

THE RELATIONSHIP OF HB_s ANTIGEN AND ANTIBODY TO ATOMIC BOMB
RADIATION IN THE ADULT HEALTH STUDY SAMPLE, 1975-77

成人健康調査対象者における HB_s 抗原及び
抗体と原爆放射線との関係, 1975-77年

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SUMMARY

A study was conducted on the frequency of HB_s positive antigen and antibody reactions as an index for determining whether there is any change in the immune competence as a late observable effect of atomic bomb exposure in Hiroshima and Nagasaki.

From among those RERF Adult Health Study participants who received medical examinations during the two years beginning September 1975, a study was undertaken of a total of 2,566 individuals about half of whom were exposed to 100 rad or more and the remainder, as controls, exposed to 0-9 rad, matched by sex, age, and date of examination.

There was no difference between the two comparison groups in the occurrence of positive HB_s antibody reactions (prevalence of HB virus). However, the frequency of positive HB_s antigen reactions (79% remained persistently antigen-positive) was significantly higher in those exposed to 100 rad or more than in the controls. The same tendency was apparent for the two exposure groups when classified by sex, city, and age, though by age the difference between exposure groups among the younger age groups (age 20 or less at the time of the bomb) was more marked. On the other hand, contrary to expectation, there was no difference between exposure groups

要約

広島・長崎の原爆放射線被曝の後影響としての免疫能に変化があるか否かを調べるための指標の一つとして, HB_s 抗原と抗体の陽性率を調査した。

放影研の成人健康調査対象者で1975年9月から2年間に受診した者のうち, 100rad以上の高線量を受けた全数と, その対照者として性, 年齢, 受診年月日を一致させた0-9rad線量群の同数を選んで, 総計2,566人について調査した。

HB_s 抗体の陽性率(HBウイルスの蔓延度)は二つの比較群間に差異はない。しかし, HB_s 抗原の陽性率(このうち, 2年間続けて陽性である, いわゆる持続性抗原陽性者は79%を占める)は100rad以上の高線量群の方が対照群よりも有意に高い。この傾向は二つの被爆群間で性, 都市, 年齢別にみても同様であり, 年齢別には若年(被爆当時20歳以下)の者に差異が著明である。しかし予想に反し, 抗原陽性者

in the distribution by high vs low titers among the antigen-positive individuals.

The above findings suggest that immune competence, using the prevalence of positive HB_s antigen reactions as an index, is depressed in the high dose group, but further careful study, including follow-up of those with persistent positive HB_s antigen reactions, is required before this tentative conclusion can be considered anything other than a working hypothesis.

There is no difference in the prevalence of positive HB_s antibody reactions between Nagasaki and Hiroshima, but the frequency of positive antigen reactions is higher in Nagasaki. With respect to HB_s antigen subtypes, adr occurs in a higher and adw in a lower frequency in Nagasaki than in Hiroshima, corresponding to earlier reports for the Japan archipelago of reverse and complementary distributions of these two subtypes.

INTRODUCTION

Among the late effects of exposure to A-bomb radiation is the development of malignant tumors such as leukemia, lung cancer, breast cancer, and thyroid cancer, but the mechanism of radiation induction is as yet virtually unknown. Though a direct effect of radiation on cells may initiate malignant changes, it is also possible that radiation may exert its effect indirectly by, for example, activating an oncogenic virus or by inducing changes in the immune defense mechanism. In view of data suggesting a high incidence of hepatic cancer in heavily exposed A-bomb survivors¹ and the relation between HB_s antigen and the development of liver cirrhosis and hepatic cancer,² it appears timely to investigate the frequency of positive antigen and antibody titers for B-type hepatitis virus as an index of immune competence and to examine these frequencies in relationship to exposure dose.

HB_s antigen titer was determined in a study of HB_s antigen and antibody on a total of about 5,000 Adult Health Study (AHS)* subjects in Hiroshima and Nagasaki for one year from November 1969.³ Because a modified Ouchterlony's microdetermination method was

の titer による分布は両被爆群間に差異は認められない。

以上の所見は HB_s 抗原の陽性率を指標とした場合、高線量群での免疫能の低下を示唆するものかもしれないが、この暫定的な結論が作業仮説の域を出るまでには、持続性 HB_s 陽性者の追跡調査を含む更に綿密な調査が必要である。

