuther's terminology) were calculated. Pregnant mice AFB (5-17 days of pregnancy) were irradiated ($^{137}$Cs, 0.1-2.0 Gy), lung tissue samples of 1-2 day 14-16 day old mice were washed, cut and type sized. Tissues were suspended in the Eagle medium, cell suspensions were filtered and seeded in the appropriate medium at the density of 1000 cells per cm$^2$ of glass cover slips in the hermetically closed bottles and maintained for 1 day. Thereafter, cells were fixed, stained, and the proportion of small spindle-shaped cells (MF I) was evaluated. It has been ascertained that radiation speeds up (in a dose-dependent manner) the process of terminal differentiation in cell populations of human fibroblasts. In clonal cultures the proportion of MF I (cells with the greatest proliferative potential) were decreased. All more or less large clones (consisting of hundreds of cells) have been grown from an initial cell of type I (MF I), because the terminal differentiation sequence has one direction and MF I is it's first step. The mean size of clones was decreased under the influence of radiation. Dynamic investigation of the living cell cultures with the aid of inverted microscope revealed that radiation accelerates the process of decreasing the proportion of the mitotic fibroblasts and increasing the proportion of the postmitotic fibroblasts in human cell population. Irradiation of mouse embryos decreased the proportion of MF I in the lung tissue of the new-born and 15-16 day old mice. These data demonstrate similar effects of radiation on the populations of cultured cells and cells of the organism. Decrease of the proportion of actively dividing cell types may reflect an important aspect of the radiation-induced acceleration of cellular aging and carcinogenesis.
LOW DOSE-RATE IONIZING RADIATION INDUCED DISORDERS OF K⁺-TRANSPORT MODULATION BY SEROTONIN IN NERVOUS TISSUE

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It is known that total low irradiation induces considerable disorder in nervous tissue functional activity, that is evidence of its substantial radiosensitivity. The earlier post-irradiation changes in the metabolic regulation systems seem to be a basis of such disturbances. For more complete understanding of phenomenological peculiarities of postirradiation CNS status and its molecular and cellular basis, it is necessary to consider the neurone functional systems taking into account their intimate interaction and interdependency. In this connection we studied the postirradiation effect of serotonin (5-HT) on membrane K⁺-transport in nervous tissue and serotonin receptor role in this process.

Male Wistar rats were irradiated with doses of 0.25 and 0.5 Gy acutely or chronically (0.01 Gy per day at the dose rate of 0.037 mGy/s). Animals were decapitated the day after irradiation was completed. Passive and active K⁺-transport processes were observed in rat brain cortex slices incubated in bicarbonate Krebs-Ringer buffer, pH 7.4, under anaerobic and aerobic conditions respectively. 5-HT (20-500 μM) and its antagonist - mianserin (MS, 50 μM), were added to the washed solution for anaerobic incubation. The Na,K-pump activity was estimated as the slice uptake ability to K⁺ from washed solution against the concentration gradient. K⁺ uptake was determined as a difference between K⁺ levels in the slices after anaerobic and aerobic incubation. K⁺ content in brain tissue was measured by method of atomic-absorption spectrophotometry.

Results showed that normally 5-HT stimulated active K⁺-transport by 55% compared to the control. The patterns of the Na,K-pump reaction to 5-HT was not changed after single X-ray exposure, but the activating effect of the mediator was reduced by 23.6% compared to control one. Under simultaneous appication of 5-HT and MS we have observed the addition of both agents’ effects, whereas normally MS had entirely abolished the 5-HT influence upon K⁺-transport. Chronic irradiation with investigated doses caused the essential modification of curves, describing the active and passive K⁺-transport parameters’ dependence on neurotransmitter concentration present in washed solution. The similar character of 5-HT influence in used concentration range upon transmembrane K⁺ transfer has been pointed for both doses. After 5-HT application under conditions of chronic exposure with a dose of 0.5 Gy, the increase of K⁺ level in nervous tissue to control values had been observed, although the intensity of its antigradient transport was significantly reduced. If, in that case, the MS or both agents were added to the incubation medium, the Na,K-pump activity was not changed due to the irradiation effect. Probably that is caused by the lack of 5-HT and MS binding with specific receptors of neuronal membrane.

It has been assumed that post-irradiation modification of the 5-HT regulative effect on the K⁺ homeostasis in brain cortex tissue was caused by membrane-tropic action of low doses irradiation, leading to damage to specific membrane receptors.
MOLECULAR LEVEL STUDY OF FUNCTIONAL DISORDERS IN CNS AFTER LOW DOSE IRRADIATION

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The health status studies (1993-1994) of patients, who took part in the clean up works at the Chernobyl NPP after the accident in 1986, showed that the both mental disorders and nervous system diseases were prevalent over others according to IDC-9. These could be a result of radiation-induced functional disturbances in nervous cells in the early terms after exposure, in particular disorders in the processes of interneuronal regulation. In this connection we investigated postirradiation changes in the receptor-mediated effects of acetylcholine (ACh) and gamma-aminobutyric acid (GABA) upon Na, K-pump in neuronal membranes, that expressed some aspect of the synaptic transduction modulation.

Wistar-rats were exposed to 0.25 Gy X-irradiation at a dose rate of 1.67 mGy/min by two methods: acutely and chronically (10 mGy/day). The Na,K-pump activity was evaluated as antigradient K⁺ uptake by brain cortex slices during 30 min incubation under the aerobic conditions. 5 min preincubation of slices with (10⁻¹⁰ - 10⁻⁵ M) ACh or GABA showed defined biphasic effects of both neuromediators upon Na, K-pump as normal, but 0.25 Gy irradiation modified them considerably.

There were different effects of single and chronic exposure to ionizing radiation upon the Na,K-pump function in nervous cells (respectively, activation by 32% and inhibition by 41%). However radiation modification of curves describing the concentration dependency of active K⁺ transport in slices from neuromediator presence in the incubation medium was obviously similar. So, both curves had maximal points in the higher concentrations ranges.

For detailed study of molecular pathways, the neuromediator modulation processes were evaluated through the specific antagonists (10⁻⁵ M) of cholino- and GABA-receptors (ChR, and GABA-R) exposed as follows: atropine to M-ChR, d-tubocurarine to N-ChR, bicuculline to GABA_A-R, 5-aminovaleric acid and phaclophen to GABA_B-R. Obtained data showed that in brain cortex slices from non-irradiated rats ACh and GABA-effects were mediated via relevant N-ChR and GABA_A-R, but after exposure to X-rays with dose of 0.25 Gy M-ChR and GABA_B-R were found to be involved in the neurotransmitter regulation processes. Replacing of the effective ionotropic receptors with metabotropic ones was more expressed in the case of chronic exposure. We supposed that this was connected with adaptive reaction of the nervous cells to the ionizing radiation influence, but essential changes in the metabolic modulation processes could lead to the neuronal activity disintegration.
Antimutagenic prevention and modulation of individual radiosensitivity with pharmaceutical preparations

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Four-month long prevention procedures were undertaken with 27 women workers from a shoe factory who were permanently exposed to the combined action of high concentrations of solvents (toluene, acetone, benzine) and Diizocyanates. 13 workers were given daily 2 tablets of the polyvitamin-polymineral containing a preparation of CENTRUM (Lederle, USA) + 1 tablet of RESPIVAX (Bulgaria) an immunostimulatory polybacterially preparation. The other 14 workers were at the same time treated with only CENTRUM + PLACEBO The antimutagenic effect and the individual radiosensitivity were estimated by the cytokinesis-block micronuclear method in peripheral lymphocytes. Individual radiosensitivity was determined in blood samples of the same persons (taken prior and following termination of prevention) "in vitro" irradiated with 1 Gy gamma rays of 137 Cs. The cytogenetic monitoring performed in the same groups of workers during the preceding 92/93 and 1994 years showed constant high micronuclei levels in lymphocytes. A group of 27 women from the administrative staff with an initial level of micronuclei 23.8±8.3% was used as control showing a 16.3±5.8% after prevention procedures. The initial incidence of micronuclei in the workers treated with Centrum + Respivax was 64.8±16.8%. Upon termination of prevention it was reduced to 31.6±8.6% and for the Centrum - Placebo treated group the decrease was from 68.1±24.7% to 40.4±11.8%. The mean micronuclei incidence values for a part of the "in vitro" irradiated blood samples with 1 Gy before starting the prevention were 160±25.5% for the Centrum + Respivax treated group and for the Centrum + Placebo treated group they were 160±40.1% After termination of prevention procedures incidence values are statistically significant in lowering to 75.3±17.6 % for the first group, and to 92.2±29.4% for the second group.

