Dose-effect relationship between the thorium lung burden and the hepatic function of the miners at the Bayan Obo Rare-earth Iron Mine

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Abstract. The purpose of this paper is to present the dose effect relationship between the thorium lung burden and the hepatic function of the miners at the Bayun Obo Rare-earth Iron Mine. **The methods** we used is to carry out the measurement of each miner's exhaled thoron activity and the thorium lung burden along with the four hepatic functions (thymol turbidity test, glutamic pyruvic transminase, thymol flocculation test and alkaline phosphatase)of the dust exposed miners in Bayun Obo Rare-earth Iron Mine. We have carried out three investigations in 1983, 1984~1987 and 1994 respectively. **Results** showed that during the period 1983-1994, 1158 measurements of thorium lung burden estimates and 1158 measurement of every four hepatic functions(altogether 4632
measurements) were performed on 638 dust-exposed miners. No adverse effects were observed. In the same time, none of the above-mentioned 638 exposed miners had a thorium lung burden higher than 11.11 Bq. **It is concluded** that if any miners' thorium lung burden not higher than 11.11 Bq, his four hepatic functions should not be affected. This first possible threshold for thorium lung burden affecting the hepatic functions was put forward by us and confirmed by the Information Center of Chinese Academy of Medical Science in 2003 after searching 23.6 million references.

KEYWORDS: Exhaled thoron activity, Portable measurement system, Thorium lung burden.

1. Introduction

In 1962, Bruce Boecker reported that there is evidence that inhalation of thorium can lead to deposition of small amounts in the liver of rats. In 1964 Yan Xiao-shan[1] reported that after a single intratracheal instillation of a certain amount of ThO_2 in a saline suspension into a rat, a small amount of ThO_2 appeared in the liver in the first few days after injection and remained for five months. In 1999, Stehney[2] reported the organ distribution of thorium in autopsy samples from one thorium worker were as follows: lung 1.74mBqg^{-1}; pulmonary lymph nodes 5.40 mBqg^{-1}; bone 0.70mBqg^{-1}; liver 0.17mBqg^{-1}.

Ibrahim Farid and Shirley A. Conibear[3] reported that changes in liver function in 273 former workers of a thorium refinery might be compatible with a toxic effect of thorium, or its daughter products on hepatocytes. The correlation of some hepatic function tests with the body burden of thorium suggests a radiation effect, although a chemical toxic effect cannot be ruled out.

In 1973, scientists from the Labor Hygiene Institute of the Baotou Steel Company reported that the enlargement of liver size and the abnormal of liver function were appearing in quite a lot of workers inhaling thorium-containing dusts for long periods. However, since at that time they had no data on the thorium body burdens of the workers they. were unable to establish any clear relationship between thorium body burden and hepatic function in these workers.

In 1983, Ibrahim Farid and Shirley A. Conibear were the first to report thorium body burden measurements on 195 former workers of a thorium refinery as well as measurements of the following hepatic function tests: aspartate aminotransferase, total protein, albumin, total bilirubin, alkaline phosphatase and globulin. The results showed that the globulin levels increased with age and with increasing levels of thorium body burden, although the relationship was not significant at the 0.05 level. However, the thorium body burden had no effect on either albumin or total protein. The thorium exposed workers showed no statistically significant association between alkaline phosphatase and thorium body burden; however, total bilirubin showed a weak association with the body burden

(R^2=0.015) that was statistically significant (P=0.043); aspartate aminotransferase also correlated significantly with thorium body burden. However, this refinery used monazite as the raw material.
The thorium body burden of 3 of the 195 workers measured reached a level as high as 75 Bq, or even more. While the highest thorium lung burden observed among the 638 miners measured at the Bayun Obo Rare-earth Iron Mine was only 11.11 Bq[4]. Therefore, we carried out a ten-year-study on the dose-effect relationship between the thorium lung burden and the five indices of hepatic function in the miners at the Bayun Obo Rare-earth Iron Mine since 1983[5]. The IRPA12 - 2008 Proceedings will be distributed at the conference on a CD-ROM. The authors are requested to submit their paper in the format described in these instructions. This is easily done by using the format in this document, which can be downloaded from http://www.irpa12.org.ar "downloads". Full Papers should have at most ten (10) pages (A4 format), including tables, figures and references. The font should be Times New Roman 11 point font. Do not reduce the font size to comply with the 10-page limit. Figures, photos and/or tables should be included within the body of the paper. The deadline for the submission of Full Papers is 1 July 2008 and must be carried out only through the IRPA12 Website. Full Papers received after this deadline will not be included in the Proceedings. At least one author must be duly registered at the Congress before sending the Full Papers.