長崎と広島では HB_s 抗体の陽性率に差異はないが、抗原の陽性率は長崎の方が高い。また抗原の subtype は、長崎は広島よりも adr の割合が多く、adw が少ない。この所見は、日本におけるこの subtype の地域分布に関する従来の報告と一致する。

緒言

原爆放射線被曝の後影響には、白血病、肺癌、乳癌、甲状腺癌などの悪性腫瘍の発現があるが、放射線による誘発の機序はまだほとんど不明である。放射線の細胞への直接的影響が悪性変化への原因になり得るが、腫瘍ウイルスを活性化したり、免疫機構に変化を誘発したりして、間接的に影響を及ぼす可能性もある。高線量被爆者に肝癌が高いことを示唆する資料、¹ 並びに HB_s 抗原と肝硬変及び肝癌の発現² との関係から見て、免疫能の指標としての B 型肝炎ウイルスに対する抗原及び抗体の陽性の頻度とその力価を調べ、被曝線量との関係を調べることは重要である。

1969年11月から1年間、広島及び長崎の成人健康調査*対象者約5,000人について実施した HB_s 抗原及び抗体の調査³で、HB_s 抗原の力価を測定した。Ouchterlony 微量定量法の変法を用いたため、抗原

*A biennial physical examination on a fixed cohort of some 20,000 subjects since 1958.

1958年以来、約20,000人の対象者からなる固定集団について、2年ごとに行われている検診。

used, the overall frequency of positive antigen reactions was quite low (0.68%) but was higher in the heavily exposed survivors than the controls (0.93% vs 0.52% but the difference is not statistically significant). A more sensitive immune adherence hemagglutination (IAHA) method used on 961 subjects examined during a 2-month period from September 1971 demonstrated no relationship to radiation dose,⁴ but the number of cases was so small (only 196 subjects exposed to 100 rad or more) that it was considered inappropriate to discuss the findings in relation to radiation dose. In this study, the relationship between exposure dose and HB_s antigen and antibody was examined on a sample including all heavily exposed AHS subjects using a more sensitive test.

MATERIALS AND METHODS

A total of 2,566 members of the AHS sample who underwent routine medical examination in the 2-year period from September 1975 to August 1977 were included in this study and were either survivors exposed to 100 rad or more or controls exposed to 0-9 rad, matched by sex, age, and date of examination. Because the sample structure of the subjects examined during the first year of the survey period had been established two examination cycles previously (4-years earlier) and because the subsequent examination rate differed somewhat by exposure dose, sex, and age, there was a slight difference between the number examined in the two exposure groups, with 1,213 in the heavily exposed (100+ rad) group and 1,353 in the control (0-9 rad) group.

Table 1 shows the composition of the two exposure groups. The distribution ratios by sex, age, and city between the two groups were almost identical.

Serum was used for the determination of the 1,359 subjects examined during the first year ending in August 1976 and plasma for those 1,207 subjects examined in the latter half of the study period. All determinations were made by the Hepatitis Group, Tokyo Metropolitan Institute of Clinical Medicine (Representative; Makoto Mayumi).

An IAHA method was used for HB_s antigen determination and a passive hemagglutination (PHA) method for HB_s antibody.⁵

の陽性頻度はかなり低かったが(0.68%),高線量被爆者では対照者よりも高かった(0.93%対0.52%であったが、この差は統計的に有意でない)。1971年9月から2か月間、961人を対象に、より感度の高い免疫付着反応法(IAHA)を用いたところ、放射線量との関係は認められなかったが、⁴例数があまりに少なかったので(100rad以上の被爆者はわずか196人)、その所見で放射線量との関係を論ずることは妥当でないと考えられた。今回の調査では、成人健康調査対象中の高線量被爆者全員を含む集団を対象に、より感度の高い検査法によって、HB_s抗原及び抗体と被曝線量との関係を調べた。

材料及び方法

本調査は、1975年9月から1977年8月までの2年間に定期検診を受けた成人健康調査対象者計2,566人を対象としたものであり、100rad以上の放射線に被曝した者とこれに性、年齢及び診察年月日を合わせて無作為に選ばれた0~9radに被曝した者を対照として実施された。しかし調査期間の最初の1年間に受診した者は、2診察周期前(4年前)に設定されていたものであり、その後の受診率は被曝線量、性及び年齢別に幾らか異なっているため、二つの被曝群中の受診者数にはわずかな差があった。すなわち、高線量被曝群(100+rad)では1,213人、対照群(0~9rad)では1,353人であった。