In 92 percent of the persons studied a strict correlation between the initial micronuclei incidence and that following termination of prevention has been established that has proven valid for the "in vitro" irradiated blood samples too.

The same picture is observed in the control group of individuals.

The results obtained give grounds for performing such a therapeutic-preventive treatment of occupationally irradiated persons as well as for a permanent treatment of irradiation accidents.
A MARKEDLY DIFFERENT APPROACH TO "RISK" ASSESSMENT

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If one has available a complete set of relevant data for any biologically effective agent, e.g., radiation energy, one can, by suitable choice of coordinates and by selecting values from the data set, construct at will either a threshold-sigmoid or a related and complementary linear function. This makes evident an internal contradiction that renders invalid the "no threshold" interpretation of the linear function, i.e., the same agent cannot at once show a classical and time-honored threshold, and yet be so incredibly toxic that "any amount, however small can be harmful and even lethal". Thus, the "no-threshold" interpretation of linear functions, key to the "linear, no-threshold" hypothesis (LNH) is false. A complete data set must provide absolute values and not just ratios for the response (ordinate), and for the physical insult (abscissa). Also needed is the mass of each subject, from which the imparted energy to subjects, groups, and populations can be calculated. The absolute number responding can then be plotted against the cumulative imparted energy to a population, to yield the only proper linear function. Essentially all of both types of function are obtained with photon radiations, i.e., the reasons for this linearity and for that observed with clearly particulate radiations such as alpha particles or highly-accelerated, stripped carbon or heavier ions are quite different. The concept of "quality" here means effectiveness as registered by the responding subject. If the mass in a system is held constant, and only the energy concentration is permitted to vary (and response and agent amount are measured at the same level of biological organization), then, unfailingly, a threshold-sigmoid function that reflects only the response as a function of quality is obtained. Conversely, if the quality is held constant at any given level of response, e.g., 0.7, then all that can vary is the mass and thus the amount of agent, in the form of either the number dosed or the equivalent in imparted energy. The inevitable result is a linear function which must terminate at one responding subject because no fewer than one subject can die from any cause. Quite relevant are the solid cancer data from the atomic bomb survivors because a linear response is observed when the proper additive independent variable, imparted energy in the system, is used. From the slope of this function, on average, about 3 kJ of energy are needed to produce one cancer, with much more required actually to observe one. This is incompatible with the LNH. The threshold-sigmoid curve originated in and is used correctly only in the context of Medicine and Toxicology (MT). The linear functions are observed only in the context of branches of Public Health (PH), and are inapplicable in MT. Thus, as expected, the two have distinctly different coordinates, which leads to the no threshold-abolishing internal consistency shown above. Some conclusions are: 1) Imparted energy is the only agent-containing quantity that can be used correctly with linear functions, 2) Neither agent concentration nor "person Gy" is an acceptable alternative, 3) The correct total number of cancers can be obtained only if the abscissa of the linear function is imparted energy, 4) Substituting the correct quantity for the present incorrect quantity used for expression of the "amount" of radiation energy reduces the "risk" coefficient by a factor of about 70, and 5) The LNH is false and must be abandoned as the keystone of radiation protection policy.

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MODERN RADIATION POLICY: PREVENTION, MONITORING AND COMPENSATION

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The main component affecting radiation policy is the risk perception of the public. While people are usually more ready to accept a common environmental toxic materials (e.g. smoking), radiation is considered a creeping silent enemy. Consequently, decision making processes with regard to use and development of nuclear energy are strongly influenced by the magnitude of the benefit/hazard ratio. Results of recent studies and several conjectures implicating low dose radiation in carcinogenesis impede the development of nuclear industry, and have led to an increasing numbers of personal and class litigations. Yet, compensation of affected individuals is not infrequently limited by a wrong interpretation of the term “probability of causation.” Two case studies of large essentially healthy people exposed to radiation in therapeutic and industrial settings are discussed in the light of current legislation. Distinction is made between voluntary and involuntary exposure, as well as the level of awareness of delayed radiation sequelae.
THE PROBABILITY OF CAUSATION AS BASIS FOR RADIATION WORKERS

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The carcinogenic risks of exposure to ionizing radiation as assessed by the ICRP (ICRP 60, 1991) and the BEIR committee are reviewed.

The concepts and quantitative parameters related to the assessment of the Probability Of Causation are introduced and discussed (the POC is defined as the chance that a specific malignant disease, diagnosed in a worker at a specific age following a specific history of occupational exposure to ionizing radiation was caused by his exposures and it is not a part of the age specific "natural" cancer morbidity).

The practical application of the quantitative values of the excess relative risk caused by exposure to ionizing radiation as assessed by the BEIR committee as a basis for a compensation scheme for radiation workers who became ill with cancer is discussed. Some actual cases of POC calculations are presented.
WHO RADIATION EMERGENCY MEDICAL PREPAREDNESS AND ASSISTANCE NETWORK (REMPAN)

G. Souchkevitch, World Health Organization

For the promotion of radiation emergency medical preparedness and for practical assistance and advice to countries in case of overexposure from any source of radiation, WHO has established 9 Collaborating Centres: in France (International Centre for Radiopathology, Paris), in the USA (Centre for Radiation Emergency Assistance, Oak Ridge), in Russia (Centre for Medical Radiation Pathology, St. Petersburg), in Australia (Centre for Radiation Protection and Radiation Emergency Medical Assistance, Melbourne), in Argentina (Centre for the Response to Ionizing Radiation Emergencies, Buenos Aires), in Brazil (Centre for Radiation Protection and Medical Preparedness for Radiation Accidents, Rio de Janeiro), in Germany (Centre for Radiation Emergency Medical Preparedness and Assistance, Ulm) in the United Kingdom (National Radiological Protection Board, Didcot) and in Japan (Centre for Radiation Effects on Humans, Hiroshima).

The centres serve as focal points for advice, training and possible medical care of radiation injuries; assist in the establishment of medical emergency plans for large-scale radiation accidents; initiate coordinated studies on human radiopathology and radiation epidemiology; and assist in the preparation of relevant documents, guidelines and meetings.

In the case of a radiation accident, the Collaborating Centres will provide a team for on-site emergency treatment; a survey team for rapid external radiation monitoring and/or contamination surveys with appropriate equipment; transportation of patients; facilities and staff for medical investigation and treatment; follow-up medical supervision and treatment.
The results of studies of health effects of the Chernobyl accident are in general terms consistent with previous findings on the impact of radiation on health status. Predictions made on the basis of knowledge of conditions soon after the accident indicated the real possibility of an increase in thyroid cancer cases. However, further findings, peculiar to this radiation catastrophe, have been obtained in ongoing studies of health effects resulting from the Chernobyl accident. In particular, the development of childhood thyroid cancer occurs during earlier periods after the accident and the number of observed cases is greater than had been suggested. By now 124 thyroid cancer cases have been detected in children and adolescents living in the most contaminated territories of Bryansk, Kaluga, Oriol and Tula regions. In the cohort of liquidators of 1986-87, twofold statistically significant increases in leukemia cases and a great increase in the number off thyroid cancer cases among liquidators of May and June 1986 have been noted. These new findings should be the subject of further collaborative studies on radiation effects.

The Chernobyl catastrophe, in contrast to other radiation events, has for the first time afforded the opportunity to study the effects of low and middle doses of ionizing radiation on huge cohorts. Studies on retrospective estimation and reconstruction of individual radiation doses to the thyroid and to the whole body, for liquidators and for people living in the contaminated areas have been performed.

An important lesson of the Chernobyl accident is recognition of the great importance of the psychological and social impacts of the radiation accident on the development of health disorders in the affected population as well as in the liquidator group.

The experience gained from the Chernobyl accident has pointed out the necessity of improving the techniques used for the prevention of thyroid cancer development using iodine, including the establishment of an effective system for treatment and rehabilitation of affected persons. The system of medical preparedness for radiation accidents should also be improved at both national and international levels.
ESTABLISHMENT OF ANSI N13.11 X-RAY RADIATION FIELDS FOR PERSONAL DOSIMETRY PERFORMANCE TEST BY COMPUTATION AND EXPERIMENT

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In the autumn of 1995 the Ministry of Science and Technology (MOST) was performed personal dosimetry performance test, which is based on the ANSI N13.11 Standard (1993), to the all of suppliers of dosimetry services for personnel potentially exposed to ionizing radiation. The test irradiation was conducted in Korea Atomic Energy Research Institute (KAERI) because KAERI is a National Secondary Standard Calibration Laboratory. So KAERI has finished to set up the ANSI N13.11 X-ray radiation fields just before the performance test started.

