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Dose-effect Relationship of Dicentric and Ring Chromosomes in Lymphocytes of Individuals Living in the High Background Radiation Areas in China

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Chromosomes of 39 healthy family members (3 generations from 13 families) living both in the high-level background radiation areas (HBRA) and the control areas (CA) were studied. Cumulative dose from birth to the time of blood sampling was estimated by calculating measured exposure rate in each individual. The cumulative doses ranged 30.9–358.9 and 6.0–59.2 mGy for HBRA and CA, respectively. Peripheral lymphocyte chromosome preparations were made according to our improved method. Dicentric and ring chromosomes (Dic+Rc) were scored in average 2,527 cells per individual in HBRA and 2,694 cells in CA under a microscope equipped with an automated stage. A positive correlation between Dic+Rc and age was found in HBRA, while no such dose relationship was clear in CA. The frequency of Dic+Rc linearly increases over lifetime due to chronic low dose exposure and it is likely that the activation of repair enzymes is not triggered in the present HBRA. Threshold dose (rate) of the induction of chromosome aberrations, if any, is below the present dose (rate) level.

INTRODUCTION

Many *in vitro* studies have been conducted with low-LET radiation at doses less than 500 mGy where dose response of the frequency of chromosome aberrations was shown to be linear. However, the dose response relationship is not clear at the very low dose and dose rate. It has been reported that a significant increase in dicentrics plus ring chromosomes (Dic+Rc) can be detected above the dose of 20 mGy[1)]. Pohl-Rüling[2)] has argued that upon reaching a certain

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level of damage the production of repair enzymes is triggered which function to lower the frequency of chromosome aberration in the very low dose level of below 3.0 cGy/year.

A number of areas with natural high background radiation are found throughout the world, such as in Brazil, India, Iran and China. Analysis of Dic+Rc in peripheral lymphocytes of people living in these areas would provide valuable data of the effect of radiation in such very low doses and dose rates. Several groups have reported that the frequency of chromosome aberrations (Dic+Rc) increased among inhabitants of high background radiation areas (HBRA) in comparison with their respective controls[3–6]. However, the reported frequencies of Dic+Rc in those HBRA are not suitably high compared with that of the generally accepted value (1 Dic+Rc/1000 cells) for the control population[7,8]. Probably a considerable number of Dic+Rc in those HBRA cases might have been lost during the time of culture in the conventional methods used in their analysis.

To obtain more accurate data in quantifying Dic+Rc, we carried out a cytogenetic study in HBRA in the south of China using recently developed techniques with improved recovery of metaphase. In our previous study, preliminary data were obtained from 28 cases[9]. In the present study, we analyzed an additional 11 cases which greatly improved the analysis.

MATERIALS AND METHODS

Study population

Members were chosen from 3 generations in each family for the present study. Twenty-two members were from 8 households living in HBRA, and 17 members were from 5 households in the control area (CA). All subjects were healthy inhabitants in HBRA and in CA. They had no history of significant medical exposure, except occasional chest X-ray examinations which contribute marginally to the cumulative dose of an individual.

Dose Estimation

Exposed dose rate in each family member was measured by a dose rate meter. The exposure to radiation is considered to be operationally constant throughout lifetime, i.e., from birth to the time of blood sampling. Details of the measurement of individual dose is reported by Yuan et al[10], and Morishima et al[11].

Cytogenetic method

The blood samples were assigned code numbers and transported to the cytogenetic laboratory within 5 hours. Chromosome preparations were made according to the improved methods for the study of the low dose range[12], with a slight modification. Since the colcemid was administrated at the beginning of the culture in this method, more than 99.5% of metaphases were in the first division[13]. To avoid scoring the same cell twice, an automated stage system was used. Metaphases having centromere counts of 46 ± 1 were analyzed under a microscope. Metaphases with definite and suspected dicentric, tricentric or centric ring chromosomes were recorded. Final judgement was made by the review of at least three scorers. For some

subjects the same set of metaphases were scored twice independently by two scorers using the automated stage system of our microscope so as to reduce possible overlooking rate.