表1に、二つの被曝群の構成を示した。この2群間の性、年齢及び都市別分布はほとんど同じであった。1976年8月までの最初の1年間に受診した1,359人の測定検査には血清を用い、次の1年間の受診者1,207人の測定検査には血漿を用いた。測定検査はすべて、東京都臨床医学研究所肝炎研究グループ(代表者:真弓忠)が行った。

HB_s抗原の測定には免疫付着反応法を、HB_s抗体の測定には受身赤血球凝集反応法(PHA)を用いた。⁵

TABLE 1 NUMBER OF SUBJECTS BY RADIATION DOSE, CITY, AGE, AND SEX

表1 対象者数;放射線量,都市,年齢及び性別

Age in years	Both Cities			Hiroshima			Nagasaki		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
100+ rad Exposure Group									
Total	No. 1213	473	740	570	240	330	643	233	410
	% 100.0	39.0	61.0	47.0	19.8	27.2	53.0	19.2	33.8
<40	No. 111	54	57	45	23	22	66	31	35
	% 9.2	4.5	4.7	3.7	1.9	1.8	5.4	2.6	2.9
40-49	No. 418	175	243	180	91	89	238	84	154
	% 34.5	14.4	20.0	14.8	7.5	7.3	19.6	6.9	12.7
50-59	No. 310	76	234	149	44	105	161	32	129
	% 25.6	6.3	19.3	12.3	3.6	8.7	13.3	2.6	10.6
60+	No. 374	168	206	196	82	114	178	86	92
	% 30.8	13.9	17.0	16.2	6.8	9.4	14.7	7.1	7.6
0-9 rad Exposure Group									
Total	No. 1353	543	810	710	264	446	643	279	364
	% 100.0	40.2	59.8	52.5	19.6	32.9	47.5	20.6	26.9
<40	No. 115	55	60	49	22	27	66	33	33
	% 8.5	4.1	4.4	3.6	1.6	2.0	4.9	2.4	2.4
40-49	No. 473	191	282	231	92	139	242	99	143
	% 35.0	14.2	20.8	17.1	6.9	10.3	17.9	7.3	10.6
50-59	No. 340	103	237	197	56	141	143	47	96
	% 25.1	7.6	17.5	14.6	4.1	10.4	10.6	3.5	7.1
60+	No. 425	194	231	233	94	139	192	100	92
	% 31.4	14.3	17.1	17.2	6.9	10.3	14.2	7.4	6.8

RESULTS

As shown in Table 2, in both Hiroshima and Nagasaki, the frequencies of positive reactions (titer 1:32 and over) for the HB_s antigen in the heavily exposed group was higher than that of the control group but no significant difference was noted in the distribution of the antigen by antigen titer. Among those with positive titers the antigen titer tended to be lower in the heavily exposed group, but the difference was not statistically significant (Table 2). The same tendency was noted by sex, but when compared by age for those less than 50 years and 50 or more, there was a difference in occurrence of positive HB_s antigen reactions between the two dose groups among the younger subjects (Table 3). The frequency of positive HB_s antibody reactions, unlike that for the HB_s antigen, showed no difference between the two exposure groups, nor was there any difference between the two exposure groups in the distribution of antibody titers among those exhibiting positive antibody reactions (Table 4).

結果

表2に示すように、広島・長崎の両市とも高線量被爆群のHB_s抗原陽性(力価1:32以上)の頻度は対照群の場合よりも高かったが、同抗原の力価分布に有意な差は認められなかった。陽性力価を示す者のうち、高線量被爆群の抗原力価は低い傾向があったが、その差は統計的に有意ではなかった(表2)。性別には男女とも同じ傾向が認められたが、年齢別に50歳未満の群と50歳以上の群とを比較したところ、前者における二つの線量群間にはHB_s抗原の陽性率に差があった(表3)。HB_s抗体の陽性の頻度は、HB_s抗原の場合と異なって、二つの被爆群間に差が認められず、また抗体が陽性なものにおける抗体力価分布についても二つの被爆群間に差はなかった(表4)。

