Diseases of the Liver and Biliary System

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Immune complexes containing HBsAg, IgG and complement have been found in the vascular lesions [64]. The presence of circulating complexes correlates with disease activity. As the lesions become less active, evidences of viral infection disappear [64].

The importance of hepatitis B virus in the whole picture of polyarteritis is probably low, perhaps representing some 10% of cases.

Glomerulonephritis. Membranous or membrano-proliferative glomerulonephritis has been found with chronic hepatitis B virus infection, either isolated or part of a generalized vasculitis [14]. The association is a rare one. Circulating HBsAg antigen–antibody complexes are found. Complexes containing HBsAg, IgG and C_3 are found in the glomeruli.

Polymyalgia rheumatica has been connected with hepatitis B infection [5], but the relationship is not clear cut [58].

Essential mixed cryoglobulinaemia. A patient with peripheral neuropathy and cryoglobulinaemia showed a cryoprecipitate with a high concentration of HBsAg. However, anti-HBsAg and complement were not found [57]. The relationship of hepatitis B to this condition has not been proved [27].

Hepatitis B carriers

Approximately 10% of patients contracting hepatitis B will not clear HBsAg from the serum within six months. Such patients become carriers and this state is likely to persist. Reversion to a negative HBsAg is rare but may develop in old age. Males are six times more likely to become carriers than females.

Persistence of antigen might be genetically determined. The dilemma of a person, such as a hospital worker, carrying the antigen and coming from an area where it is prevalent in apparently healthy persons is a very difficult one. The extent of his infectivity and the medico-legal implications of his employment are not yet clear. The HBsAg carrier of today must not replace the leper of yesterday. Hospital staff who develop HBsAg-positive hepatitis clear the antigen from the blood and are immune to type B hepatitis. They become particularly valuable members of staff. If they become carriers, the position is a difficult one. The extent of the infectivity of surgeons, dentists or indeed any hospital worker to patients and casual contacts has not been established but cannot be very great.

Although apparently healthy, carriers usually show histological changes on liver biopsy [47]. These run from simple non-specific minimal abnormalities through to chronic active hepatitis and cirrhosis [74]. The extent of the changes is not reflected by serum biochemical tests and may only be revealed by liver biopsy. A positive antigen test, however, can persist for many years without apparent clinical detriment.

The healthy carrier is said to show excess of the tubular and spherical antigen particles whereas the person incubating the disease or with an established chronic hepatitis shows more of the Dane particles, i.e. the complete virion [67, 69]. Serum HBcIgMAb and HBeAg positively indicate infectivity and ongoing disease. Mechanisms of chronicity are discussed in Chapter 16.

NON-A, NON-B HEPATITIS

The elimination of hepatitis A and hepatitis B from transfused blood did not eliminate post-transfusion hepatitis. Some of the cases were due to cytomegala infection, but the majority were due to another virus or viruses termed non-A, non-B. This infection now accounts for about 75% of post-transfusion hepatitis and possibly 15–20% of sporadic hepatitis, depending on the geographic location. Haemophiliacs receiving factor concentrates obtained from commercial sources are particularly at risk [18]. Non-A, non-B hepatitis is largely blood spread [25, 93]. It has also been reported with drug abuse, renal transplant recipients [93], in dialysis centres [36] and in donors used for plasmapheresis. It may affect recipients of commercial blood transfused at the time of coronary bypass surgery [4] (table 38). Waterborne epidemics in India resemble hepatitis A.

Table 38. Hepatitis after open heart surgery (Alter *et al* 1979).

	Transfused	Controls
Number	533	108
Hepatitis B	3	1
Non-A, non-B	43	0

Intra-familial spread has been described from Costa Rica [88]. Vertical transmission is also likely. The epidemiological pattern resembles type B hepatitis.

The agent has not been conclusively identified. It has been transmitted to chimpanzees [83]. These animals show double-walled 27 nm intranuclear particles, the nature of which is uncertain. An antigen appears within 7–10 days of infection. Antibody response is weak, and this may account for the difficulty in diagnosis. The identity of this agent remains uncertain [89] and some episodes may be modifications of type B.