This paper describes the establishment of ANSI N13.11 X-ray filtered radiations by computation which was modified the Kramer's theory with target attenuation and backscatter correction and by experiment which was measured the spectral distributions with a HPGe semiconductor detector. Corrections for measured pulse height distributions were made with photopeak efficiency, compton fraction and K-escape fraction.

The average energies and conversion coefficients were calculated from the above computational and experimental X-ray pulse height distributions and compared with the ANSI N13.11 and the recent published NIST X-ray beams (1995), and a good agreement was achieved within 3% between the corresponding values.
ORGANIZATION AND FUNCTION OF AN AMBULATORY CARE FACILITY IN NETANYA, ISRAEL SERVING IMMIGRANTS FROM THE CHERNOBYL AREA: INITIAL CLINICAL IMPLICATIONS

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Aim: Since the Chernobyl disaster some 15,000 immigrants from affected areas of Belarus, Ukraine and Russia have settled in the city of Netanya. Precise information about the current health status of immigrants and health risk assessment of their potential history of radiation exposure is lacking.

Methods: In order to provide a dedicated clinical facility where health issues specifically related to this population can be dealt with, a facility was established in 1995 at Sanz Medical Center-Laniado Hospital. A potential patient is referred to the clinic by The Netanya Municipality Information Center. Logistic support is provided by the regional office of the Ministry of Health.

In addition, a study has been initiated, within the clinical facility, to evaluate the incidence of hematological malignant diseases among immigrants. This was done initially by reviewing the records of all patients examined by the hospital’s hematologist during 1993-1996 and by comparing with expected incidence rates in the local population.

Results: During the first 6 months of operation, preliminary data have been obtained among 100 self-referred patients, forty-three percent of whom were children. More than half had arrived in Israel between 1990-1992. Main countries of origin were Ukraine (58%) and Belarus (24%). Diagnoses of malignant diseases consisted of 14 tumors of various localisations, including colon, ventricle, rectum, liver, larynx, brain, breast, uterus, and thyroid; in addition, melanoma and skin lymphoma were found in two patients.

Thyroid pathology (multinodular goiter, hyperplasia and hypoplasia) was present in 15 patients. With regard to hematological neoplastic diseases, 23 patients had a diagnosis of various types of leukemia. These immigrants constituted 76% of all patients that had been examined in the city by the same hematologist and had been given a diagnosis of leukemia.

Conclusion: Initial clinical impressions indicate a high frequency of tumors in immigrant patients from the Chernobyl area, particularly in organs known to be targets for radiation exposure. These observations require epidemiological confirmation. In one instance, the diagnosis of leukemia was made at the dedicated clinic following several visits by the patient to various health care facilities where attention was not focused on possible radiation induced injury. Moreover, there is a need for a system of permanent medical management of immigrants from high-risk radiation areas such as cancer screening for adults, and a program with attention to the thyroid gland for children. Given the long latency period for induction of diseases caused by radiation, continuous surveillance is essential.
CHRONIC LYMPHATIC LEUKEMIA (CLL) IMMUNOPHENOTYPING IN SURVIVORS OF THE CHERNOBYL NUCLEAR REACTOR ACCIDENT - INITIAL OBSERVATIONS

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CLL is characterized by progressive accumulation of mature B lymphocytes with phenotypic markers including low-surface density monoclonal immunoglobulins mainly of IgM type, the CD 20 marker, and the pan-T-cell marker CD 5. In a study of patients, who were potentially exposed to radiation from the Chernobyl region, 14 were diagnosed with CLL. Seven CLL patients with B cell surface markers were thoroughly studied and compared with markers from 41 native CLL patients, who had been examined at the same medical facility. The results are shown in the table.

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<th>B cell surface antigens among survivors from the Chernobyl nuclear reactor accident and comparsion subjects.</th>
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<td>POPULATION</td>
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The major difference between the groups was that among the Chernobyl survivors, IgG appeared as the dominant immunoglobulin instead of IgM. In 3 of the 7 patients from this group, secondary malignancies including carcinomas of the stomach, colon and prostate, were the most prominent clinical manifestations. None in the comparison group had a secondary neoplasm. Although the significance of the observed elevated B cell IgG surface immunoglobulins is not readily apparent, and while there is no evident connection between these markers and secondary malignancies, special attention should be paid to this latter finding. The fact that the patients with these characteristics had resided in the Chernobyl region at the time of the disaster should also be considered.
SIMILARITY OF EFFECTS INDUCED BY ELF AMPLITUDE MODULATED RF FIELDS AND ELF MAGNETIC FIELDS ON PHB IN VITRO

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Aim: This work intends to confirm and to extend the results obtained by Leyle D.B. (Bioelectromagnetics, 4, 1983), concerning the suppression of T-Lymphocyte cytotoxicity following exposure to amplitude modulate RF fields, in the context of a low level but long term exposure of people residing in the neighborhood of a TV broadcasting station, and to observe possible similar results, following PHB exposure to ELF in vitro.

Method: PHB samples taken from 40 health people, living in the vicinity of a broadcasting station in Conversano, Italy, were employed in cell proliferation tests, induced after 72 hours stimulation by PHA ConA, PWM. In addition to this, cytotoxicity tests, NK or ADCC mediate tests were performed, over a period of 4 hours. Portions of PHB samples were re-irradiated in vitro by RF (639.25 MHz, 12V/m average, 50 Hz amplitude modulated, 50% duty cycle) while other portions were re-irradiated in vitro by ELF (50 Hz, 6.7 Gauss). All irradiation were performed at 37° C, in a CO₂ (5%) atmosphere, 98% relative humidity. Control samples were provided by volunteers of the University of L’Aquila, and were processed with the same tests at the same time (June 1995).

Results: The samples from Conversano showed a statistically significant lower stimulation (70%) induced by PWM. Moreover, significant (p < 0.5) increased stimulation induced by ConA was observed, in comparison with controls, following exposure to ELF. RF re-irradiation did not induce statistically significant effect during proliferation tests. Cytotoxicity tests showed a significant (p <0.001) reduced NK-activity of samples from Conversano in comparison with controls, when the cells were exposed to RF (up to 30%) and to ELF (up to 70%). The same effect was observed during ADCC-cytotoxicity test of cells exposed to RF.

Conclusion: The tests showed similarity of effects induced by ELF amplitude modulated RF and by ELF magnetic fields on PHB in vitro.
Cancer in fifty-four nuclear workers: Preliminary findings

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We constructed job-exposure profiles and assessed quality of health care in 54 current and ex-workers from a nuclear installation in the Negev who referred themselves to us for assessment of the possible work-relatedness of their tumors. The workers, mostly male, (avg age: 49.3; range 39-69) began employment at varying times from onset of the reactor's construction, and were engaged in varying tasks in laboratory research, construction, maintenance and services. It was possible to provide a partial picture of past exposures to radiation and chemical agents from interviews, chart reviews, Geiger and dosimeter records and radionuclide examinations. Most of the workers reported up to three job settings during their employment, and described a trend toward progress in exposure control, personal protection, information delivery and medical surveillance, especially in the mid-80's, although there appeared to less than full understanding of the risks for cancer from low exposures to radiation and the zero-threshold principle. In 26 of the 54 workers, latency between onset of exposure and first appearance of illness from tumor was 24.6 y (r 9-31). In the 54 workers, the tumor distribution was: gastrointestinal, 14; pulmonary, 10 (5 known smokers); brain, 3; bone, 2; skin, 3; renal-urinary, 7, hematolymphatic, 5; breast, 2 (one male); unspecified, 8. Many of the patients first became clinically ill after 1989, the last year of follow-up for tumor risk of a previously reported study. Interviews and clinical records indicated that patients found by their own doctors to have gross hematuria and diagnosed as having urogenital cancer shortly after being told that their urine assays were negative for microscopic hematuria. The findings suggest the need for external quality control of the internal surveillance of nuclear workers and improvements in information delivery.
The principle of boron neutron capture therapy (BNCT) is the nuclear reaction that takes place upon capture of low energy 'thermal' neutron (0.025 ev) by a stable isotope boron-10 to yield high energy helium nuclei (α particles) and recoiling lithium-7 nuclei according to the reaction:

\[
^{10}\text{B} + n, h \rightarrow ^{11}\text{B} \rightarrow ^{7}\text{Li} (0.87 \text{ Mev}) + ^{4}\text{He} (1.52 \text{ Mev}) + \gamma (478\text{Kev})
\]

BNCT is based on the proposition that mainly 10B is activated following neutron irradiation, so that only cells which are specifically boronated will be destroyed but the non-boronated cells or tissues near the boronated cells will be much less affected. Hence the problem is to achieve the binding of sufficiently large number of boron atoms per cell in order to reach the required concentration for BNCT. Theoretical calculation of neutron capture by boronated cells have determined that about 10^9 boron atoms are needed per target cell in order to support an effective BNCT reaction. We are therefore working on developing new methods to bring high amounts of boron atoms to cells. Two directions have been pioneered in our laboratory:

1. The uptake of certain porphyrins by cancer cells suggests the possibility of a method which could bring boron in large quantities into cells using boronated porphyrins. We have developed a method for radiolabeling of boronated porphyrin (BOPP) with indium-111. By this method it is shown that stable radioactive In-BOPP complexes can be prepared and isolated.