TABLE 2 HB_s ANTIGEN BY RADIATION DOSE AND CITY表2 HB_s 抗原; 放射線量及び都市別

Dose in rad	Total	Negative	Positive (Titer)					Statistical* Test
			Total	32	64	128	256+	
Both Cities								
Total	No. 2566	2498	68 (2.7%)	14	5	3	46	.05 > P > .02
	%		100	20.6	7.4	4.4	67.6	
0-9	No. 1353	1326	27 (2.0%)	4	3	1	19	
	%		100	14.8	11.1	3.7	70.4	
100+	No. 1213	1172	41 (3.4%)	10	2	2	27	
	%		100	24.4	4.9	4.9	65.9	
Hiroshima								
Total	No. 1280	1255	25 (2.0%)	6	1	2	16	P > .10
	%		100	24.0	4.0	8.0	64.0	
0-9	No. 710	699	11 (1.6%)	1	1	1	8	
	%		100	9.1	9.1	9.1	72.7	
100+	No. 570	556	14 (2.5%)	5	0	1	8	
	%		100	35.7	0.0	7.1	57.1	
Nagasaki								
Total	No. 1286	1243	43 (3.3%)	8	4	1	30	.10 > P > .05
	%		100	18.6	9.3	2.3	69.8	
0-9	No. 643	627	16 (2.5%)	3	2	0	11	
	%		100	18.8	12.5	0.0	68.8	
100+	No. 643	616	27 (4.2%)	5	2	1	19	
	%		100	18.5	7.4	3.7	70.4	

* χ^2 test for difference in positive reactions (>32) between 0-9 rad and 100+ rad groups.0-9 rad 群と100+rad 群との陽性反応(>32)の差についての χ^2 検定.

The frequency of the positive HB_s antigen reaction in Nagasaki was about 1.5 times higher than that of Hiroshima (Table 2). However, there was no difference in the occurrence of the positive antibody reaction (1:4 and over) between the two cities (Table 4). There was also no difference in the distribution of HB_s antigen and antibody titers between the two cities (Tables 2 and 4).

When the difference in the frequency of positive HB_s antigen reactions between the two cities was examined by age, the occurrence of positive reactions was greater in the age group less than 50 in Nagasaki compared to Hiroshima, but no difference was apparent between the two cities in the older group (Table 5).

In studying the relationship between HB_s antigen and HB_s antibody, it was found that HB_s antibody reaction was negative in all subjects with a positive HB_s antigen reaction,

長崎におけるHB_s抗原の陽性の頻度は、広島の場合より約1.5倍高かった(表2)。しかし抗体の陽性率(1:4以上)には、両市間に差はみられなかった(表4)。またHB_s抗原及び抗体の力価の分布にも、両市間に差はなかった(表2及び4)。

両市間におけるHB_s抗原陽性の頻度の差を年齢別に調べた場合、長崎の50歳未満の年齢群では、広島に比べて陽性率が高かったが、50歳以上の群では両市間に明白な差は認められなかった(表5)。

HB_s抗原とHB_s抗体との関係の検討では、HB_s抗原の反応が陽性である者全員がHB_s抗体反応は

TABLE 3 HB_s ANTIGEN BY DOSE, SEX, AND AGE表3 HB_s 抗原; 線量, 性及び年齢別

Dose in rad	Total	Negative	Positive (Titer)					Statistical* Test
			Total	32	64	128	256+	
Male								
Total	No. 1016	979	37 (3.6%)	12	2	1	22	.05 > P > .02
	%		100	32.4	5.4	2.7	59.5	
0-9	No. 543	530	13 (2.4%)	4	1	-	8	
	%		100	30.8	7.7	-	61.5	
100+	No. 473	449	24 (5.1%)	8	1	1	14	
	%		100	33.3	4.2	4.2	58.3	
Female								
Total	No. 1550	1519	31 (2.0%)	2	3	2	24	P > .10
	%		100	6.5	9.7	6.5	77.4	
0-9	No. 810	796	14 (1.7%)	-	2	1	11	
	%		100	-	14.3	7.1	78.6	
100+	No. 740	723	17 (2.3%)	2	1	1	13	
	%		100	11.8	5.9	5.9	76.5	
Age < 50								
Total	No. 1117	1082	35 (3.1%)	5	3	2	25	.10 > P > .05
	%		100	14.3	8.6	5.7	71.4	
0-9	No. 588	575	13 (2.2%)	-	3	-	10	
	%		100	-	23.1	-	76.9	
100+	No. 529	507	22 (4.2%)	5	-	2	15	
	%		100	22.7	-	9.1	68.2	
Age 50+								
Total	No. 1449	1416	33 (2.3%)	9	2	1	21	P > .10
	%		100	27.3	6.1	3.0	63.6	
0-9	No. 765	751	14 (1.8%)	4	-	1	9	
	%		100	28.6	-	7.1	64.3	
100+	No. 684	665	19 (2.8%)	5	2	-	12	
	%		100	26.3	10.5	-	63.2	

*See footnote Table 2 表2の脚注参照

while the HB_s antigen reaction was negative in all those with a positive HB_s antibody reaction.

