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An Epidemiological Investigation of Mutational Diseases in the High Background Radiation Area of Yangjiang, China*

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Data from the epidemiological investigation on mutation-based diseases in the High Background Radiation Area (HBRA) of Yangjiang, China, were analyzed. Although the gamma exposure level in the HBRA is three times that of the Control Area (CA) and about ninety percent of the families in the HBRA have lived there for more than six generations, there was no significant difference between the HBRA and CA in cancer mortality and the total incidence of 31 kinds of hereditary diseases and congenital defects. The frequency of chromosomal aberrations in peripheral lymphocytes of inhabitants in the HBRA was statistically higher than that in the CA, and a higher reactivity of T-lymphocytes was found in the HBRA youngsters. The comparative study of factors believed to influence the occurrence of mutation-based diseases has thus far not revealed any dominant factors that could be affecting disease prevalence.

It is a great honor and pleasure for us to be invited to participate in this Annual Meeting and to have an opportunity to make a presentation. This talk will consist of six parts.

BACKGROUND

An investigation of the high background radiation area in Yangjiang County, Guangdong Province, China, was begun in 1972 for the purpose of studying the human health effects of exposure to high background levels of radiation in the natural environment. The different aspects of this study include ascertainment of the level of high background radiation, estimation of human absorbed dose, evaluation of the health status of inhabitants, and identification of confounding factors that may either mask or falsely imply the existence of a radiation effect. The first three stages of this study were conducted between 1972–84. The study is currently in its fourth stage.

The high background radiation area in Yangjiang County includes two regions, Donganling and Tongyou, separated a short distance from each other. It encomposes a total area of about 540 square kilometers, and more than 80,000 of the inhabitants belong to families who have lived in the area for more than two generations. The control area also has two regions, Sanhe and Wudianmeihua, located fairly close to the high background radiation area (Figure 1).

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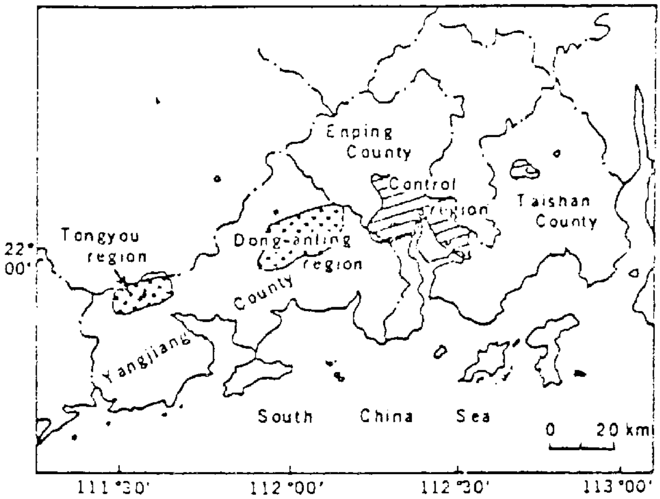

Fig. 1. Locations of the high background radiation and control regions.
High background radiation area
Control area

About 80,000 inhabitants live in the control area[1].

Results from various parts of this investigation have been presented by members of the High Background Radiation Research Group at previous Annual Meeting of the Radiation Research Society of Japan and elsewhere[1-3]. This paper presents results from an epidemiological study investigating whether or not there is a higher rate of mutation-based diseases in inhabitants exposed to high levels of background radiation versus those who are exposed to normal levels of background radiation in the control area. In this paper, the term "mutation-based diseases" refers to cancer, hereditary disease, and congenital defects, all believed to be the result of some form or component of mutation.

DOSIMETRY

Both the measurement of gamma exposure rate using RSS-111 High Pressure Argon Ionization Chamber System and Gamma-ray Spectrometry, and the measurement of individual cumulative exposure using thermoluminescent dosimeters (TLD) and silver-activated metaphosphate glass dosimeters (RPL) revealed that the gamma radiation in the high background radiation area was about three times that found in the control area. The annual individual external exposure to the environmental gamma radiation was 330 mR/yr in the high background radiation area and 114 mR/yr in the control area (Table 1)[4-6].