RESULTS AND DISCUSSION

Subject, age, dose rate, cumulative dose, scored cells and the frequency of detected Dic+Rc are listed in Tables 1 and 2. A total of 55,595 cells for HBRA subjects and 45,799 cells for CA subjects were analyzed. Frequencies of Dic+Rc per 1, 000 cells were 0.49−5.45 for HBRA and 0−2.86 for CA. A considerable number of Dic+Rc which did not accompany a fragment was observed in both groups. When the frequency of Dic+Rc per 1000 cells was plotted against the age of each individual, an obvious trend of increase with age appeared in the HBRA group (frequency of Dic+Rc = 0.5717 + 0.04444 × year, R^2 = 0.7441) but not in the CA group (frequency of Dic+Rc = 0.7227 + 0.0137 × year, R^2 = 0.2111) (Fig. 1). The cumulative dose increased with the age of an individual. There was more than a 3 times difference in the slopes of the age response relationship, i.e., 0.0444 in HBRA and 0.0137 in CA. Therefore it was considered that the increase of Dic+Rc was mainly attributable to the increase in the cumulative

Table 1. Age, dose (air kerma) and the result of chromosome analysis of each family member in HBRA

Case	Age (y)	Dose/y (mGy)	Total Dose (mGy)	Cells Scored	Dic + Rc in 1000 cells		
					With Frag.	Without Frag.	Total
A01	64.1	3.68	235.9	3092	5 (1.62)	8 (2.59)	13 (4.20)
A03	37.1	3.57	132.4	1781	4 (2.25)	2 (1.11)	6 (3.40)
A09	9.4	3.29	30.9	2037	1 (0.49)	0	1 (0.49)
B01	68.9	3.28	226.0	3043	3 (0.99)	6 (1.97)	9 (2.96)
B05	33.3	3.56	118.5	3011	2 (0.66)	5 (1.66)	7 (2.32)
B11	11.6	3.40	39.4	2044	1 (0.49)	2 (0.98)	3 (1.47)
D01	72.8	3.00	218.4	3020	10 (3.31)	1 (0.33)	11 (3.64)
D03	34.1	3.28	111.8	3060	3 (0.98)	4 (1.31)	7 (2.29)
D12	11.2	3.54	39.6	2047	1 (0.49)	1 (0.49)	2 (0.98)
E01	80.8	2.74	221.4	2569	7 (2.73)	7 (2.73)	14 (5.45)
E08	11.5	3.56	40.9	2004	0	2 (1.00)	2 (1.00)
F01	80.7	3.89	313.9	2970	10 (3.37)	5 (1.68)	15 (5.05)
F07	13.2	4.21	55.6	2030	1 (0.49)	1 (0.49)	2 (0.99)
G01	77.2	3.52	271.7	2966	3 (1.00)	4 (1.35)	7 (2.36)
G06	10.9	3.54	38.6	2256	0	3 (1.33)	3 (1.33)
X01	74.5	4.23	315.1	3502	7 (2.00)	4 (1.14)	11 (3.14)
X02	34.4	4.31	148.3	2960	4 (1.37)	1 (0.34)	5 (1.69)
X03	11.4	4.44	50.6	2992	3 (1.00)	0	3 (1.00)
Y01	89.5	4.01	358.9	791	3 (3.79)	0	3 (3.79)
Y2a	46.6	4.01	186.9	3282	12 (3.66)	1 (0.30)	13 (3.96)
Y2b	19.9	4.07	81.0	1743	1 (0.57)	0	1 (0.57)
Y03	10.8	4.19	45.3	2395	2 (0.67)	0	2 (0.67)

Table 2. Age, Dose (air kerma) and the result of chromosome analysis of each family member in the control

