Editorial

Delta-Virus Hepatitis

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DELTA-VIRUS HEPATITIS

In 1977, when Rizetto et al. (1) reported a new hepatitis-B associated antigen which they named delta antigen, the response from the scientific community was far from enthusiastic. Doctors were already confused and disillusioned by the large array of hepatitis B markers and their antibodies, and nobody outside Italy was able to demonstrate the new antigen. Six years later, however, intensive research has vindicated Rizzetto's observations and has brought to light some fascinating facts.

Delta antigen has been revealed as an autonomous though defective virus which has a molecular weight of approximately 68,000 daltons and which induces the production of anti-delta (anti-D). Experiments in chimpanzees have shown that delta virus can exist only in association with hepatitis B virus, the latter being needed to supply the defective virus with its indispensable shell, namely HBs Ag (Fig. 1). Chimpanzees (2) which have anti HBs, and are therefore immune to hepatitis B, cannot contract delta-virus infection, though asymptomatic carriers of hepatitis B virus develop acute delta virus infection after inoculation, and subsequently show a fall in the titre of HBs Ag, this being partially used up by delta virus. The same phenomenon also blocks the multiplication of hepatitis B virus to a considerable extent.

During the acute phase of infection delta virus remains detectable in the serum for about a month, but disappears rapidly when produc-
tion of anti-D begins. In cases of chronic delta-virus infection, on the other hand, anti-D positive sera may remain infectious for some time (2).

Delta virus can be demonstrated in liver biopsies and indeed in liver cell nuclei by immunofluorescence or by the peroxidase-antiperoxidase technique. Anti-D in serum can be detected by radioimmunoassay or the ELISA test. There is also a specific test for anti-D IgM.

In our latitudes the transmission of delta antigen is mainly parenteral, but where hygiene is poor, as in Southern Italy, Africa and the Middle East, it is also transmitted by close bodily contact. An epidemic of this kind has recently been observed among the Yupca Indians in Venezuela. Markers for delta virus infection have been found in 31 to 64% of European drug addicts who are HBs Ag positive and who inject their drugs intravenously (4). Among haemophiliacs in Italy and the USA the prevalence is 50% (5). A few years ago Northern Europe was still free from this infection, but delta virus has now reached the region, probably carried by drug addicts. Only a few isolated cases of delta virus infection have been found in Japan.

Clinically, there are two possibilities:

1. Hepatitis B virus and delta virus may be transmitted simultaneously. The resulting illness does not usually differ from hepatitis B, although the delta virus may cause a second peak in the clinical course and fulminating cases are somewhat more frequent (Fig. 2). Dual infections are nearly
always misdiagnosed as acute hepatitis B.

2. Delta virus infection may occur in an HBs Ag carrier. Such cases not infrequently follow a fulminating course, or may become chronic. Patients with pre-existing liver disease, such as chronic aggressive (chronic active) hepatitis B in the cirrhotic stage, are at special risk. Surprisingly enough, most such patients are anti HBe-positive HBs Ag carriers (Fig. 3). Delta virus infection in HBs Ag carriers simulates acute hepatitis B.

Like acute hepatitis B, combined infection with delta virus and hepatitis B virus is normally a self-limiting disease which does not require drug therapy. For chronic infections, on the other hand, some form of treatment would be highly desirable. Immunosuppressive therapy has been tried but the results have been discouraging. Other therapeutic approaches have so far been equally disappointing, and the problem of treatment is still completely unsolved. The best means of preventing delta virus infection is immunization against hepatitis B.

REFERENCES

Fig. 1 Delta viral components
Fig. 2  HBV/δ coinfection. HBV/δ are introduced simultaneously. After appearance of HBsAg in serum, δ agent develops. Its synthesis, however, is limited by the transient HBs antigenemia, which δ agent cannot outlive. Hepatitis is mainly due to the HBV damage. The immune response to δ infection is usually brief and low-titered, often represented by a transient primary IgM antibody response. ALT, SGPT. From Rizzetto M (5).

Fig. 3  δ superinfection of an HBV carrier. Prior HBs antigenemia provides immediate rescue for δ agent, whose pathogenic potential can be expressed at full. This results in a severe acute hepatitis, due to the virulence of δ agent. Continuing HBs antigenemia may also maintain the persistence of δ agent replication and acute hepatitis progresses to chronicity. Development of chronic δ hepatitis is paralleled by a rise of the IgG antibody to δ in high titers. From Rizzetto M (5).