Clinical course (fig. 248)

The incubation period is about seven weeks, although a short incubation type (one to four weeks) is also seen. The acute episode is usually mild and often anicteric. Extra-hepatic manifestations do not occur. Fulminant hepatitis is rare. The serum bilirubin and transaminase levels tend to be lower than with acute virus A or virus B infection. The serum immunoglobulin M is normal. The course may be prolonged, with serum transaminase levels waxing and waning for many months. A mild, chronic hepatitis develops in about a quarter, but this usually improves with time [8]. Circulating immune complexes may contribute [28]. Cirrhosis can develop.

In liver biopsies, in addition to the general

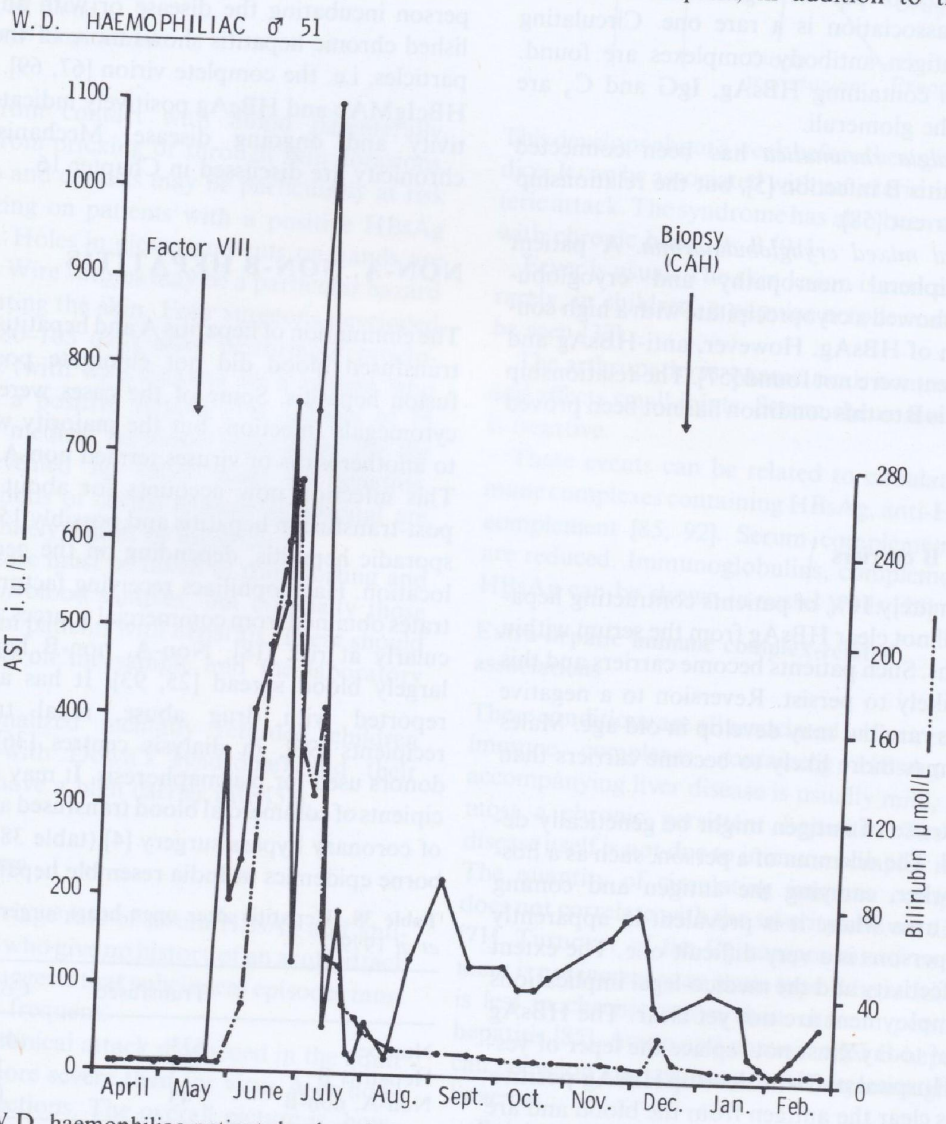

Fig. 248. W.D. haemophiliac patient developed acute hepatitis three weeks after a factor VIII concentrate known to cause non-A, non-B hepatitis. Serum HBsAg and hepatitis A IgM antibody were absent. Note very high serum bilirubin and aspartate (AST) levels. Serum bilirubin returned to normal, but aspartate transaminase fluctuated over the next seven months. Liver biopsy showed that a mild chronic active hepatitis (CAH) had developed. Normal AST = 5–15 i.u./l; normal bilirubin = 5–17 μmol/l.

features of acute virus hepatitis, the picture is one of marked sinusoidal and portal zone cellular infiltration, somewhat resembling infectious mononucleosis. Fatty change and evidence of bile duct damage may sometimes be seen [84].

Non-A, non-B hepatitis often progresses to a mild chronic hepatitis. The prognosis of this is, at the moment, uncertain but probably benign.

TREATMENT

Prevention

Compulsory notification leads to earlier detection and hence identification of methods of infection, for instance, food or water contamination.

VIRUS A

Control lies in perfect sanitation. The virus is particularly resistant to ordinary methods of water sterilization, including chlorination; boiling for 10 minutes is a safeguard. Ultimate control lies in general hygiene, safe disposal of faeces and control of insect vectors. The virus is excreted in the faeces for as long as two weeks before the appearance of jaundice. It is also probable that the anicteric patient may excrete the virus for a similar period. Virus may therefore be widely disseminated in a community before the diagnosis is made. For this reason isolation and quarantine of patients and contacts cannot be expected to influence significantly the spread of hepatitis.