Case	Age (y)	Dose/y (mGy)	Total Dose (mGy)	Cells Scored	Dic + Rc in 1000 cells		
					With Frag.	Without Frag.	Total
A01	64.1	3.68	235.9	3092	5 (1.62)	8 (2.59)	13 (4.20)
L02	55.8	0.72	40.2	2006	0	2 (1.00)	2 (1.00)
L06	26.7	0.68	18.2	3081	1 (0.33)	2 (0.65)	3 (0.97)
L07	8.2	0.90	7.4	3056	1 (0.33)	2 (0.66)	3 (0.98)
M01	70.5	0.84	59.2	2016	3 (1.49)	0	3 (1.49)
M04	37.8	0.67	25.3	3021	1 (0.33)	2 (0.66)	3 (0.99)
M08	10.3	0.75	7.7	3032	2 (0.66)	2 (0.66)	4 (1.32)
N01	64.9	0.74	48.0	2010	3 (1.49)	1 (0.50)	4 (1.99)
N04	32.9	0.76	25.0	2823	2 (0.71)	2 (0.71)	4 (1.42)
N08	8.2	0.73	6.0	2009	2 (1.00)	1 (0.50)	3 (1.50)
P01	64.4	0.69	44.4	1908	3 (1.57)	0	3 (1.57)
P02	56.3	0.60	33.8	1889	0	0	0
P05	30.8	0.63	19.4	3104	3 (0.97)	2 (0.64)	5 (1.61)
P08	9.8	0.64	6.3	2125	1 (0.47)	0	1 (0.47)
T01	70.6	0.65	45.9	3145	3 (0.95)	6 (1.91)	9 (2.86)
T2a	47.3	0.65	30.7	4249	6 (1.41)	0	6 (1.41)
T2b	37.7	0.66	24.9	3309	4 (1.20)	1 (0.30)	5 (1.51)
T03	10.4	0.66	6.9	3016	0	0	0

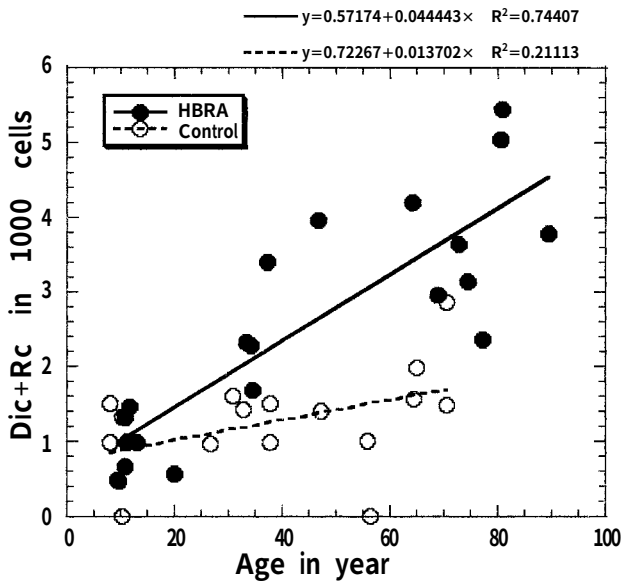

Fig. 1. Age response in the yield of Dic+Rc in HBRA and CA.

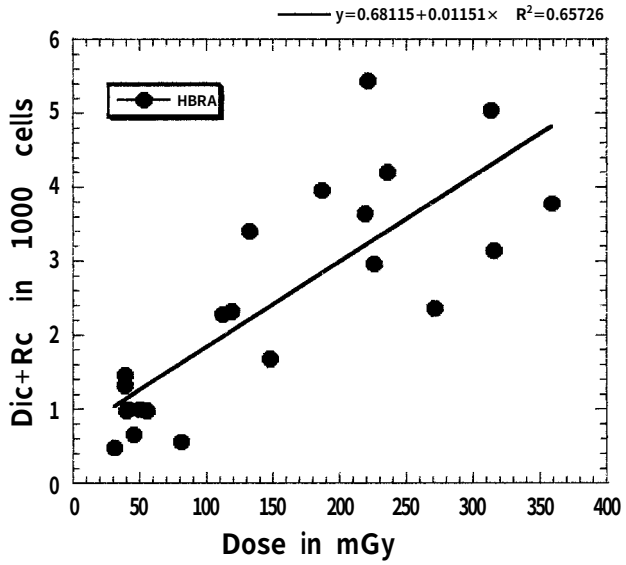

Fig. 2. Dose response in the yield of Dic+Rc in HBRA.

dose. The yield of Dic+Rc was plotted against cumulative doses in HBRA cases. It is clear that the frequencies increased in proportion to the cumulative doses (Fig. 2). The result of regression analysis shows that the dose-effect relationship between cumulative doses (D) and the yield of Dic+Rc (Y) fits well with the linear equation ($Y = 0.6812 + 0.0115D$, $R^2 = 0.6573$). The estimated rate of increase is 1.15×10^{-5} per mGy per cell and this is in good agreement with reported data[14,15]. The linear increase in the frequency of Dic+Rc indicates that activation of repair enzymes is not triggered by exposure to radiation in HBRA. Threshold dose (rate) of the induction of chromosome aberrations, if any, is below the present dose (rate) level.

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