Of the 1,359 subjects examined during the first year, 1,242 had a determination of HB_s antigen and HB_s antibody two years earlier (though antibody determination was not possible on three cases). The HB_s antigen and antibody determinations of the previous and current examinations are compared in Table 6. Of the 30 subjects, 26 (86.7%) who were antigen-positive (titer 32 and over) in the previous determination were again positive in this current determination.

陰性であり, HB_s 抗体の反応が陽性である者はすべて HB_s 抗原反応が陰性であった。

最初の1年間に受診した1,359人のうち, 1,242人はそれより2年前にHB_s 抗原及び抗体の測定が行われていた(ただし, うち3例では抗体測定が行われなかった)。前回と今回のHB_s 抗原及び抗体の測定結果の比較を表6に示す。前回の検査で抗原が陽性(力価1:32以上)であった30例中26例(86.7%)は, 今回の測定でも陽性であった。

TABLE 4 HB_s ANTIBODY BY DOSE AND CITY表4 HB_s 抗体; 線量及び都市別

Dose in rad	Total	Negative	Positive (Titer)					Statistical* Test	
			Total	4	8	16	32		64+
Both Cities									
Total	No. 2561	1715	846 (33.0%)	62	138	156	194	296	P > .10
	%		100	7.3	16.3	18.4	22.9	35.0	
0-9	No. 1349	910	439 (32.5%)	36	61	92	104	146	
	%		100	8.2	13.9	21.0	23.7	33.3	
100+	No. 1212	805	407 (33.6%)	26	77	64	90	150	
	%		100	6.4	18.9	15.7	22.1	36.9	
Hiroshima									
Total	No. 1279	869	410 (32.1%)	25	45	78	100	162	P > .10
	%		100	6.1	11.0	19.0	24.4	39.5	
0-9	No. 709	487	222 (31.3%)	14	21	50	56	81	
	%		100	6.3	9.5	22.5	25.2	36.5	
100+	No. 570	382	188 (33.0%)	11	24	28	44	81	
	%		100	5.9	12.8	14.9	23.4	43.1	
Nagasaki									
Total	No. 1282	846	436 (34.0%)	37	93	78	94	134	P > .10
	%		100	8.5	21.3	17.9	21.6	30.7	
0-9	No. 640	423	217 (33.9%)	22	40	42	48	65	
	%		100	10.1	18.4	19.4	22.1	30.0	
100+	No. 642	423	219 (34.1%)	15	53	36	46	69	
	%		100	6.8	24.2	16.4	21.0	31.5	

* χ^2 test for difference in positive reactions (>4) between 0-9 rad and 100+ rad groups.0~9 rad 群と100+rad 群との陽性反応(>4)の差についての χ^2 検定TABLE 5 HB_s ANTIGEN BY AGE AND CITY表5 HB_s 抗原; 年齢及び都市別

Age in Years	Total	Negative	Positive (Titer)					Statistical Test for Difference between Cities
			Total	32	64	128	256	
Hiroshima								
Total	No. 1280	1255	25 (2.0%)	6	1	2	16	.10 > P > .05
< 40	No. 94	93	1 (1.1%)	0	0	0	1	.05 > P > .02
40-49	No. 411	404	7 (1.7%)	2	1	1	3	.10 > P > .05
50-59	No. 346	340	6 (1.7%)	1	0	0	5	P > .10
60+	No. 429	418	11 (2.6%)	3	0	1	7	P > .10
Nagasaki								
Total	No. 1286	1243	43 (3.3%)	8	4	1	30	
< 40	No. 132	122	10 (7.6%)	1	1	0	8	
40-49	No. 480	463	17 (3.5%)	2	1	1	13	
50-59	No. 304	299	5 (1.6%)	2	0	0	3	
60+	No. 370	359	11 (3.0%)	3	2	0	6	

TABLE 6 CHANGE IN HB_s ANTIGEN & HB_s ANTIBODY TITER DURING 2-YEAR PERIOD表6 2年間におけるHB_s抗原及びHB_s抗体の力価の変化

HB _s Antigen Titer							
II	I					Total	
	< 32 (neg.)	32	64	128	256+		
< 32 (neg.)	1205	1	3			1209	
32	2	1				3	
64	1	1	2			4	
128	1			1		2	
256+	3		9	8	4	24	
Total	1212	3	14	9	4	1242	

