

# Hepatitis Delta Virus: Epidemiology, Natural Course and Treatment

Philippe Sultanik and Stanislas Pol\*

*Department of Hepatology, Paris Descartes University, France*

\*Corresponding author:

and sub-tropical areas and decreases in tempered areas. HDV is endemic in Mediterranean area (Southern Italy), in the Near East, in South America (Amazon Basin), in sub-Saharan or Central Africa and in East Europe. Despite a high HBV prevalence in South-East Asia, HDV infection is rare except in Vietnam and in the Pacific islands; we cannot exclude that "Asian" HBV genomic variations of B or C HBV genotypes could limit their auxiliary function for HDV replication. In Africa, individuals are contaminated during childhood and teen age by vertical transmission from mother to child or horizontal transmission with tattoos, acupuncture, ritual scarifications, traditional medicine... In the Mediterranean area, people are mostly contaminated later during the fourth decade. In the United-States and in North Europe, low endemic areas, HDV has been introduced in the 1970s, mostly by the intra-venous drugs users (IVDU), with a rapid expansion -in France, 70% of the IVDU and 15% of the MSM who carried HBs antigen (HBsAg) were infected by HDV at the beginning of 1980s [13]. This

histological findings the absence of difference of severity between HBV or HVB/HDV carriers [28-31] and occurrence of hepatocellular carcinoma is the same (3 to 5%/year) than in B or C viral cirrhosis.

In the French Deltavir study [32], 28% of patients had a biopsy-proven cirrhosis at enrollment, 15% had at least one episode of cirrhosis decompensation and 2.7% had a HCC. After a median follow-up of more than 4 years, 20% of patients have developed cirrhosis, 10% had a decompensation of cirrhosis and 6.5% a HCC. In multivariate analysis, age, GGT level and detectable HDV RNA were predictor of cirrhosis decompensation and ASAT level was predictor of cirrhosis development.

The association of serum HBsAg, anti-HBc IgG antibodies positivity with anti-HBc IgM negativity makes the diagnosis of HDV superinfection. HBV DNA is usually undetectable or with very low levels. The delta antigen is present in the liver, with nuclear localization, sometimes cytoplasmic, except in fulminant presentations where it is mostly undetectable. HDV RNA is detectable in liver and serum. The constant positivity of anti-delta IgM antibodies (monomeric [75]) with a titer of anti-delta IgG antibodies above 1/1000 signs chronic delta infection.

## i e e g e m l

**Fulminant hepatitis** Fulminant presentations of acute delta hepatitis

Pilot studies reported a decrease of liver

**Other therapies** In the setting of decompensated cirrhosis, liver transplantation can be proposed. The HDV infection relapse on the liver graft is frequent (70%) but with a better prognosis than the infection on the native liver or than the relapse with HBV alone. An immune-prophylaxis, as already cited, is justified to decrease the risk of HBV relapse after transplantation. The 5-year survival rate is around 90% [18]. When hepatocellular carcinoma is established, the best therapeutic strategy may be the liver transplantation that cures the tumor and the cirrhosis, with a low risk of tumor recurrence at 2 years if the tumor size is small (<3 cm). The surgical resection for small tumor provides a similar 2-year survival rate but tumor recurrence is frequent (around 60%), suggesting a lower efficacy on long survival than liver transplantation. The best treatment of delta hepatitis virus infection remains prevention with vaccination against HBV; efficiently

34. Samuel D, Muller R, Alexander G, Fassati L, Ducot B, et al. (1993) Liver transplantation in European patients with the hepatitis B surface antigen. *N Engl J Med* 329: 1842-1847.
35. Buti M, Jardi R, Allende H, Cotrina M, Rodriguez F, et al. (1996) Chronic delta hepatitis: is the prognosis worse when associated with hepatitis C virus and human immunodeficiency virus infections? *J Med Virol* 49: 66-69.
36. Piroth L, Pol S, Lacombe K, Mialhes P, Rami A, et al. (2010) Management and treatment of chronic hepatitis B virus infection in HIV positive and negative patients: the EPIB 2008 study. *J Hepatol* 53: 1006-1012.
37. Aragona M, Macagno S, Caredda F, Crivelli O, Lavarini C, et al. (1987) Serological response to the hepatitis delta virus in hepatitis D. *Lancet* 1: 478-480.

38