The Hepatitis B Antigen and Antibody of Healthy Donors in a Farm Area.

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Ausria II-125 and Ausab were used for testing 1,000 sera from apparently healthy blood donors living in a geographically relatively isolated farm area in the northern part of Shikoku-island. Hepatitis B surface antigen was detected in 2.1% of the donors. The prevalence of antibody to the antigen was 19%. A significant excess of the antigen carriers was detected among males and among donors aged 20-29 years. The frequency of detectable antibody against the antigen increased with advancing age. There was no significant differences in the prevalence of the antibody between males and females. Only 9 male donors were found to have elevated serum glutamyl-oxalacetic-transaminase level. Of these donors with elevated transaminase level, one was with positive antigen and five were with positive antibody.

Key Words: Ausria II-125, Ausab, Glutamic-oxalacetic-transaminase, Glutamic-pyruvic-transaminase, Serum bilirubin, Alkaline phosphatase, Radioimmunoassay, Liver disease, Age and sex differences, and Epidemiology.

Many articles have described the close relation between hepatitis antigen (HBAg) and hepatitis (1-3). The incidence of HBAg and anti-HBAg (HBAb) in normal population have been reported in several regional studies (4-9). These prevalence were described ranging from 1% to 3.5% and 11% to 25%, respectively. The technique used for these studies were micro-Ouchterlony (MO), single radial immunodiffusion (SRI), immune adherence hemagglutination (IAHA), immunoelectro-osmophoresis (IEOP), passive hemagglutination (PHA), reversed passive hemagglutination (RPHA) or hemaggluti-

nation inhibition (HAI).

Recently a radioimmunoassay (RIA) technique followed by chromatoelectrophoresis was reported that increased the sensitivity of detection of HBAg by at least 100-fold and of HBAb by at least 20-fold in comparison with complement fixation technique (CF) (10). Further modification of the radioimmunoassay procedure were achieved by using double antibody precipitations (RIA-DAP) (11, 12) and solid phase techniques (RIA-SP) (12, 13). A commercial product based on the latter technique became available, but limitations of the assay for HBAg were discussed in several reports because of the presence of false positive (14-17). Modification of the method by changing incubation time, temperature, or adding normal guinea pig serum to the reaction mixture at second incubation, re-

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duced the non-specific reaction (18). Recently, an improvement of the technique was achieved by using heterologous pig-human antibody sandwich technique (19).

This report summarizes data on the age- and sex-specific prevalence of HBAG and HBAb in apparently healthy donors who live in a geographically restricted farm area by using commercial products, Ausria II-125 and Ausab which techniques are based on the heterologous sandwich principle.

MATERIALS AND METHODS

Donors were enrolled during the period between June 1975, and March 1976, who underwent donation at Mitoyo General Hospital. All donors live in the western part of Mitoyo, Kagawa Prefecture in which part the population is about 50,000. Mitoyo is a farming county in the northern part of the Shikoku-island surrounded by the Seto-inland sea and mountains. Most residents are engaged in farming and don't go another province for work. The Japanese old customs are still lingering on this district. It is a custom of this area from early times that the eldest son succeed to his father's farming and the other go to city for work. The social and hygienic conditions are moderately good compared to the ones of the average Japanese countryside. One thousand donors, about 2% of the population were tested for HBAG and HBAb. In all instances serum was taken from persons having no signs or symptom of liver disease. The samples were collected at the central laboratory in glass tubes and they were frozen until ready for testing.

Assays for HBAG and HBAb were done by Ausria II-125 and Ausab as indicated by the manufacturer. All specimens were also tested for glutamic-oxalacetic transaminase activity, glutamic-pyruvic transaminase activity, bilirubin, and alkaline phosphatase activity.

RESULTS

Table 1. Prevalence rate according to age and sex of hepatitis B antigen among blood donors.

Age group	Males			Females			Both		
	Total No.	No. with HBAG	Rate per 100	Total No.	No. with HBAG	Rate per 100	Total No.	No. with HBAG	Rate per 100
<20	32	1	3.13	19	0	0	51	1	1.96
20-29	306	15	4.90	89	1	1.12	395	16	4.05
30-39	231	1	0.43	52	0	0	283	1	0.35
40-49	150	0	0	53	0	0	203	0	0
50	60	3	5.0	8	0	0	68	3	4.41
Total	779	20	2.57	221	1	0.45	1,000	21	2.10

Table 2. Prevalence rate according to age and sex of hepatitis B antibody among blood donors.

Age group	Males			Females			Both		
	Total No.	No. with HBAb	Rate per 100	Total No.	No. with HBAb	Rate per 100	Total No.	No. with HBAb	Rate per 100
<20	32	6	18.8	19	3	15.8	51	9	17.6
20-29	306	45	14.7	89	10	11.2	395	55	13.9
30-39	231	48	20.8	52	9	17.3	283	56	19.8
40-49	150	43	28.7	53	9	17.0	203	52	25.6
50	60	14	23.3	8	4	50.0	68	18	26.5
Total	779	156	20.0	221	35	15.8	1,000	190	19.0

Table 3. Relationship of HBAG, HBAb and S-GOT.