2. The binding of boronated polylysine to antibodies which can be used for the radiolabeling cells, thus rendering them sensitive to thermal neutrons. Our objective has been to attach boronated polylysine (BPL) to a polyclonal antibody with specific affinity to a 'sandwiched' monoclonal antibody, bound in turn to a specific cell surface antigen. To reduce interference with antibody binding sites BPL was bound to oligosaccharide moieties on IgG at some distance from the antibody combining sites. The immunoreactivity of the BPL-IgG complex was measured by two methods, the first being a modified luminescence procedure, and the second a modified double antibody IRMA procedure for serum TSH. The results obtained showed that binding affinity to antigen remained unaffected by attached BPL. The total measured boron per BPL bound IgG molecule was greater than 10^3 atoms.
Prompted by the increasing awareness to potential radiation hazards caused by hospitalized patients, who have undergone diagnostic nuclear medicine procedures, we decided to carry out a pilot study in selected non-radioactive wards of the medical center.

The aim of the project was to monitor the personnel radiation doses to the staff (medical and paramedical) for 3 months, and to measure the dose distribution around the patients' beds for the commonly used radioisotopes, in order to estimate the dose to other patient in the room, and to visitors. According to the number of patients referred to several departments, 3 wards were selected: Internal medicine C, internal medicine E, children A. The staff members for each category (doctors, nurses and paramedics) were selected according to the maximum time they spend with the patients. Thirty personnel monitoring badges were distributed between these 3 categories, for a period of 3 month. Questionnaires were distributed after this period, to try to establish some trends like: full use of the badge during the whole 3 months, if other radioactive procedures like portable x-ray films were applied, etc. From dose-rate and integral dose measurements around the patients' beds, normalized isodose lines were drawn for Tc-99m, Ga-67, Tl-201 and I-131 (mR/mCi), for different distances from the patient. The maximum dose to the staff was 30 mRem in a 3 month period. Complete results on the doses received by other patients in the room and by visitors will be presented.
THE INFLUENCE OF EXPOSURE TO LOW DOSES RADIATION ON SOME INDICES OF LYMPHOCYTE GENOME OF THE SELF-SETTLERS IN THE CHERNOBYL NPP ALIENATION ZONE.


For January 1, 1996 in 30 km zone of alienation Chernobyl NPP 600 persons live who have independently returned to native villages in some months after their evacuation on May 4, 1986.

It was represented expedient to investigate some genome indices of the people who are living about 10 years in the conditions of extended exposure to low doses radiation. The inhabitants of the five villages of a zone at the age of 24 to 60 were examined. The residents of Kiev of the same ages were the group for comparison. It was investigated the DNA contents (DNA index), frequency and distribution of micronuclei in lymphocytes of the peripheral blood.

Flow cytometry analysis of the DNA content in lymphocytes of the self-settlers of the alienation zone has shown availability total cell population with coefficient variation of the G1 peak about 3%. Deviation from the DNA diploid content was not found in the examined individuals.

The micronuclei analysis in lymphocytes of self-settlers was founded the valid increase of an average index of total content of micronuclei in 1000 binuclear cells (14.0±0.8) in comparison with the residents of Kiev (10.8±0.8). The cells, containing two micronuclei were founded in 19% of examined self-settlers. The distinctions in frequency of micronuclei were detected in self-settlers living on the territories with different level of radionuclide contamination. According to the data of the contamination with 137Cs and 90 Sr the territories, the doses of irradiation on the whole body and the red bone marrow of self-settlers were calculated for 9.5 years of their inhabitation. The changes of doses in period 1986-1995 is submitted. It is shown that the main doses on the whole body were obtained during the first year of the accident. The doses on the red bone marrow decrease slowly and in 1995 were 30-45% at different areas in comparison with the doses of 1986. Valid mutational effect in lymphocytes of self-settlers blood was founded from doses 152mSv on the whole body (external and internal totally) and 89mSv on the red bone marrow. The correlation analysis between the frequency of micronuclei in self-settlers lymphocytes and the level of radionuclides contaminated territories of their inhabitancy the more high level of correlation with 90Sr contamination was founded (coefficient of correlation for 90Sr =0.62 and 137Cs=0.51; p=0.99).
Radioiodines I-125 and I-131 are extremely volatile even in the form of the relatively stable iodine anion. This property renders frequent airborne contamination and sometimes accidental inhalation of the radioiodine by personnel heavily involved with its handling.

In order to detect radioiodine contamination as early as possible, the laboratory and its surroundings are constantly air monitored, surfaces are monitored according to a predetermined regime and personnel is being checked upon completion of a job or upon leaving the laboratory.

Follow-up, routine or in special occasions, is performed by health-physics personnel who reports to the radiation medicine department.

We report here the measures and means used to monitor a case of an accidental inhalation of I-125 due to an externally contaminated NaI[I-125] commercial package.

The contamination was found using a hand held detector (thin NaI (TI) crystal) with Minimum Detectable Activity (MDA) of 2.7 Bq for one minute count. Accurate quantitative measurements were performed using a Phoswich Detector calibrated with a Phantom and placed in a shielded room.

During the first two weeks, 5 urine analyses were performed. The curve of the dose of I-125 in the thyroid as detected by the Phoswich detector coincides with the expected decay for I-125 in the thyroid. The semi-quantitative measurements taken by the hand held detector show lower activity.

The calculated internal Dose was as follows:

<table>
<thead>
<tr>
<th></th>
<th>Dose (SV)</th>
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<tbody>
<tr>
<td>CEDE</td>
<td>4.7x10⁻³</td>
</tr>
<tr>
<td>CDE to thyroid*</td>
<td>0.15</td>
</tr>
<tr>
<td>Internal Intake Activity**</td>
<td>777kBq</td>
</tr>
</tbody>
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*CDE = Committed Dose Equivalent
** Calculated to the day of exposure

The results of the urine analyses were scattered and differed from the predicted decay pattern. The values obtained for internal exposure were lower than those described above.

The contamination was discovered too late for KI treatment. The absorbed dose was lower than the Annual Limit of Intake (ALI) for I-125, which is 2mbq (27 μCi), therefore no special steps were taken. However, TSH and T3 were measured 6 months later, for thyroid function determination, and found normal.
COMPARATIVE ANALYSIS OF PROCEDURAL ARRANGEMENTS: HEALTH EFFECTS OF RADIATION

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Recently, a procedural agreement has been reached regarding the evaluation of probability of causation in lawsuits of 15 radiation workers in a nuclear research center. These arrangements could apply also to similar lawsuits.

The purpose of this paper is to overview existing legal arrangements in several countries, including England, Germany, the United States, and Israel, concerning the determination of health effects caused to workers from their exposure to radiation and their compensation.

The paper will describe the British Compensation Scheme which was conceived and developed by BNFL (which operates several licensed nuclear sites in the UK) and its recognized trade unions. Thereafter this paper will focus on the legislation in England: the "Workers Compensation Act."

Further on, the German Occupational Disease Decree of 1968 and the German Workers Compensation Law will be described.

This paper will further focus on the procedural arrangement in the United States as reached in the case of David Day v. NLO (the Fernald Case).

Finally, the Israeli arrangement which was recently concluded will describe the establishment of a panel (which will include two physicians and a third expert in the filed of radiation of in the field of hazardous substances) the method of determining the probability of causation of suffering cancer due to the plaintiff's exposure to radiation, and the legal status of the panel's findings.

The paper will show that there is a need, in addition to the legislation in the field of protection from the harmful effects of ionizing radiation, for a voluntary procedural arrangement which enables both the worker and the employer to faster and easier methods of determining the probability of causation concerning occupational diseases of radiation workers.
DNA REPAIR AND CELL CYCLE IN UV-IRRADIATED MOUSE FIBROBLAST AND NEUROBLASTOMA CELLS

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There is much current interest in the relationship between cell cycle check points, UV sensitivity and DNA repair in UV-irradiated eukariotic cells. Exposure to UV light causes the formation mainly of cyclobutane pyrimidine dimers (PD) in cellular DNA that results in mutagenic, carcinogenic and lethal response in a variety of organisms. During DNA replication on a template with nonexcized UV-induced photoproducts, PD including, premutation and potential carcinogenic DNA alterations may appear. Eukaryotic cells with nonexcized PD can synthesize error-free DNA (without gaps) after a prolonged postirradiation period.