HB _s Antibody Titer							
II	I					Total	
	< 4 (neg.)	4	8	16	32		64+
< 4 (neg.)	775	2	10	4	1		792
4	43	3	1				47
8	54	16	11	1	1		83
16	31	10	16	5	1		63
32	18	18	35	15	5	2	93
64+	10	3	37	40	54	17	161
Total	931	52	110	65	62	19	1239

Furthermore, of the 1,212 subjects showing a negative antigen titer in the previous determination, 7 (0.57%) were positive in the current determination making the rate of conversion to positive in this population about 0.3% per year.

The 26 cases (78.8%) among the 33 subjects whose antigen determination in the current test was positive (titer of 32 or more) were cases who remained positive. The proportion of the persistent positive cases to the positive cases was 12/16 (75.0%) in the heavily exposed group and 14/17 (82.4%) in the controls, a difference which is not statistically significant. Further, in the 2-year period, the rate of conversion to positive in the heavily exposed group was 4/581 (0.69%) and in the controls 3/631 (0.48%), which is not a statistically significant difference.

Study of temporal changes in HB_s antibody reaction (Table 6) shows that of the 308 subjects who were positive at the previous determination, 17 (5.5%) were negative in the current determina-

更に、前回の測定で抗原力価陰性を示した1,212例のうち、7例(0.57%)は今回の測定で陽性であった。これにより本集団における陽性転化率は年間約0.3%であることが分かった。

今回の検査で抗原が陽性(力価1:32以上)であった33例中26例(78.8%)は、引き続き陽性であった例である。持続性陽性例対陽性例の比は、高線量被爆群では12/16例(75.0%)、対照群では14/17例(82.4%)であり、その差は統計的に有意ではなかった。また、その2年間における陽性転化率は、高線量被爆群では4/581例(0.69%)、対照群では3/631例(0.48%)であり、これも統計的に有意な差ではなかった。

HB_s抗体反応の時間的变化に関する調査(表6)では、前回の測定で陽性であった308例のうち17例(5.5%)は、今回の測定で陰性であることが認められた。前回

tion. Of the 931 subjects who were negative in the last determination, 156 (16.8%) changed to positive in the current determination. The temporal changes in antibody value were classified into five groups:

1. Titer unchanged since previous determination

前回の測定以来力価に変化のないもの 816 65.9 %

2. Elevated by 1 serial dilution

1回の連続希釈で上昇したもの 144 11.6 %

3. Elevated by 2 or more serial dilution

2回又はそれ以上の連続希釈により上昇したもの 256 20.7 %

4. Depressed by 1 serial dilution

1回の連続希釈で下降したもの 7 0.6 %

5. Depressed by 2 or more serial dilution

2回以上の連続希釈で下降したもの 16 1.3 %

Total 合計 1,239 100.0 %

No significant differences were noted in negative conversion rate, positive conversion rate, or temporal change by dose, city, sex, or age between the comparison groups.

DISCUSSION

The frequency of positive HB_s antibody reactions was 32.1% in Hiroshima and 34.0% in Nagasaki and thus there was no significant difference in the prevalence of HB virus between the two areas. However, the rate of positive HB_s antigen reactions in Nagasaki of 3.3% was higher than the 2.0% in Hiroshima. In autopsy cases, no difference between Hiroshima and Nagasaki was observed for the prevalence of liver cirrhosis (post hepatitis liver cirrhosis)⁶ but the prevalence of primary liver cancer, especially liver cancer with liver cirrhosis⁷ in Nagasaki is about 3 times higher than in Hiroshima. Further, the proportion of liver cancers with post hepatitis liver cirrhosis which comprises the majority of liver cirrhosis cases is higher in Nagasaki (7/17 = 41.2%) than in Hiroshima (5/44 = 11.4%), which may be partly explained by the higher frequency of positive HB_s antigen reactions in Nagasaki than in Hiroshima.