HBAG and HBAb	Males			Females			Both		
	Total No.	No. with normal GOT	No. with elevated GOT	Total No.	No. with normal GOT	No. with elevated GOT	Total No.	No. with normal GOT	No. with elevated GOT
HBAG(+)	20	19(95.0%)	1(5.0%)	1	1(100%)	0(0%)	21	20(95.2%)	1(4.8%)
HBAb(+)	156	151(96.8%)	5(3.2%)	35	35(100%)	0(0%)	191	186(97.4%)	5(2.6%)
HBAG(-) & HBAb(-)	603	600(99.5%)	3(0.5%)	185	185(100%)	0(0%)	788	785(99.6%)	3(0.4%)
Total	779	770(98.8%)	9(1.2%)	221	221(100%)	0(0%)	1,000	991(99.1%)	9(0.9%)

The frequency of HBAG, detectable by the RIA, in sera from normal blood donors is summarized in Table 1. HBAG was detected in sera of 21 of the 1,000 donors. The antigen was found more frequently in male donors than female donors. The overall prevalence rate was 2.57% male donors and 0.45% female donors. In both sexes, the highest prevalence was observed in the group 20-29 year of age.

Table 2 shows the incidence of HBAb in the donors. 190 individual sera from 1,000 healthy donors were found to be HBAb positive. The prevalence of the antibody was slightly higher among male than female. HBAb was detected in 20.0%

of male in comparison to 15.8% of female. The frequency of the antibody increased with advancing age.

Elevated glutamic oxalacetic transaminase levels were observed in 9 males (Table 3). Of these donors, HBAb were detectable in one donor and 5 donors, respectively. In all sera from female donors, serum transaminase activities were within the normal range. None of specimen from the donors showed an elevation of alkaline phosphatase or bilirubin level.

DISCUSSIONS

The geographic distribution and sex-and age-specific prevalence of HBAg in normal population were described in several reports (1, 20). The antigen was quite rare in normal Americans and was not uncommon in several tropical populations. It also occurred in Japanese and Mediterranean population in lower frequency (about 1%). West African population contained the antigen in high frequency (1, 20). The frequency was invariably higher in the younger than in the older age groups, and in males than in females in nearly all the population (1, 20).

The incidence of HBAg in blood donors by MO technique was reported from Paris (6.2%) (21), Minnesota (0.06-1.47%) (22), Copenhagen (0.18%) (23), Tokyo (1.0%) (4) and from Taiwan (3.1%) (24), and by IEOP technique was reported from Glasgow (0.08%) (25), New York (0.15%) (26), New Orleans (0.7%) (27), Mainz (0.12%) (28) and from American Red Cross donor population (0.10%) (29). Following the original study in Tokyo by using MO technique, IAHA method was developed and resulted in a 2-fold higher incidence of HBAg (5) than by MO technique (4).

More recently RIA techniques were described that increased the sensitivity of detection of HBAg (10-19) by at least 3 to 8 times as many positive sera as the CF, MO or IEOP technique. The Ausria II-125 methodology which was used in our study had demonstrated a very high degree spe-

cificity when compared with the earlier RIA technique (19).

As shown in Table 1, a slightly higher incidence (2.1%) was found in Mitoyo than in Tokyo (2.0%). The actual prevalence rates in these areas will be in the same order since IAHA technique is quite sensitive (5). The incidence of HBAb in the other parts of Japan was reported to be 3.5% in Akita (6) (by IAHA), 2.1% in Oku-Hida (7) (by IAHA), 2.1% in Gifu (8) (by RPHA), and 2.3% in Aki (9) (by IAHA). An excess prevalence of HBAb among male donors and young adults was observed as reported by the other authors (1, 5-8, 20, 23, 26).

HBAb carriers will increase as exposure to HBAb increases (30-33). It was stated that HBAb exposure became apparent when pre-existing HBAb increased in its titer or when seroconversion from HBAb negative to positive is noted (32). Therefore the prevalence rate of HBAb would suggest the extent of exposure to HBAb (24, 34). We obtained a lower incidence of HBAb in Mitoyo by the most sensitive method (Table 2) than in Akita (24.8% by PHA) (6), in Oku-Hida (25.8% by PHA) (7) and in Aki (22.2% by IEOP) (9). The result suggests a lower extent of past exposure to HBAb in Mitoyo than the other parts. An association of HBAb with age (age group: 20-29) was observed in Mitoyo as described in the other parts of this country (6, 7, 9, 23).

The incidence of donors with elevated serum transaminase activity was only 0.9%. Strikingly, all sera from 221 female donors were found to have normal serum transaminase levels. A more higher prevalence rate of elevated serum transaminase activity was observed in Oku-Hida (3.7%) (7) and Aki (19.0%) (9). The elevated serum transaminase activity was determined in 4.8% of donors with HBAb. A lower incidence was detected in Oku-Hida (0.4) (7) and higher incidences were determined in Aki (38.5%) (9) and in New York (23%) (26). A significantly lower incidence of HBAb carrier with elevated serum transaminase acti-

vity was determined in Mitoyo (2.6%) than Oku-Hida (8.5%) (7) and Aki (18.4%) (9).

Since a recent report (35) suggested that normal serum transaminase activity in HBsAg or HBsAb carrier does not exclude significant chronic damage which may be detected histologically, we are planning a follow-up study including liver biopsy of these carriers.

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