Our aim was to study DNA repair on a cellular level (cell survival and mitotic cycle recovery) and that on a molecular one (postreplication repair, PRR, and postreplication bypass of lesions) in UV-irradiated cells in mouse fibroblasts L929 and neuroblastoma N-2a. Flow cytometry and sucrose gradient techniques have been used.

In L929 cells resistance to UV light correlates with free DNA synthesis, with a slight delay in S phase and no G1 delay during progress of irradiated cells through the mitotic cycle. In differentiated N-2a cells, also resistant to UV light by a cell survival, a deficiency in a free by-pass of lesions correlates with a more effective PRR of DNA, with a G1 phase delay and a more prolonged delay in S phase. One can assume operating of some intrinsic mechanisms, proper to N-2a cells, during cell transit through the cycle and DNA repair which compensate deviations in opposite directions of N-2a cells from L929 ones, thus resulting in one and the same cell killing.

The results obtained point to a positive correlation between an alteration of S phase and a cell ability to synthesize error-free DNA on a damaged template some time after UV irradiation. These data do not seem occasional since they may result in possible premutation and potential carcinogenic DNA alterations which may appear after exposure to UV light in the living N-2a cells during the DNA replication on a damaged template.
CHEMICALS AND THE PHENOMENON OF PSEUDOMUTAGENESIS

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The prognosis of mutagenic and carcinogenic action of environmental factors is based on linear extrapolation of dose-effect curves and on the assumption of additivity of effects. However, the data is available on anomalous effects at low radiation doses, on cases of considerable synergism or antagonism between certain mutagens, on existence of chemicals with strongly nonlinear concentration-effect dependence. Our aim is to draw attention to some of these questions.

We have studied cytogenetic effect of the cell metabolic inhibitors using seedlings of Crepis capillaris and human lymphocytes as test systems. Large number of inhibitors and vast experimental material allowed us to notice very specific regularities which appeared to be general for all the chemicals tested. These results can be explained based on the assumption that all the used chemicals increased aberration frequency as compared to control level by inhibition of repair of spontaneous genetic lesions. Therefore the observed chromosome mutations merely represent unrepaired spontaneous injuries. Such chemicals or factors were called by N.V. Luchnik (1978) "pseudomutagens" because they do not produce clastogenic effect, but enhance aberration level. All the chemicals tested (aminopterin, 5-Fluorodeoxyuridine, hydroxyurea, thymidine, caffeine, cycloheximid, actinomycin D, I - β - D - arabinofuranosylcytosine, aphidicolin) revealed the following specific regularities: a) increase of aberration frequency above control level; b) independence of the induced mutation frequency with dose (concentration) of the inhibitors in a rather wide concentration range; c) similarity of the induced aberration "spectrum" to the "spectrum" of spontaneous aberrations, d) independence of aberration quantity and quality on the cell cycle stage; e) the same effect of different chemicals on the same organism; f) the absence of additivity between two such factors applied for combined treatment; g) combined treatment with "true" mutagens may produce synergistic effect because pseudomutagens inhibit not only the repair of spontaneous lesions but also that of radiation induced damage. It is evident that a number of chemicals regarded at present as weak mutagens are in fact pseudomutagens. This phenomenon should be considered in estimation of damaging effects of environmental pollutants because of the possibility of potentiating of effect of true mutagens by pseudomutagens.
A SCIENTIFIC PANEL FOR DETERMINING HEALTH EFFECTS OF RADIATION WORKERS AT ISRAEL'S NUCLEAR POWER RESEARCH FACILITIES

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It is unknown how many workers have been employed at the two nuclear research facilities in Israel, one in Yavneh and the other near Dimona. It is known, however, that close to 100 past and present employees have developed different types of cancer. These workers came to me to file suit against their employer for exposing them to radiation and other dangerous substances as a cause for cancer. My understanding of the legal system led me to suggest that instead of a typical court proceeding, there be a proceeding not yet tested in the courts in Israel, and possibly not anywhere else in the world. The following is a brief explanation of the creation of that system.

A major problem in determining causation effects of workers exposed to dangerous substances is proving the types and level of exposure to named dangerous substances, in order to determine cause and effect. Once information has been received or obtained from an employer, it is fairly easy to get scientific evidence concerning the potential health or environmental effects of that substance on a person or ecosystem. The problem in the nuclear research facilities in Israel is that information on any aspect of a worker's job routine, including exposure to dangerous substances, is a state secret. The information is not given out by the employer, and the employee is sworn to secrecy and is unable to tell even his attorney the extent and type of exposure and the name of the substance to which he was exposed.

It was, therefore, incumbent upon me to file a request to the courts for information to be obtained from the nuclear research facilities. A case was filed in the District Court of Jerusalem against Israel's Atomic Energy Commission demanding that the Commission submit information and data concerning worker exposure at the nuclear research facility. After several months of debate, the Atomic Energy Commission agreed that if the employer filed an individual case in court, they would agree to naming a scientific expert with security clearance who could review all data and make a submission of evidence to the court or other bodies.

In addition, it was agreed that a case could be filed without attaching a medical opinion, which is always necessary in these cases, but unable to be filed in this case because no information had been supplied. Of course, at the same time, there would be no need to file defense papers because a medical opinion had not been filed.

Based on this agreement which was given the effect of a court decision, the parties met over a period of a year and worked out the creation of a scientific panel with security clearance who could review worker data from the nuclear research facilities and determine a causation effect between exposure and cancer.

Only recently were the parties able to agree on a framework whereby the scientific panels have been created in the following manner:

- Each side chooses a physician who has some knowledge in the field of radiation and its effects on humans.
- The two physicians then choose a third person chosen from a list drafted by the two parties, that person being an expert either in radiation or other dangerous substances.
- The panel is to receive written materials from the parties prior to their deliberation.
- The panel is entitled to interrogate and question a worker and even enter the nuclear research facility, if necessary, and after proper security clearance.
• The panel will then make a determination if the cancer from which the patient suffers or has suffered (in the case of a claimant who is not alive) is connected to his exposure to radiation or any other dangerous substance at the nuclear research facility.
• Once this determination has been made, a claim will then be processed for compensation.
• If the panel determines there is no connection, a claim for compensation will not be filed.
• At the same time, it was agreed that each worker would file a claim for national insurance with the National Insurance Institution of Israel. This would insure that if the worker is found to have a claim for exposure to dangerous substances at work, he or his widow will be compensated by National Insurance.

This system was designed to work in a situation where security matters are of utmost importance where workers have been exposed to dangerous substances. The genius of the system is the following: It enables information to be supplied to an objective scientific panel with security clearance to make the hard decision about causation; it reduces the number of cases in court; it reduces the time that cases have to be filed and processed; it enables a single panel to review numerous cases, in this particular situation, over 100 cases, hopefully in a shorter period of time than it would take for the court to review the same number of cases. At the same time, it keeps the question out of the courts and, therefore, away from the tremendous exposure that these kinds of cases would have in the local press and communications media. This is also an important issue for the Atomic Energy Commission.
USE OF ANTIOXIDANTS FOR PROPHYLAXIS OF UNFAVORABLE CONSEQUENCES OF RADIATION AND STRESS EFFECTS


Antioxidants (B-carotene, vitamins E and C, selenium) neutralize toxic influence of free radical products of lipid peroxidation. We tested, in experimental and clinical studies, the ability of preparations containing water-dispersed forms of B-carotene and vitamins E and C to reduce consequences of radiation and stress effects on organism.

Exposure of white mice (genetically type Swiss, males, weight 18-22 gr.) to doses of 50 or 10-0 rad, as well as stress action (holding under conditions of limited mobility without food and water during 24 hours), resulted in decrease of weight, number of cells in thymus and in chromatin degradation. Introduction of the preparations Lecar (3% B-carotene and 3% vitamin C) or Vetoron (2% B-carotene, 0.67% vitamin C, 0.67% vitamin E) into the food reduced the lympholytic effects of radiation and stress. Preliminary use of Vetoron-enriched food (31 mg of B-carotene per 100 gr. of the food) during one week provided 50% protection of mouse thymus against destruction. It was shown that the enrichment of the ration with the preparations Vetoron and Lecar decreased radiation-induced chromatin degradation in thymocytes and increased the effectiveness of DNA repair in the spleen.