2. Methodology

2.1 The measurement of exhaled thoron activity.

The measurement of exhaled thoron activity was carried out by an electrostatic negative high voltage exhaled thoron decay products measurement system[6].

2.2 Medical and routine hepatic function examinations.

After the exhaled thoron activity measurement during one week, each subject went to the hospital to undergo a physical examination by a senior medical doctor, as well as routine hepatic function tests， which were carried out by two experienced technicians. The tests were repeated whenever any abnormality appeared.

2.3 The five hepatic function tests and their normal ranges.

T.T.T. (Thymo turbidity test) - Normal range 0-6 units (Shank); T.F.T. (Thymol flocculation test) - Normal range (-) (+) (++) (+++) (n.a.); G.P.T (Glutamin Pyruvic transminase)- Normal range 0-40 units/L (Karman); TBIL (Total Bilirubin) – Normal range 0.1-1.0 mg% (Jendrassik); ALP (Alkaline phosphates) – Normal range: 3-13 units/L (King. J) （1983-1987 study）; Normal range: 20-30 units/L (n.a.) （1994 study）

3. Results

3.1 The results in the 1983 study

3.1.1 The general condition of the subjects

The subjects in this investigation were selected by a stratified random sampling method from the main dust-generating posts. Out of 31 dust-exposed miners, 25 having a working history of more than 21 years were selected as the observed group. Six young miners having working histories of less than 5.5 years were regarded as the control group. The thorium lung burdens of 31 miners were estimated using the highly sensitive electronic exhaled thoron activity collection measurement system.
The older miners having a thorium lung burden of 1.85Bq or higher (nearly reaching 1 investigation level) were assigned to Group I, those with lung burdens ranging from 0.74Bq to 1.85Bq to Group II and those with less than 0.74Bq to Group III. The young miners were assigned to Group IV (the controls).

Table 1 The group classification of the workers in the crushing workshop.

Group	Number	Age(years)	Working history (years)	Thorium lung burden（Bq）	
				Range	Mean ±SD
I	3	49.4±3.39	25.3±1.28	2.05～3.60	2.44±0.49
II	12	46.1±4.03	25.3±1.48	0.79～1.82	1.16±0.25
III	5	45.1±3.21	25.2±1.3	0.23～0.73	0.49±0.18
IV	6	25.7±1.51	4.4±1.02	0.10～1.29	0.56±0.42

3.1.2 The relationship between the thorium lung burden and 4 parameters of hepatic function.

The results for the 5 parameters of hepatic function in the 4 groups with different thorium lung burdens are listed Table 2.

There were significant differences (P＜0.01～0.001) among the thorium lung burdens of groups I, II and III except for the comparison between Groups III with IV. This result showed that the above classification was correct.

Table 2 The hepatic function of the different groups (Mean ±S.D.)

Group	TTT (units)	Total bilirubin (mg%)	Alkaline phosphates (units/L)	**G.P.T.** (Units/L)	**T.F.T.**
I	4.1±1.0	0.24±0.09	5.69±2.49	＜40	(-)
II	4.3±0.9	0.45±0.31	5.74±2.17	＜40	(-)
III	5.0±0.7	0.24±0.12	6.30±2.67	＜40	(-)
IV	4.3±1.0	0.26±0.15	6.97±2.08	＜40	(-)

In Table 2, it is difficult to find any relationship between the thorium lung burden and the TTT, TBIL and ALKP parameters of hepatic function. All the values of above parameters were within normal limits in the 31 miners studied (P>0.05). In addition another parameter TFT was tested and the results were all negative. The results for GPT among most miners in Group I were normal except that one man whose GPT value was 480 U/L and another in Group II with a value of 350 U/L: one miner in the control group had a value of 250 U/L. One month later, the above GPT value had all returned to normal. Therefore, no definite relationship could be found between the above 3 subjects' GPT values and their thorium lung burdens.