Linen and other items of clothing soiled by patients should be autoclaved or boiled if this will not damage the fabric. Contamination of food, water and milk directly or indirectly by contacts or patients or by sewage should be prevented. Contacts need not be quarantined, but those who are food handlers should be given specific advice on personal hygiene.

VIRUS B

Virus B hepatitis is controlled by avoiding the use of blood products unless really indicated (one unit blood transfusions are never necessary). Where possible, sterile disposable equipment should be used for medical, dental and public health procedures and non-disposable equipment should be thoroughly washed and sterilized before use. This implies boiling for at least 10 minutes or subjecting to steam under pressure or to dry heat. Whole blood cannot be sterilized of the hepatitis virus. Routine thorough washing of endoscopes is sufficient to prevent infections [49].

All prospective blood donors should be screened for HBsAg by radioimmunoassay. This will not, of course, eliminate transfusion hepatitis, due to other hepatitis viruses, such as non-A, non-B.

Blood donors should be rejected if they have been in contact with hepatitis in the previous six months or if their blood is suspected of having been responsible for a case of post-transfusion hepatitis. The safest donor is one who has previously given blood many times without being responsible for a case of post-transfusion hepatitis.

Exclusion of commercial and HBsAg-positive donors reduces the frequency of post-transfusion hepatitis from 33% to 5%. Four of ten of the patients developing hepatitis were of non-A, non-B type, but six were HBsAg positive. Current tests, including radioimmunoassay, cannot detect all donors capable of transmitting hepatitis. The positive HBsAg donor with acute or chronic hepatitis may be more infectious than the so-called healthy carrier [41].

Immune-globulin prophylaxis (table 39) [77]

VIRUS A

Immune serum globulin (ISG) is effective in preventing or modifying type A virus hepatitis. When administered before or within one to two weeks of exposure in a dose of 0.02 ml/kg intramuscu-

Table 39. Immunoprophylaxis of virus hepatitis in adults.

Type	Globulin	Indication	Regime
A	Conventional	Close exposure to virus Travel to 'dirty' areas	3 ml within ten days 6 ml every six months
B	Immune	Exposure to HBsAg +ve blood Sexual consorts	5 ml within 48 hours and 28 days