Biochemical Findings Compared with Histologic Observations in Carriers of Hepatitis B Antigen (37312)

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The studies on the hepatitis B antigen (HB Ag) have established the fact that, depending on the geographic location, a variable number of people are chronic carriers of the antigen without any apparent clinical symptoms (1, 2). These carriers may harbor subclinical liver disease that can be demonstrated histologically and/or biochemically. Microscopic examination of liver biopsy specimens from HB Ag carriers indicated various degrees of abnormality in the majority of the carriers (3). Biochemical data are useful to detect occult abnormalities in asymptomatic carriers for appropriate management. The purpose of this report is to present the biochemical findings and histologic observations in 31 asymptomatic HB Ag carriers.

Experimental. Out of a group of 109 clinically asymptomatic HB Ag carriers, who were detected among 2190 healthy blood donors 20–25 years old, 31 volunteered for this study. The 31 carriers were hospitalized and subjected to clinical examination and liver biopsy; blood was drawn for chemical analysis. Liver biopsy specimens were obtained by the technique of Menghini (5). Histologic examination was performed after the specimens were fixed in a mixture of equal parts of 10% formalin and 96% ethanol, embedded in paraffin wax and stained routinely in hematoxylin-eosin (H & E). Serum glutamic-pyruvic transaminase (GPT) activity was determined by the modified method of Henry *et al.* (6), lactate dehydrogenase (LDH)-isozymes by our quantitative electrophoretic technique (7). Quantitative determination of serum immunoglobulins was performed by a radial immunodiffusion method (8) using commercial immunoplates.

Results. Physical examination of the 31 HB Ag carriers did not reveal any remarkable clinical signs with the exception of slight hepatomegaly in the majority of the cases. None of these carriers was a professional blood donor or had any history of blood transfusion or hepatitis.

The histologic evaluation of the biopsy specimens showed two cases with no apparent histologic abnormality and 29 cases with morphologic changes. Figure 1 is representative of 4 cases with moderate chronic portal inflammation and parenchymatous reaction, which is observed in chronic persistent hepatitis (9). The remaining 25 cases showed slight inflammatory infiltrations mainly in the portal tracts.

Liver is rich in LDH isozyme-5 and GPT. The combined determination of these enzymes in serum served as a double-check for the evaluation of liver abnormality and for checking each other. The normal range for GPT given by the method used is 6–34 Wroblewski units. In a control series of 37 normal HB Ag negative subjects the same range was found in this study. Taking into consideration this control range, in 14 carriers, serum GPT activity was higher than the normal. A good correlation in these 14 cases was found between increased activity of GPT and increased density of LDH isozyme-5. The percent distribution of LDH-isozymes in normal serum by quantitative densitometry (7) was found 30-40-20-6-4 for isozymes 1 to 5, respectively; one is the anodic and 5 the cathodic isozyme. LDH-5 was consistently demonstrated in normal serums by this technique. The low intensity of LDH-5 zone allows the detection of small deviations from the normal.

Determination of serum immunoglogulins

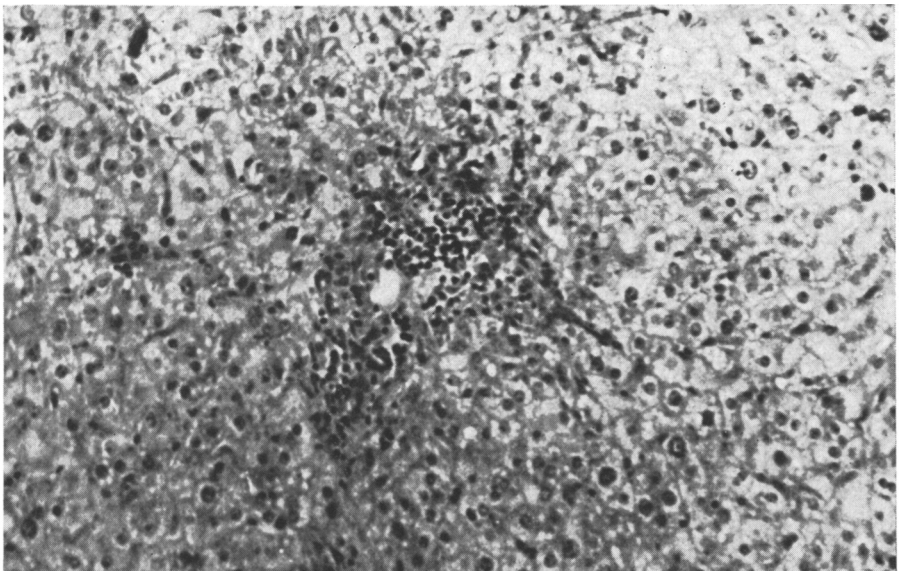

FIG. 1. Histologic section of a liver biopsy specimen showing chronic inflammation with the appearance of inflammatory cells (chronic persistent hepatitis) H & E × 120.