The values in Table 1 and Table 2 showed that the five parameters of hepatic function were not obviously changed when the thorium lung burden of miners was less than two investigation level (4.44Bq).

3.2 The results of the 1984－1987 study.

The preliminary observations and analyses on the relationship between the thorium lung burden and hepatic function in the 31 thorium-dust-exposed miners in the crushing workshop of the Baiyun Obo mine were done in June 1984. The working histories of 25 miners out of the 31 were above 25 years.. The results showed that there were no adverse effects on the hepatic function of the miners inhaling thorium-containing dusts[7]; but there were very few cases and, in addition that there was only one set of observations. In order to make clear the relationship between the thorium lung burden and hepatic function, we began to expand the number of subjects to be examined and since 1985 not only were another 66 older miners from the crushing mill observed in the same way, but also the observations on the 51 older miners randomly chosen from the above 66 miners were continued for four years. The young miners were treated as the control each year. The results were as follows.

3.2.1 The general situation of the subjects.

Most of the 51 old miners were randomly sampled from the main posts (the crushing mill and the belt), and all of them had a working history over 21.53 years. The individual thorium lung burdens of these miners were determined by the exhaled thoron collection and measurement system[6]. The group classification was based on their thorium lung burden estimates. Group I had a thorium lung burden over 1.48Bq or reaching towards 1 investigation level -2.22Bq. Group II ranged from 0.74Bq to 1.48Bq; Group III was ＜0.74Bq，and the young miners were regarded as Group IV "the controls". General physical examinations (height of body, weight, blood pressure, chest and abdomen, clubbed finger）and hepatic function tests were carried out on all of them. The parameters of hepatic function included G.P.T.，T.T.T.，T.F.T，Total bilirubin and alkaline phosphates. In 1984 we carried out Type A ultra sonic examination to detect the size of the liver; in addition, since 1987, we carried out Type B ultra sonic examination to observe the shape, size and the presence or not of abnormal parenchyma in different sections. The purpose of these examinations was to understand the relationship between the thorium lung burden and the hepatic function parameters, as well as look for injury of the liver.

3.2.2 The relationship between the thorium lung burden and the hepatic function parameters

The measurements of hepatic function parameters and the Type B ultra sonic examination in 1987 of the different groups are listed in Table 3 and Table 4.

Table 3 The hepatic function of different groups (1984-1987)

Group	**Year**	**Case**	**Alkaline phosphates** (Units /L)	**T.T.T. (Units)**	**Total bilirubin. (mg%)**	**G.P.T.** (Units/ L**)**	**T.F.T.**
I	84	17	5.4 ±1.5	4.0 ± 1.1	0.29 ± 0.22	＜40	(-)
	85	20	3.9 ± 1.2	4.3 ± 1.8	0.37 ± 0.22	＜40	(-)
	86	18	7.4 ± 3.0	4.3 ± 0.1	0.30 ± 0.08	＜40	(-)
	87	18	7.9 ± 4.8	4.7 ± 1.9	0.33 ± 0.20	＜40	(-)
II	84	22	7.1 ± 2.7	3.5 ± 1.5	0.29 ± 0.22	＜40	(-)
	85	20	4.4 ± 2.1	3.6 ± 1.3	0.37 ± 0.15	＜40	(-)
	86	23	6.2 ± 2.2	4.3 ± 1.1	0.30 ± 0.06	＜40	(-)
	87	15	3.7 ± 2.5	4.2 ± 1.0	0.30 ± 0.10	＜40	(-)
III	84	12	5.7 ± 1.6	3.8 ± 1.6	0.32 ± 0.31	＜40	(-)
	85	11	3.8 ± 1.4	4.5 ± 1.7	0.40 ± 0.17	＜40	(-)
	86	10	6.5 ± 2.2	5.1 ± 2.4	0.33 ± 0.07	＜40	(-)
	87	18	7.4 ± 2.5	5.2 ± 1.7	0.40 ± 0.14	＜40	(-)
IV	84	6	7.0 ± 2.1	4.3 ± 1.0	0.26 ± 0.15	＜40	(-)
	85	5	3.3 ± 0.8	4.3 ± 1.2	0.69 ± 0.51	＜40	(-)
	86	4	11.2 ± 7.2	4.5 ± 1.3	0.28 ± 0.05	＜40	(-)
	87	4	7.6 ± 1.9	4.0 ± 1.5	0.23 ± 0.10	＜40	(-)

For all the groups tested the liver function parameters were within normal limits, Table 3 and there were no significant differences between the different groups (P larger than 0.05).