Although the occurrence of positive HB_s antigen reactions differs between Hiroshima and Nagasaki, the composition of the heavily exposed group and the controls do not differ significantly from

の測定で陰性を示した931例のうち156例(16.8%)は、今回の測定で陽性に変化していた。抗体価の時間的変化を次の5群に分類した:

比較群間では陰性転化率、陽性転化率、及び線量、都市、性、又は年齢別による時間的変化に有意な差は認められなかった。

考 察

HB_s 抗体の陽性の頻度は広島で32.1%、長崎で34.0%であったので、両市間のHBウイルスの有病率に有意な差はなかった。しかし、長崎におけるHB_s 抗原の陽性率3.3%は、広島の2.0%より高かった。剖検例では肝硬変(肝炎後性肝硬変)⁶の頻度に広島・長崎間の差はなかったが、長崎の原発性肝癌、特に肝硬変を伴う肝癌⁷の頻度は、広島より約3倍高い。更に、肝硬変例の主体である肝炎後性肝硬変に肝癌を伴う頻度は、長崎(7/17=41.2%)の方が広島(5/44=11.4%)より高いが、これは長崎におけるHB_s 抗原の陽性の頻度が広島より高いことによって一部説明できるかもしれない。

HB_s 抗原の陽性率は広島・長崎間で異なるけれども、高線量被爆群と対照群の構成は表1で示すように性、

one another by sex, age, or city as shown in Table 1. Therefore, the significantly higher rate of positive HB_s antigen reactions among the heavily exposed group compared to the controls is not ascribable to differing distributions of these three factors. The greater prevalence of positive antigen reactions in the heavily exposed group is observed consistently regardless of location by city, sex, or age. When classified by age, a stronger relation to radiation dose is noted in the less than 50 age group (age less than 20 at the time of the bomb, ATB) than in the 50 or more age group. This is consistent with the general trend for radiation effects (especially radiation-induced cancer) to be more marked among those exposed at younger age.¹

On the contrary, the occurrence of positive HB_s antibody reactions is about 33% and there is no difference between the two exposure groups. According to a recent RERF study of A-bomb survivors conducted more than 30 years after exposure, using phytohemagglutinin response of T lymphocytes as an index, the immune competence of a heavily exposed group appeared to be depressed below that of controls.⁸ Thus, although there is apparently no difference between the comparison groups in the occurrence of HB viral infection, it may be that the increased prevalence of positive HB_s antigen reactions among the heavily exposed group is possibly ascribable to radiation-induced depression of immune competence.

On the other hand, the distribution of antigen titers among the antigen-positive subjects was somewhat lower in the heavily exposed group than in the controls, the frequencies of antigen titers 256 or over being 65.9% in the former, and 70.4% in the latter; however, the difference is not statistically significant. In other words, it might be expected that the proportion having a high titer would be higher among those with depressed immunotolerance due to radiation exposure, but no such tendency is apparent here.

Of the 68 antigen-positive individuals, 33 had been tested two years earlier and 26 (78.8%) were positive at that time and thus are considered as persistent antigen-positive cases. The prevalence of persistent antigen-positive cases was 12/16 (75.0%) in the heavily exposed group and 14/17 (82.4%) in the control group, which is not a statistically significant difference. Further follow-up study of the positive HB_s

年齢又は都市別で有意な差はない。したがって、高線量被爆群におけるHB_s抗原の陽性率が対照群に比べて有意に高いのは、これら三つの因子の分布の差にはよらない。高線量被爆群に抗原の陽性率が高いことは、都市、性又は年齢別分布とは無関係に一貫して認められる。年齢別に分類すると、50歳未満群(原爆時20歳未満)に認められる放射線量との関係は、50歳以上群のそれよりも強い。これは、放射線の影響(特に放射線誘発癌)が若年時の被爆者により著明である一般的傾向¹と一致している。

これに対してHB_s抗体陽性率は約33%で、二つの被爆群間に差はない。放影研で原爆被爆者を対象に、被爆後30年以上も経ってTリンパ球の植物性血球凝集素反応を指標に用いて行った最近の調査によれば、高線量被爆群の免疫能は対照群のそれよりも低下しているようであった。⁸したがってHBウイルス感染率では、二つの比較群間に差がないようであるが、高線量被爆群におけるHB_s抗原の陽性率の増加は、恐らく放射線による免疫能の低下に起因するものと思われる。

他方、抗原陽性者における抗原力価の分布は、対照群よりも高線量被爆群の方が幾らか低く、1:256以上の抗原力価の頻度は、被爆群で65.9%、対照群で70.4%であったが、その差は統計的に有意ではない。換言すれば、放射線被曝によって免疫耐性が低下している者では、高力価を有する者の割合が大きいたことが期待されるが、そのような傾向はここでは認められない。

抗原が陽性である68例のうち33例は2年前に検査されており、26例(78.8%)はその当時陽性であったので、抗原陽性の持続例と考えられる。持続性抗原陽性例の頻度は、高線量被爆群では12/16(75.0%)、対照群では14/17(82.4%)であったが、これは統計的に有意な差ではない。肝臓疾患(肝炎、肝硬変及び肝癌)の発現との関係をより明らかにするために、

antigen cases and particularly of the persistently positive cases is necessary to discern a clearer relationship with the development of hepatic diseases (hepatitis, hepatocirrhosis, and hepatic cancer).