Measurements were taken of ^{226}Ra and ^{228}Ra in foodstuffs, drinking water, and adult teeth; similar measurements of ^{222}Rn and ^{220}Rn were taken from samples of exhaled air. The data indicated that the concentration of ^{226}Ra and ^{228}Ra in human bones in the high background radiation area was about 3–5 times higher than that in the control area[4]. Direct meas-

Table 1. Annual external exposure measured by different methods (mR/yr)

Measurement method	High background radiation area	Control area	Ratio*	Year of measurement
RSS-111**	337.1 ± 60.6	115.7 ± 21.2	2.9	1982
TLD				
$CaSO_4$ (Tm)	351.4 ± 56.8	120.3 ± 27.2	2.9	1978
LiF(Mg, Ti)-M	330.0 ± 55.1	103.3 ± 23.6	3.2	1978
$CaSO_4$ (Dy)	330.0 ± 52.8	119.0 ± 29.4	2.8	1975
RPL	330.0 ± 35.6	119.4 ± 24.6	2.8	1975

*High background radiation area/Control area
**Results produced by Field Gamma-ray Spectrometry were similar to those obtained with the RSS-111 method.

urement of ^{226}Ra and ^{228}Ra in human bones of the deceased has been conducted since 1982. These measurements have been used to derive preliminary dose estimates of the radiation delivered to bone tissue as a result of radionuclides present in the environment. Although the sample size is too small (6 cases in the high background area and 8 cases in the control area) to make any statistical conclusion, the ratio of ^{226}Ra and ^{228}Ra in human bones for inhabitants of the high background radiation area compared to the control area was more than three. These results showed agreement with previous estimates of bone tissue doses based on the radiochemical analysis of human teeth (Table 2)[5].

Results from the Investigation of Mutation-based Diseases

Once again, it is emphasized that the term "mutation-based diseases" refers to cancer mortality and the prevalence of both hereditary diseases and congenital defects.

Cancer mortality in the high background radiation area and the control area has been investigated for more than 14 years. The early data (1970–1978) were obtained by means of a retrospective survey. In 1979, a cancer registry system was established for the study areas whereby local physicians, with the help of many hospitals and administrative organizations, report all incident cancer cases and cancer deaths to the registry. Diagnoses are confirmed by an expert group who meet to evaluate cases once or twice a year. Up to the end of 1983, 326 cancer deaths were found among 764,696 person-years (pyr) at risk in the high background radiation area, resulting in a cancer mortality rate of 42.63 deaths/10^5 pyr. The corresponding figures in the control area were 412 cancer deaths, 777,482 pyr, and a crude cancer mortality rate of 52.99 deaths/10^5 pyr. Using the combined population of the two areas as a standard, standardized mortality rates were 44.60 deaths/10^5 pyr and 51.00 deaths/10^5 pyr for the high background radiation area and control area respectively. For site-specific cancers, the standardized mortality rates in the high background radiation area were also lower than that of the control area except for osteosarcoma and cancers of the uterus and nasopharynx. However, neither the total nor site-specific mortality rates showed statistically significant differences between the two areas (Table 3)[5, 7]. Further studies with the accumulation of more person-

Table 2. Annual doses delivered by ^{226}Ra, ^{228}Ra, and their decay products based on measurements taken from various sources (mrad/yr)

Source	High background area		Control area	
	Bone marrow	Bone surface	Bone marrow	Bone surface
^{226}Ra and its decay products				
Bone	0.50	2.76	0.15	0.81
Teeth	0.38	2.74	0.11	0.80
Foodstuff	1.51	8.28	0.49	2.96
Exhaled air	3.25	17.88	0.65	3.58
^{228}Ra and its decay products				
Bone	1.20	6.60	0.36	2.00
Teeth	1.86	9.89	0.53	2.80
Foodstuff	2.08	11.48	0.55	3.00
Exhaled air	0.70	3.84	0.23	1.00

Table 3. Cancer mortality (per 10^5 pyr) in high background and control areas (1970–1983)

Site of cancer	High background area			Control area		
	No. of deaths	Mortality averaged	Mortality standardized	No. of deaths	Mortality averaged	Mortality standardized
Nasopharynx	79	10.33	10.80	86	11.06	10.60
Esophagus	6	0.78	0.82	15	1.93	1.83
Stomach	43	5.62	5.90	41	5.27	5.02
Liver	78	10.20	10.70	107	13.76	13.30
Intestine	10	1.31	1.37	19	2.44	2.34
Lung	23	3.01	3.17	27	3.47	3.31
Breast	6	0.78	0.81	8	1.03	1.00
Uterus	10	1.31	1.39	5	0.64	0.61
Leukemia	21	2.75	2.75	27	3.47	3.57
Osteosarcoma	3	0.39	0.40	3	0.39	0.38
Other	47	6.15	6.34	74	9.52	9.05
Total	326	42.63	44.60	412	52.99	51.00

Note: NS (non signifidant, namely $P > 0.05$) for all.
High background area: 764,696 person-years
Control area: 777,482 person-years

years are necessary.