Table 4 The hepatic measurements for the different groups by ultra sonic examination (B type) in 1987 (Mean±S.D.)

Group	Case	Length of the left lobe of the liver (mm)	Original diameter of the left lobe of the liver (mm)	Obligue diameter of the right lobe of the liver (mm)	Original diameter of the right lobe of the liver (middle line of the clavicle) (mm)
I	14	67.2 ± 6.8	74.4 ± 10.8	130.3 ± 11.1	85.3 ± 8.6

II	13	68.5 ± 7.6	79.7 ± 15.7	125.2 ± 10.1	82.8 ± 7.9
III	17	70.5 ± 7.3	73.4 ± 10.0	131.6 ± 9.2	87.6 ± 9.2
IV	4	67.5 ± 4.7	70.0 ± 17.2	122.5 ± 5.2	85.0 ± 6.2

The t-test for the average values of the ultrasound measurements listed in Table 4 showed that the differences between the average values of the groups were not significant (P value larger than 0.05).
Based on the results of A and B type ultra sonic examinations, none of the 51 miners from the crushing workshop had an enlargement of his liver or the injury to the parenchyma of the liver. In addition, that the results of 5 hepatic function parameters were also normal. Therefore we again confirmed that if the thorium lung burdens of the old miners from the crushing workshop of the Bayun Obo mine were at a level of about 1 investigation level (2.22Bq) or less than 2 investigation levels (4.44Bq) for a long time, the amount of thorium transferred to the liver from the lung still did not reach the level needed to affect the hepatic function. This view was confirmed by the observation over the four years.

3.3 The result of the 1994 study

Based on the 1993 investigation, the air dust concentration in the crushing workshop of the Bayun Obo Mine ranged from 1.6 mg/m^3 to 74.0 mg/m^3, the average value was 17.11 mg/m^3, these levels were higher than those in the other 6 dust-exposed workshops. The other workshops were as follows: main mine, east mine, railway transportation, bus transportation, electricity, highway.
The range of air dust concentration at these workshops was from 1.2 mg/m^3 to 16.4 mg/m^3. The average value was 5.7 mg/m^3. In this year's study, 136 miners were chosen by stratification random sampling from among 2390 male miners from the seven dust producing workshops. A total of 64 miners were from the crushing workshop where the air dust concentration was the highest. For the control, 20 miners were selected from the main mine, 17 from the east mine, 10 from railway transportation, 10 from the bus transportation; 7 from the high way and 8 from the electricity workshop.

3.3.1 The general situation of the subjects

The age ranges of the crushing group (64 miners) and internal control group (72 miners) were 30 to 57 years and 34 to 59 years old respectively. The average ages were 49.3±4.8 years and 48.0±5.6 years respectively. There was no statistically significant ($P<0.05$) difference between the average ages of the two groups and the age range was about the same.
The exposure histories of the crushing and internal control groups ranged from 8 to 36 years and 17 to 36 years respectively with averages of 28.3±6.2 and 27.0±5.0 years, respectively. There was no statistically significant difference between the exposure histories among the two groups ($P<0.05$).

3.3.2 The relationship between the thorium lung burden and the hepatic function parameters of the miners

To make clear the relationship between the thorium lung burden and its health effects in miners, the above-mentioned 136 miners were divided into two groups: the crushing group (64 miners) and the internal control group (72 miners from the other six workshops). This was because the difference of the thorium lung burden between the two groups was very significant. According to the level of thorium lung burden, the crushing group was further divided into Crushing Groups 1, 2 and 3. The thorium lung burdens of the above-mentioned three crushing groups and their internal control group are listed in Table 5.

Table 5 The thorium lung activity of the 3 crushing workshop groups and their internal controls group.

Group	Case	Thorium lung burden（Bq）	
		Range	Mean ±SD
Crushing 1	36	0.132～1.45	0.82±0.41

Crushing 2	10	1.520～2.18	1.74±0.23
Crushing3	18	2.380～7.26	3.76±1.24
Internal control	72	0.112～1.45	0.58±0.32

The comparison of hepatic functions between the above-mentioned four groups is shown in Table 6..