Among those tested two years ago, HB_s antigen adw, and adr subtypes⁹ were also determined for 25 of the antigen-positive individuals. In Hiroshima, the percentage of those with the adw subtype is greater than in Nagasaki (Hiroshima 2/10 = 20%, Nagasaki 2/15 = 13%), while for adr it is lower (Hiroshima 80%, Nagasaki 87%). Though the numbers are small, these differences are in agreement with an earlier study where opposing clines were reported for the Japanese, decreasing for adw subtypes from north to south, and increasing for adr subtypes (Okinawa excluded: few adr are found there). This distribution of the HB_s antigen subtypes is interpreted as an indication of "vertical" or maternal-to-fetus transmission of the HB virus.⁹

HB_s 抗原陽性例, 特に持続性陽性例について更に追跡調査を行う必要がある。

2年前に検査を行った者のうち, 抗原が陽性を示した25例については, HB_s 抗原 adw 及び adr の subtype⁹ の決定も行った. 広島では, adw subtype を有する者の百分率は長崎より高い(広島 2/10 = 20%, 長崎 2/15 = 13%)が, adr の方は低い(広島80%, 長崎87%). 例数は少ないが, これらの差異は日本人に認められる二つの相反する地域的な差異, すなわち北から南に下るにつれて adw subtype が減少し, 反対に adr subtype が増加する(ただし, ほとんど adr が認められない沖縄は除外)と報告されている別の調査結果と一致している. この HB_s 抗原 subtype の分布は, HB ウイルスの "垂直感染" すなわち母親から胎児への感染を示すものと考えられている.⁹

REFERENCES

参考文献

1. BEEBE GW, KATO H, LAND CE: Studies of the mortality of A-bomb survivors. 6. Mortality and radiation dose, 1950-1974. *Radiat Res* 75:138-201, 1978 (RERF TR 1-77)
2. 平山 雄, 西岡久寿彌: Hepatitis B ウイルス感染症における問題点. *内科* 34: 918-26, 1974 (HIRAYAMA T, NISHIOKA K: Some problem on infection by Hepatitis B virus. *Naika-Intern Med*)
3. BELSKY JL, KING RA, ISHIMARU T, HAMILTON HB, NAKAHARA Y: Hepatitis-associated antigen in atomic bomb survivors and nonexposed control subjects: Seroepidemiologic survey in a fixed cohort. *J Infect Dis* 128:1-7, 1973 (ABCC TR 30-71)
4. BELSKY JL, OKOCHI K, ISHIMARU T, HAMILTON HB: Hepatitis-associated antigen and antibody in A-bomb survivors and nonexposed subjects, Hiroshima and Nagasaki. *Radiat Res* 52:528-35, 1972 (ABCC TR 12-72)
5. 真弓 忠: B型肝炎ウイルスについて. *日本医師会雑誌* 80: 618-26, 1978 (MAYUMI M: Hepatitis B virus. *Nihon Ishikai Zasshi-J Jpn Med Assoc*)
6. SHREIBER WM, KATO H, ROBERTSON JD: Cirrhosis of the liver, Hiroshima-Nagasaki, 1 October 1961-31 December 1967. *ABCC TR* 17-69
7. SHREIBER WM, KATO H, ROBERTSON JD: Primary carcinoma of the liver in Hiroshima and Nagasaki, Japan. *Cancer* 26:69-75, 1970 (ABCC TR 15-69)
8. YAMAKIDO M, AKIYAMA M, DOCK DS, HAMILTON HB, AWA AA, KATO H: T and B cells and PHA response of peripheral lymphocytes among atomic bomb survivors. *RERF TR* 23-81
9. 宮川侑三, 真弓 忠: オーストラリア抗原 (HB_s 抗原) の Subtype. *内科* 34: 927-34, 1974 (MIYAGAWA Y, MAYUMI M: Subtype of Australian antigen (HB_s antigen). *Naika-Intern Med*)