demonstrated increased concentration of IgG in the majority of the cases. As shown in Table I, elevation of IgG was found in one of the two cases with normal liver histology, in 3 out of 4 cases with chronic persistent hepatitis, and in 17 of the 25 cases with inflammatory reaction. On the contrary, elevation of IgA was found in 2 cases and IgM only in 5 of these cases. The ranges of the immunoglobulins found in 37 HB Ag negative subjects from the same group of volunteer blood donors is also given in the Table I for comparison. These normal ranges are similar to those given by the commercial source of immunoplates.

Discussion. While the reason for the persistence of HB Ag in the chronic carriers is unknown, the existence of these carriers in the society has created a new clinical entity, potential risk in public health, and a problem to the physician for their management. Since the incidence of HB Ag carriers in the general population in Greece is much higher, 3–4% (10), than in other countries, (USA 0.1%, Denmark 0.2%), these problems are much greater in this country. Histologic evidence indicated clearly (Fig. 1) that in 4 of our cases, the pathologic changes are similar with the findings described by other investigators (9) and classified as persistent hepatitis. In the rest of our cases, a mild scattered reaction was observed.

This investigation was directed towards the determination of SGPT and LDH isozyme-5 for the detection of liver tissue changes, and in the study of immunoglobulins, which reflected the overall immune response to the antigen in the hosts. The increased activities of these serum enzymes and IgG found in many cases, raises the question as to whether they are transient, as in certain types of hepatitis, or permanent, associated with persistent antigenemia. This question is under investigation.

The useful information gained in this preliminary study is that there are definite histologic and biochemical abnormalities in carriers; sensitive methods and closely controlled studies may yield more information as to the nature and extent of these changes.

Summary. Histologic examination of liver biopsies and biochemical analysis of serum samples were performed in 31 hepatitis B antigen carriers. The histologic evaluation revealed 4 cases with chronic persistent hepatitis and in the majority of the cases an interlobular inflammatory reaction. Increased activity of serum glutamic pyruvic trans-

TABLE I. Histologic Observations in Liver Biopsies and Biochemical Data from Serum Analysis of 31 Hepatitis Associated (Australia) Antigen Carriers (HB Ag).[a]

Nr	Histology	GPT	LDH-5	IgG	IgA	IgM
1	N	24	N	1800	230	110
2	N	31	N	1000	215	85
3	PH	190	I	2200	330	100
4	PH	108	I	1100	80	100
5	PH	96	I	2000	330	320
6	PH	37	I	1600	210	190
7	IR	90	I	1800	400	200
8	IR	100	I	1300	110	80
9	IR	160	I	1600	200	190
10	IR	80	I	2000	510	500
11	IR	60	I	2200	190	170
12	IR	83	I	1800	170	150
13	IR	64	I	2000	150	150
14	IR	48	I	1600	180	90
15	IR	38	I	2000	240	120
16	IR	44	I	1350	170	40
17	IR	20	N	2200	300	170
18	IR	33	N	2200	300	110
19	IR	33	N	1700	200	90
20	IR	34	N	1800	100	120
21	IR	34	N	1900	110	100
22	IR	32	N	2200	280	80
23	IR	32	N	2000	230	120
24	IR	31	N	1800	200	110
25	IR	26	N	2000	190	85
26	IR	24	N	1000	250	120
27	IR	22	N	1100	290	80
28	IR	26	N	1300	150	85
29	IR	20	N	1500	150	42
30	IR	26	N	1400	230	110
31	IR	26	N	1250	200	90
Normal ranges		6–34	—	700–1520	150–350	50–170

[a] N = Normal; PH = Persistent hepatitis; IR = Inflammatory reaction; I = Increased; GPT = Glutamic pyruvic transaminase, Wroblewski units; LDH-5 = Lactate dehydrogenase isozyme-5; IgG, IgA and IgM = Immunoglobulins mg/100 ml.

aminase and lactate dehydrogenase isozyme-5 was found in 45% of the carriers, and the concentration of immunoglobulin-G was elevated in 68% of the same subjects.

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