Vetoron was used for the treatment of victims of the Chernobyl NPP accident who had cardio-vascular, gastric intestinal diseases and inflammatory processes in their lungs. The patients received the preparation for 14 days, in the dose of 40 mg of B-carotene per day. As a result of receiving Vetoron the concentration of B-carotene in blood plasma of the patients increased by the factor 3.9 (from 83±16 to 320±24 ug/100 ml), showing a good acquisition of the preparation. B-Carotene is an antioxidant able to protect the organism against the action of toxic products of lipid peroxidation. The increase of the B-carotene concentration in blood plasma of malonic acid dialdehyde which reflects the formation of lipid peroxidation products. The biochemical study showed that 85% of the patients revealed the reduction of the concentration of malonic acid dialdehyde in blood plasma by 18%.

The inclusion of Vetoron in the complex of therapeutic procedures increased their effectiveness and improved the condition of the patients. The symptoms of physical disability were reduced, dizziness disappeared, sleep and appetite improved. Normalization of the blood pattern was noted and characteristics of the state the of cardio-vascular system and breathing. Liver function (enzyme probes) showed a distinct improvement.

The obtained results allow us to conclude that the use of antioxidants (B-carotene, vitamins C and E) can be recommended for reduction of consequences of radiation and stress action on the organism.
EFFECTS OF γ-LINOLENIC ACID ON THE DRUG METABOLIZING LIVER FUNCTION AFTER γ-IRRADIATION


We studied the therapeutic effects of Boragoglandin 100 containing γ-linolenic acid (GLA) radiation on lipid peroxidation and monooxygenase functions in rat liver microcosmes. Rats were treated with single doses of radiation (1 Gy) and decapitated 1 and 3 days following treatment. Boragoglandin 100 (150 mg GLA/ml) was administered intragastrelly 1 hour after irradiation, per os. 1 time a day, over 1 and 3 days. The malondialdehyde (MDA) content in serum was significantly increased in the irradiated group after 1 and 3 days, whereas in rat liver microsomes this parameter was increased after 1 and 3 days and decreased after 3 days. The amount of cytochrome b5 and P-450 in liver microcosms and level of steroid hormone in blood did not change after irradiation, whereas the NADPH oxidation rate was significantly decreased by 29% and the activity of NADPH-cytochrome P-450 reductase was decreased by 30%.

GLA progressively decreased the microsomal MDA content as well as the NADPH- and NADPH-oxidase activities. The NADPH-cytochrome P-450 reductase activity was normalized by GLA in 24 hours, whereas the cytochrome P-450 and b5 content was lowered by 60% and 26%, respectively, 72 hours after irradiation.

The data obtained suggested that the antioxidative effect of GLA can be realized via changes in the microsomal cytochrome P-450 and b5-dependent systems which are important sources of free oxygen radicals in the liver.
THE EFFECT OF COMBINED ACTION RADIATION AND HIGH PRESSURE OF OXYGEN ON TESTIS OF MICE

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In recent years a method of high oxygen pressure (HBO)-therapy has been widely used in medical practice in treating oncologic diseases. For this reason irradiation is used together with the method of HBO therapy. In earlier work (Tchebotarev, e.a. 1991) it is shown that the modifying effect of oxygen lowers the cytogenic effect of radiation in somatic tissues.

Mice of the CBA line were exposed to radiation Co 60 500 rad, then to five days of exposure to HBO-therapy (0.3 MPA/per hour). Cytogenetic analysis showed that the HPO-therapy did not induce increased chromosome aberration (ChA) in spermatocytes of the I and II order in mice. Treatment by ionized radiation did not provoke an authentic increase of chromosome aberration quantities in spermatocytes of Order I, neither alone nor by the combined effect with GBO-therapy. However, a considerable increase of ChA was registered in spermatocytes of Order II: 13.6% after irradiation and 14.4% after a combined method of irradiation and GBO (the control level - 0.6%). Moreover, the chromosome aberration spectrum was mostly represented by chromatide bridges. Such an increase of chromosome aberration in Order II meiosic divisions can be connected with the increase of chromatid exchanges in the state of late prophase of the meiosis. The results give evidence of the absence of a modifying effect of HBO-therapy on testicular tissues.
IL9606155

RADON REDUCING ACTION IN TALPIOT SCHOOL, JERUSALEM.


The radon concentration of 10000 Bq/m$^3$ was obtained at one of the ground class rooms at Talpiot school, Jerusalem. The measurements at the neighbor classes gave 840 and 250 Bq/m$^3$. In the class with 10000 Bq/m$^3$ two open pipes (diameter of 30 cm) was found at one of the walls. The measurements with charcoal canisters in these pipes determined 137000 and 10000 Bq/m$^3$. According to the preliminary architecture plan one more class room was planned attached to the wall and the pipes should have been connected between the two classes. During the building period, the plan was changed, but the pipes were remained in case it would be decided to add one more class room. However, the pipes were remained open to the ground which is riched by phosphate.

![Image](164)

Figure 1. The changes of radon concentration in the teacher's class at Talpiot school, Jerusalem.

It was decided to seal the pipes and to insert the ventilation system in the classes. The repeat measurements with charcoal canisters give a result of 34 and 51 Bq/m$^3$. The similar result was observed at the neighbor classes.

The school was built on a slope with terraces, therefore almost all class-rooms have some contact with the ground, including the upper floors of the building.

The measurements of all the class rooms have shown that some classes of upper floors have a higher radon level than the lower classes. At some ground flour locations the radon level was less than at the upper classes. At the first stage we have recommended to seal all possible cracks and gaps around the pipes of water, sewage, electric power cable and so on. Unexpectedly, after the sealing the radon concentration has increased at some classes (Fig. 1).

Investigation of the building has shown that the walls in school have double layers with air gap between them. The school was built about 30 years ago and this air gap was used to make a heat safe construction. Number of holes was drilled at the walls and the measurements of radon were carried out using the sniffer mode by Niton Rad 7 system. The results have determined the higher concentration in the wall's holes than at the class room itself: 200-300 Bq/m$^3$ in the walls, 0-40 Bq/m$^3$ in the class room. The ventilation of gap space between the wall layers has decreased the radon concentration from 205-1166 Bq/m$^3$ before the ventilation to 37 Bq/m$^3$ after it. Although the sniffer mode is not accurate for radon measurement its was successfully used for searching "hot" spots.
At 1990 the radon measurement at Alon school in Carmiel’s school has found radon concentration of 10000 Bq/m$^3$ in the janitor room. It was determined that the electric power pipe was the source of radon. This pipe has connected the outside electric power line with the distribution board located at the janitor room. The pipe was sealed with concrete and it has successfully decreased the radon level. During 1990-1994 the repeated measurements was carried out to control the situation, no large concentration has been registered until 1996 (figure 1).

![Figure 1. The measurements of radon concentration at the janitor room at one of the Carmiel's school during 1990-1996.](image)

At January 1996 the Radiation Safety Division has recommended to check all class-rooms that has some contact with the ground. The repeat measurements has determined 10500 Bq/m$^3$ in the janitor room. We suggest that the earthquake in November 1995 (6.2 magnitude at Richter scale), with the epicenter near Elat, has crashed the concrete which sealed the electric power pipe. The radon level was increased in the nearest class-rooms too.

At the art class-room, which is located under the janitor room, the concentration of 318 Bq/m$^3$ was determined; at the teacher room, which is a neighbor to a janitor room, the concentration of 1169 Bq/m$^3$ was registered; the other nearest rooms has determined 653, 591 and 421 Bq/m$^3$. For the low art room we have recommended to insert the ventilation system with two entrances: one should to insert free outside air and an other should exit the inside air. It was recommended that the volume of inserting air should be 10 times more then the volume of exciting air. The repeat measurements has determined 39 Bq/m$^3$.

At the same time the electric power pipe has been sealed with the plastic-caulking sealant "Silicone" to prefer the radon entrance. It was also recommended to insert an open pipes with 20 cm diameter at the floor level in order to increase the ventilation. In the nearest rooms the same pipes was inserted and it decreased the radon.

We have measured the earth sample near the building and has determined 126 Bq/kg of Radium-226 at the ground. According to geologist this part of city situated on the layers reached of uranium and radium. It was recommended to plan the future building in such way that it should prefer the radon entrance in the building.

In Israel every school building has a shelter. Frequently, these shelters is used as a general class-rooms. A great radon concentration can be observed in these classes. During the shelter building attention paid to the strength of the roof and the walls, and generally, the floor is not planning to prefer the radon entrance. Radiation Safety Department has recommended to check all shelters, which are frequently occupied by population.
The use of "liquid gloves" (SAF-T-SKINN cream) substantially reduced skin contamination and percutaneous absorption of radioiodine in a production group. Additional information regarding the use of the protective cream with radioiodine was gathered and its usefulness against iodine adherence to the skin, established. Concomitantly, a test for the applicability of the cream to the reduction of Tc99m skin contamination was initiated in the Nuclear Medicine Department of Soroka Medical Center.