Information was gathered on the prevalence of thirty-one kinds of hereditary diseases and congenital defects from a sample of children seen during one of two years (1975 and 1979) whose age at the time of exam was twelve or below. The rate of hereditary diseases and congenital defects was almost identical in the two areas, 22.64 cases/10^3 people in the high background radiation area (N=13,425), and 22.54 cases/10^3 people in the control area (N=13,087).

However, the frequency of Down's Syndrome in the high background radiation area (1.04 cases/10^3) was significantly higher ($P < .05$) than that in the control area (0.31 cases/10^3) (Table 4)[4].

Examination of Peripheral Lymphocytes in Inhabitants

While investigating some of the mutation-based diseases, cytogenetic examinations and immune function studies have been undertaken using samples of peripheral lymphocytes taken from inhabitants.

Previous results of cytogenetic studies have been presented at past Annual Meetings of the Radiation Research Society of Japan[2, 4]. Subsequent studies have confirmed that the rate of chromosomal aberrations in peripheral lymphocytes is higher for inhabitants of the high background radiation area compared to those in the control area (Table 5)[5, 8-10].

Examination of immune function showed that the morphologic transformation rate of lymphocytes and B-lymphocyte count of the 16–25 years group in the high background radiation area is significantly higher than that in the control area (Table 6)[5, 11]. It suggested that the reactivity of T-lymphocytes of the youngsters in the high background radiation area is higher than that in the control area.

Factors Possibly Affecting the Assessment of a Radiation Effect on the Health Status of Inhabitants

In order to correctly assess the effects of elevated natural radiation on diseases believed caused by some form of mutation, a comparison of various factors either accepted or believed to influence the occurrence of such diseases was undertaken in the two areas using two different approaches.

The first approach consisted of a case-control study. Cases and controls were selected from the high background radiation and control areas respectively using two-stage sampling. Controls were matched to cases by sex and age. The factors studied can be divided into two categories: (A) those which have been confirmed to be related to diseases caused by mutations, e.g. – smoking, alcohol consumption, and occupational exposure to such items as poisonous

Table 4. Prevalence rate of 31 kinds of hereditary diseases and congenital defects in children of the two areas (1975, 1979)

Item	High background area	Control area	P
Numbers of examinees	13425	13087	
Total 31 kinds of diseases			
Numbers of cases	304	295	
Prevalence rate (cases/10^3)	22.64	22.54	NS
Down's Syndrome			
Number of cases	14	4	
Prevalence rate (cases /10^3)	1.04	0.31	<0.05

Table 5. Chromosomal aberrations in peripheral lymphocytes (1982)

Method of analysis	High background area	Control area
Conventional		
Total chromosome aberration rate (per 100 cells)	0.47 (n=122, c=24400)	0.33 (n=99, c=19800)
Rate of stable aberrations (per 100 cells)	0.045 (n=122, c=24400)	0.005 (n=99, c=19800)
G-banding		
Total chromosome aberration rate (per 100 cells)	3.21 (n=34, c=1711)	1.94 (n=40, c=2006)
Sister Chromatid Exchanges (per cell)	12.97 (n=126, c=2520)	11.05 (n=124, c=2480)

Note: (A) NS for all
(B) n=number of individuals examined
c=number of cells analyzed

Table 6. Immune function studies (1982)

Item	High background area	Control area	P
T-lymphocyte count (%)	56.4±1.93 (n=83)	56.2±1.17 (n=85)	NS
^{3}H-TdR incorporation into lymphocytes (CPM/0.1 ml)	51780±1316 (n=83)	49569±1346 (n=85)	NS
Morphologic transformation rate of lymphocytes (%)			
16–25 and 45–55 years group	75.0±0.90 (n=148)*	70.6±0.99 (n=148)*	<0.01
16–25 years group	77.2±1.12 (n=82)	71.3±1.28 (n=84)	<0.01
45–55 years group	72.2±1.40 (n=66)	69.8±1.57 (n=64)	NS
B-lymphocyte count (%)			
16–25 and 45–55 years group	11.5±0.62 (n=78)	10.2±0.35 (n=83)	NS
16–25 years group	11.7±0.85 (n=39)	9.7±0.44 (n=41)	<0.05
45–55 years group	11.2±0.93 (n=39)	10.8±0.54 (n=42)	NS

*Combined with early results (1979)

or noxious substances, pesticides, medical X-rays, etc. (B) those which may not have any direct cause-effect relationship with the formation of mutations, such as socioeconomic status, educational level, etc. The data for this study were collected by interview. 459 case-control pairs were available for analysis.