Table 6 The comparison of the hepatic functions the 3 crushing Workshop groups and their internal controls (Means ±SD)

Group	Case	T.T.T（unit）	G.P.T（units/L）	ALP*（units/L）	TFT
Crushing 1	36	5.0±2.8	16.8±2.6	18±4	（—）
Crushing 2	10	5.0±1.6	19.6±4.7	19±7	（—）
Crushing 3	18	4.5±0.9	17.8±3.6	19±6	（—）
Internal control	68	5.0±1.0	16.0±3.0	28±13	（—）

* ALP：Alkaline phosphates

The result in Table 5-6 show that the hepatic function parameters of above-mentioned 4 groups were all normal and there was no statistically significant difference between any two groups ($P<0.05$). None of them had even one abnormal index. This could be explained by the fact that the absorption of ThO_2 through the respiratory tract is only $0.0001d^{-1}$, so that the amount of insoluble ThO_2 entering the blood circulation and deposited in the liver was very small. In addition, the highest thorium lung activity was only 7.26Bq among the above 136 miners in this investigation.

Including the above investigations in 2004, Chen Xing-an[7] reported the results of 4 hepatic function parameters（T.T.T、G.P.T、T.F.T and alkaline phosphates）of 1158 measurements from 638 dust-exposed miners at the Bayan Obo Mine in 1983-1994, which showed that no adverse effects were observed. The highest thorium lung burden of the above 638 miners was 11.11Bq. In the other words, if the thorium lung burden of the person was not over 11 Bq, his hepatic function parameters would not be affected.

4. Discussion

Most of the data on human effects of thorium came from the long-term follow-up study on the patients, aged 30 to 50 years, injected with Thorotrast during the 20th Century. According to Mori et al's study[8] reported in 2004, from 1945 to 2002, autopsies had been performed on 404 Thorotrast-treated-patients-392 injected intravascularly with Thorotrast and 12 injected by other routes. In the intravascularly injected autopsy cases, 266 liver malignancies (67.9%), 28 cases of liver cirrhosis (7.1%), 12 cancers of the extrahepatic bile duct (3.2%), 30 hematopoietic malignancies /(7.7%), 2 bone sarcomas (0.5%), 16 lung cancers (4.1%), one hamangiosarcoma of the spleen (0.3%), 4 malignant peritoneal tumors (1.0%), and 7 sarcomas at the injection site (1.8%) were found, The relative risk estimate of liver malignancies and hematopoietic malignancies was significantly higher in the autopsied Thorothrast patients than in the autopsied controls. After intravascular injection ThO_2-aggregates accumulate in the reticuloendothelial system (RES). The average diameter of the particles in commercial Thorotrast measured about 5.5 nm. The distribution of ^{232}Thorium in a standard patient was estimated by Kaul and Noffz[9] and found to be: liver 59%, spleen 29%, red bone marrow 9%, calcified bone 2%, lungs 0.7% and kidneys 0.1%. The concentration of ThO_2 in the regional lymph nodes near the liver and spleen was high but very low in other lymph nodes of the body. However, owing to the difference in entry route, the above-mentioned data could not be used directly to assess the biological effects of inhaling thorium compounds.

Owing to the potential importance of thorium as an energy source in the thorium -232 – uranium- 233 fuel cycle and partly from the need to evaluate the possible hazards of residual radioactivity at sites where thorium is produced, the scientists at the Center for Human Radiobiology of ANL published the first paper concerning hepatic function in exposed thorium refinery workers in 1983. Since the

disappearance of the Center for Human Radiology in the mid-1980s, the later papers dealing with the relationship between the thorium lung burden and its health effects were all published by our research group. We were the first to report that when the thorium lung burden of the dust exposed miners not higher than 11 Bq, the hepatic function would not be affected. This result has been published in national and international journals [4][7].

5. Conclusions

Between 1983 and 1994, 1158 measurements of thorium lung burden and 1158 measurements of four indices of hepatic function were carried out on 638 dust-exposed miners from the Bayun Obo Mine. The results showed that when the thorium lung burden of any miner not higher than 11 Bq, the above-mentioned four indices of hepatic function would not be affected.

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