Technetium pertechnetate is extremely difficult to remove from the skin, and is absorbed via the dermis if not removed. It is therefore essential to remove Tc99m contamination as quickly as possible in case of an accidental spillage on the skin, which happens frequently during daily routine.

**Method:** In the Nuclear Medicine Dept., the cream was tested for 6 months by 5 persons who are using Tc99m on a daily basis. In the production lab using I-125 and I-131, the experiment was conducted for 18 months by 8 persons. The cream was used on alternate months by all participants.

When used, the cream was applied every morning covering the hands and the arms up to the elbow. Upon termination of each job, the hands were monitored using a portable Geiger Counter for Tc99m and with a RAM DA (ROTEM Ind.) detector, capable of detecting 3.7 Bq (3 times background), for the radioiodines. In case of contamination the hands were washed with water and a detergent and monitored again. The hands were washed if contaminated until complete removal or until no further reduction in radiation reading could be detected.

**Results:**

1. In all cases (10 cases) where no cream was used and an accidental Tc99m contamination had occurred the isotope could not be removed even partially, by washing. Whereas, applying the liquid gloves enabled a complete removal of accidental spillage of Tc99m on the hands in 5 registered cases.

2. In 20 cases of accidental radioiodine contamination occurred after the application of liquid gloves, the hands were completely cleaned with 1-3 washings in all cases. Whereas, out of 19 cases of contamination with no previous application of the cream, 7 could not be removed by washing with water and detergent only.

**Conclusion:** For Tc99m: although a very small number of cases was registered at the present, the preliminary results strongly indicate that the use of an additional protective layer supplied by the liquid gloves is highly recommended for Nuclear Medicine staff working with Technetium, since the layer formed by it seems to prevent the adherence of the pertechnetate to the skin. The experiment is being continued and will be extended to additional isotopes.

For radioiodines: Considering the highly favorable results, the “liquid gloves” are now routinely used by all personnel involved in radioiodine production.
BIOLOGICAL TRANSFER OF 110m-Ag TO FOETUSES AND NEWBORNs IN RATS

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The radionuclide 110m-Ag has been discharged from the Hungarian nuclear reactor in increasing amounts in recent years. In 1989 the airborne release of Ag was higher than that of Cs-137, I-131 and Co-60 combined (50Mbg). In 1994, 1221 Mbq Ag-110m was released as aerosol, 58 % of 2092 Mbq total. It has therefore been necessary to try to develop predictable models for the movement of 110m-Ag within the environment. However, this is difficult because previous data on the environmental transfer of 110m-Ag is sparse.

In preliminary studies the transfer of different silver compounds to body tissues was studied in rats exposed to 100m-Ag by inhalation or ingestion as well as the biological half-lives were established.

More recently detailed studies were initiated on the movement of 110m-Ag from mother to foetuses and newborns both by circulation and mother’s milk.

In pregnant rats injected intravenously at the 17-18th day of pregnancy, 10 % of the injected 110m-Ag was accumulated in the foetuses and was present in newborns. The initial body burden of newborns was increased by 10-15 % during the suckling period.

In the case of exposure of mothers just after delivery, about 20-25 % of IBB was transferred to newborns by milk during the first day. This ratio was further increased by an additional 20-30 % by the end of a 10 days suckling period.

The elimination and accumulation of 110m-Ag from newborns and by milk was also studied using inactive mothers for active newborns as well as inactive newborns for active mothers.

About 80 % of the initial body burden of active newborns (max. activity 160-180 Bq/g bw.) was eliminated during the first 4-5 days after delivery. The accumulation of radioactive milk from mothers to inactive newborns reached a maximum value of 100 Bq/g bw. followed by a decreased rate of elimination.
CHROMOSOMAL ABERRATIONS IN LYMPHOCYTES OF CHERNOBYL CLEAN-UP WORKERS AND THEIR SIGNIFICANCE

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On the basis of our unstable chromosome aberrations studies of peripheral blood lymphocytes of clean-up workers (protracted exposure), of residents of the exposed (chronical exposure) and unexposed (background) areas, of unexposed patients with hematological diseases (exposure to chemicals because of treatment) and of normal blood irradiated in vitro (acute exposure) in comparison with literature data it is stated that a lot of pitfalls should be taken into consideration while estimating the obtained cytogenetic findings. Giemsa stained slides prepared after blood cell culturing were scored for dicentrics and other unstable chromosome aberrations. The yield of centric rings was very low comparing to that of dicentrics. More than half of the observed residents who had continued to live in contaminated areas had lymphocytes with chromosome aberrations (dicentrics in 38.1%, dicentric yield per cell was 0.0048). Aberrant lymphocytes were found in 31.9% of liquidators (dicentrics in 24.5%, dicentric yield per cell for various groups of liquidators was from 0.0014 - 0.0100). The possibility of internal irradiation of residents because of incorporated radionuclides was confirmed by direct Cs irradiation measurement. As a rule internal irradiation of liquidators was minimal and they were examined in 3 - 6 years after their emergency work. When dividing up the liquidators based on year and duration of work at Chernobyl and on postexposure assay time we confirmed that unstable aberrations frequency (dicentrics) in blood lymphocytes of liquidators was postexposure time dependent and there was some correlation in general with certain limitations with officially recorded doses or working time intervals. All the observed liquidators and the inhabitants of the more-contaminated areas were admitted to the hospital for health disorders. They suffered from various diseases and more frequently from cardiovascular, gastrointestinal diseases and blood picture disorders. However, the frequency of chromosome aberrations and health disorders incidence were not correlated. Blood picture changes were seen in groups of liquidators with and without chromosomal aberrations. Unquantifiable uncertainties made the results of cytogenetic studies not enough decisive for individual biological dosimetry. Other sources of dosimetric information were not fully reliable. The presence of unstable chromosome aberrations such as dicentrics in lymphocytes of presumably exposed people years after exposure indicates that they have been overexposed. In the absence of chromosome aberrations under study (dicentrics) in the persons involved in the emergency work it is impossible to reject overexposure in the past. Other techniques may augment to some extent current unstable chromosome aberrations data.
ACTION OF CHRONICAL IRRADIATION ON THE CYTOGENETIC DAMAGE OF HUMAN LYMPHOCYTE CULTURE

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Action of chronical (dose rate 2.9 Gy/day) irradiation on human lymphocyte culture was investigated. Whole blood was irradiated at a temperature of 37°C. 0.2 ml of whole blood was cultivated by the micromethod. A medium including PHA was added immediately after irradiation. All structural chromosome-type and chromatid-type changes were recorded. The experimental data showed that the conditions of irradiation of lymphocytes affected neither the background level of chromosome damage nor their radiosensitivity. The obtained dose-response curve of chromosome aberrations was described by a step function. At very low doses, the curve could be fitted by a linear regression, then turned to a plateau. There is no statistically significant difference between the results for the low doses (10-50 cGy) of chronical and acute radiation. The absence of dose rate effect in the low-dose region is discussed.
THYROID CANCER IN CHILDREN OF UKRAINE

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After the Chernobyl accident, beginning from 1980 a significant increase in thyroid cancer incidence in children and adolescents has been noted in Ukraine.

The rate of growth of incidence is the highest in the children having been operated at the age 0 to 14. So, if for 1981-1985 25 cases of thyroid cancer were registered in children of Ukraine, from 1986 to 1994 this number reached 211. The most pronounced increase has been noted beginning from 1990 (26 children in 1990, 22 in 1991, 47 in 1992, 43 in 1993 and 39 in 1994). In 1995 only at the Institute of Endocrinology and Metabolism 40 children with primarily revealed thyroid cancer have been operated, what points out that the disease remains on the level of last three years.

Per 100 thousand children's population the number of cases of thyroid cancer in children of Ukraine for 1981-1985 fluctuated within 0.04-0.06. In the subsequent years this index significantly increased, exceeding the "pre-Chernobyl" level by 6.5-10 times. For certain most affected regions of Ukraine the above index is much higher and averaged for the period 1990-1994: 1.6 for Kiev region, 1.7 for Chernigov, 0.9 for Zhitomir, 0.9 for Cherkassy, and 0.5 for Rovno regions. Besides, a significant increase in the incidence has been noted in the city of Kiev: 0.9 case per 100 thousand children's population.

In absolute values in 1986-1994 it has been registered in Kiev region 36, Chernigov - 22, Zhitomir - 14, Cherkassy - 14, and in Rovno region - 8 cases. In the city of Kiev 26 cases have been revealed. It should be noted that in 1981-1985 thyroid cancer in children of these regions (beside Cherkassy region) was not registered at all.