Results of comparisons for factors in category A showed no significant differences between the two areas except for medical X-ray exposure, where a greater proportion of people in the control area received medical X-rays than those in the high background radiation area (Table 7)[5, 12]. In the comparison of factors in category B, results showed that the economic and educational level of the control group were better than those of the high background

Table 7. Comparison of factors known to affect the occurrence of diseases caused by a mutation process

Factors	Constituent ratio (%)			Odds ratio*	
	High back-ground area	Control area	P	Matched analysis	Unmatched analysis
Pesticide use	62.3	63.6	NS	1.00	0.95 (0.72–1.24)
Occupations involving the use of poisonous and noxious substances	1.5	2.0	NS	0.60 (0.15–2.47)	0.77 (0.29–2.09)
Smoking	37.9	37.6	NS	1.06 (0.71–1.58)	1.01 (0.88–1.16)
Alcohol consumption	37.2	38.6	NS	0.85 (0.60–1.21)	0.90 (0.64–1.27)
Medical X-ray exposure	20.0	26.4	NS	0.62 (0.45–0.87)	0.70 (0.51–0.95)

*Figures in parentheses represent 95% confidence intervals

group. In addition, the population of the high background radiation area was more stationary than that of the control area, as evidenced by the higher proportion of families in the high background radiation area who have lived in the local area for more than five generations (Table 8)[5, 12].

The second approach to compare factors between the two areas consisted of a commune survey. The survey covered topics related to the natural geography of the area, population structure, pollution resulting from improper treatment of industrial waste, amount of medicine and pesticides used in the commune, amount of insecticide residue and aflatoxin B_1 present in food, diet and dietary habits, and the amount of trace elements present in samples of soil, human hair, etc. Results showed that the two areas were similar to each other with respect to these factors[4, 5, 13, 14]. One noted exception was the significantly higher amount of manganese found in the hair of inhabitants in the high background radiation area than that in the control area (Table 9)[14].

In order to find possible explanations for the difference in incidence of Down's Syndrome between the two areas, investigation of various factors associated with the disease was conducted. One finding showed that the age distribution for all children examined differed for the two areas. Since examinees in the high background radiation area were younger than those in the control area, this might have provided a better chance to detect more of the children who were actually afflicted with this syndrome (Table 10)[5, 15].

Results also showed that the maternal age at the time the afflicted child was born tended to be high in both areas (Table 11)[5, 15]. It is well-known, that the incidence of Down's Syndrome in children born to older mothers is higher than that for women of younger maternal age.

Table 8. Comparison of the number of generations a family has lived in the local area

Area	2–5 generations		>5 generations	
	No. of families	%	No. of families	%
High background	61	25.5	178	74.5
Control	99	41.6	139	58.4

$P < 0.01$

Table 9. Amount of trace elements (ppm) in the hair of inhabitants by study area

Element	Number of samples	High background area	Control area	P
Pb	10	2.771 ± 3.861	4.337 ± 4.118	NS
Cd	10	0.077 ± 2.182	0.109 ± 1.690	NS
Co	10	0.037 ± 2.218	0.043 ± 2.624	NS
Ni	10	0.477 ± 1.469	0.543 ± 1.262	NS
Cu	10	7.970 ± 1.262	8.037 ± 1.025	NS
Cr	10	0.372 ± 1.208	0.393 ± 1.167	NS
Fe	10	19.780 ± 1.300	20.390 ± 1.268	NS
Mn	10	10.477 ± 2.761	4.448 ± 1.972	<0.01
As	10	0.155 ± 2.851	0.132 ± 2.393	NS
Zn	10	236.7 ± 1.5	236.1 ± 1.2	NS
Hg	10	1.145 ± 1.489	1.660 ± 1.250	NS

Table 10. Comparison of the age distribution of the children in two areas

Area	Age group (years)			
	≤5		7–12	
	No. of examinees	%	No. of examinees	%
High background	7070	52.7	6355	47.3
Control	6356	48.6	6731	51.4

$P < 0.01$

Table 11. Distribution of Down's Syndrome by maternal age

Area	Cases	≥33 years	<33 years
High background	14	13	1
Control	4	4	0

Interim Conclusions

1. Although a definitive conclusion cannot be made, higher rates of diseases believed caused by mutation were not demonstrated for inhabitants of the high background radiation area.

2. The higher incidence of Down's Syndrome in the high background radiation area may reflect the advanced age of the mothers at the time of birth as well as the age distribution of the children examined.

3. The analysis of annually collected data continues to support the claim of lower cancer mortality in the high background radiation area.

4. According to the examinations of cytogenetics and immunology, it is believed, under certain conditions, that within the lymphocytes of inhabitants two different kinds of reactivities can simultaneously occur and compete with each other. This competition may be the reason that an increase in the rate of diseases believed caused by mutations has not been found in the high background radiation area.

5. Further studies are needed to substantiate suppositions and arrive at firm conclusions.

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