As a whole, the "contribution" of the above regions in thyroid cancer incidence in children aged under 15 years in Ukraine for 1990-1994 made over 60%, and for 1995 more than 70%.

When comparing the age of patients during the operation and during the accident, it should be noted that 50% of children operated later on were aged under 4 years at the moment of accident.
Among the remote after-effects of radiation exposure due to the Chernobyl accident may be hypothyroidism, autoimmune thyroiditis, benign and malignant tumors of thyroid gland.

Our investigations have shown that in the first months after the accident a dose-dependent hyperthyroxinemia without clinical manifestations of thyrotoxicosis was noted in children. The thyroxinemia was directly proportional to the dose of iodine radionuclides absorbed by the thyroid and inversely proportional to the children’s age. The level of blood thyrotropin in children with a high absorbed dose of radiiodine was decreased. This seemed to have a compensatory character and was due to a high thyroxine content in blood.

In 6 to 12 months after the accident thyroxine and thyrotropin content in blood of children was normalized and remained on this level till now.

It has been revealed no changes, as compared to the control, in the content of antithyroglobulin antibodies and microsomic fraction of thyroid in children having been exposed to radiation.

Thus, clinical observations and analysis of individual indices of children’s blood content of thyrotropin, total and free thyroxine, antibodies to thyroid antigens point out that such possible after-effects of radiation exposure as hypothyroidism and autoimmune thyroiditis have not manifested till now. At the same time, one may not exclude their appearance later on.

Beginning from 1983 it has been noted a significant increase in the number of thyroid cancers in Ukraine in children who were aged 0 to 18 years at the moment of the accident. If for five years before the accident (1981-1985) 59 cases of thyroid cancer were registered in Ukraine in children of this age, for the period 1986-1995 this number exceeded 600. In the subsequent years one may expect a further increase in the number of thyroid cancers in the children who were 0 to 18 years at the moment of the accident.

In this connection, annual screenings of all children of Ukraine aged 0 to 18 (at the moment of the accident) and having been exposed to radiation are necessary. These screenings include: examination by an endocrinologist, assay of blood content of thyrotropin, thyroxine, antibodies to thyroid antigens, ultrasound investigation; in the presence of tumors exceeding 5 mm - fine needle aspiration biopsy under sonoigraphic control followed by cytological and, if necessary, immunocytochemical study of the punctate are indicated.
This paper is devoted to analysis of psychological aspects in the problem of human interaction with nuclear objects. In previous works [1, 2] computer methods of creative thinking testing were described. They are based on a new mathematical model of creative thinking. Computer testing games were worked out and each of these games corresponds to concrete schemes of creative thinking. It was shown that one can obtain a set of new psychological parameters for creative thinking by using mentioned computer methods. These parameters characterize creative thinking structure of a person in detail (for instance: intuition (I), logics processing (LP), volume of thinking space, volume of long time memory (VM) etc). New testing methods are suitable in cases when we are interested to check person's abilities to fulfil a certain creative task. By and large we always can choose special computer testing problems that include corresponding logic schemes.

Operator of nuclear reactor works in special conditions. Nuclear reactor is a new type of industrial plant. Processes in this physical object have a probability character. In the case of Chernobyl accident electrical engineers assume control of the reactor to test a generator's capacity to power emergency systems as it coasts after steam is shut off. As a result of control rods were lowered into the core the thermal-energy level drops from normal 3,200 MW to 1,600 RMW. The emergency core-cooling system, which would draw power and affect test results, was shut off. Monitoring systems were adjusted to low power levels, but the operator failed to reprogram the computer to maintain power at 700 to 1,000 MW. Power failed to the dangerously low level of 30 MW. The majority of control rods were withdrawn to increase power, but xenon has built up in the fuel rods. This by - product absorbed neutrons and "poisoned" the reaction. In this situation virtually all control rods were withdrawn. Power climbs and stabilized briefly at 200 MV. To ensure adequate cooling after the test, all light pumps were activated. The combination of low power and high flow necessitated many manual adjustments. The operators turned off emergency shutdown signals. The computer indicated excess reactivity. But operators reserved the possibility of rerunning the test by blocking the only remaining trip signal just as it is about to shut down the reactor. The test has began and power started to rise. At this dangerously low power level any small increase in power triggers an even larger increase. Water expanded to steam and absorbed neutrons. The power began rise faster. Facing catastrophe, operators began insertion of all control rods. The rods, however, have five meters of graphite at their ends. The reaction speed was strongly displaced. In the next four seconds power surged to 100 times the reactor's capacity. The uranium fuel disintegrated, bursted through its cladding, and came into contact with cooling water. An enormous steam explosion shears 1,600 water pipes, flings the reactor's cap aside, blows through the concrete walls of the reactor hall, and throws burning blocks of graphite and fuel into the compound. Radioactive dust rised high into the atmosphere. These processes are not localized in space and are not uniformly distributed. So operator must analyse the local situation in nuclear reactor and do prognosis for the whole plant. Operator cannot completely rely upon computer data. In some cases computer needs about several minutes to give an account of reactor's state. Operator cannot wait for computer data and must act in no time. In these conditions it is very important for operator to have not only a high professional level but also adequate psychological characteristics. Typical difficulties of operators in the case of Chernobyl accident are anylized. We know that operators had enough preknowledge in physical processes that take place in reactor. Their mistakes in given situation may be explained by structure of their creative thinking. What did operators' mistakes show?
  - They were not able to comprehend the situation at a glance.
  - They did not foresee results of each stage of experiment by using previous information.
  - Their interaction with computers was faint.
  - They could not to compare many parameters of nuclear processes at the same time.

Proceed from comparison of general characteristics of operator's creative thinking and real activities of operators during Chernobyl events we concluded that creative thinking structure of operators in this concrete case was not suitable for their tasks. It goes without saying that their function I(R) was wrong. We may assume that their parameters of thinking space volume (VTS) and critical potential (CP) were small. Earlier [2] we have shown by using of our computer tests that for operators who carry out computer modelling of radiation defects creation in solids it is important to check such parameters as I0 and mutual influence of different domains of thinking space. The scheme of computer testing methods application is proposed.
CHERNOBYL: TEN YEARS AFTER

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In April of this year, the 10th anniversary of the tragic events at the Chernobyl plant took place. This anniversary gave rise to several important international meetings, including major conferences of the World Health Organization (WHO) on health consequences, and of the European Commission, Belarus, Russia and Ukraine which focused on environmental consequences and emergency planning. The International Atomic Energy Agency (IAEA) played host to the summing up conference, at which the results of those various meetings were reported and integrated into an international consensus about the consequences of the accident. The conference, presided over by Germany's Federal Minister for the Environment, Nature Conservation and Nuclear Safety, Ms. Angela Merkel, was sponsored by the European Commission, the WHO and the Agency; five other organizations of the United Nations family and the Nuclear Energy Agency of the OECD co-operated in its preparation and organization. The conference attracted high-level political participation, including the President of Belarus, the Prime Minister of Ukraine and Ministers from Russian and France. More than 800 experts from 71 countries participated, nearly half of the experts coming from developing countries, a much larger number than originally anticipated. The conference was also attended by 208 journalists from 31 countries, the level of media coverage being unusual for technical meetings of the Agency.

A summary of the key results of the conference will be presented. The results confirmed the assessment made in 1990 by the International Chernobyl Project of the general radiological situation in the area most affected by the accident. There had been consensus on the number and types of acute health effects clinically attributable to radiation exposure as a result of the accident. Furthermore, there had been verification of an increase in the incidence of thyroid cancer among those exposed individuals who had been children in 1986, confirming the concerns expressed by the International Chernobyl Project. So far, no increase in the incidence of any other malignancy that could be attributed to the accident had been detected. The conference had confirmed that there was a high incidence of psychological health disorders in the population affected by the accident. These disorders were unrelated to radiation exposure and difficult to distinguish from psychological effects associated with economic hardship and the dissolution of the Soviet Union. The dramatic social, economic, institutional and political impact of the accident on the affected countries had been reviewed. The conference had indicated that no sustained severe impacts on ecosystems had been observed, but the possibility and significance of long-term genetic effects on some plants and animals in local environments remained to be studied. Finally, the conference had reviewed the safety of RBMK reactors in general, and in particular of the Chernobyl nuclear power plant and the containment structure of the destroyed reactor, the so-called sarcophagus. the results of the conference had confirmed the hope that it would be possible for competent experts from around the world to reach a broadly accepted assessment of the major consequences of the accident.

The summary of the Conference results deserves wide dissemination in the interests of fostering an accurate international understanding of the consequences of the Chernobyl accident.