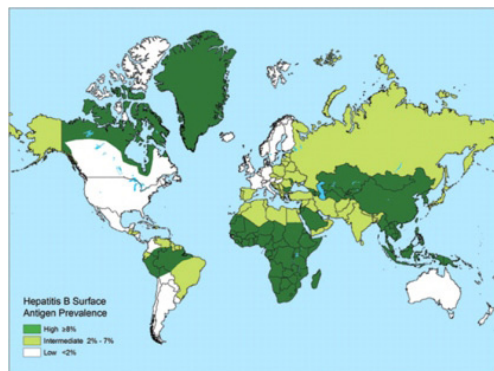


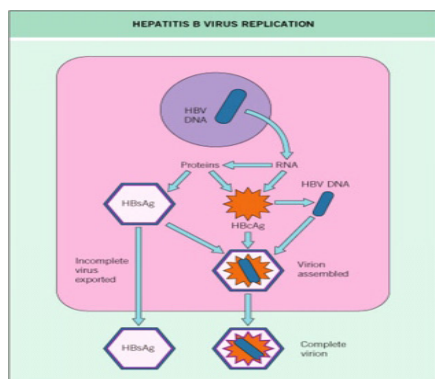
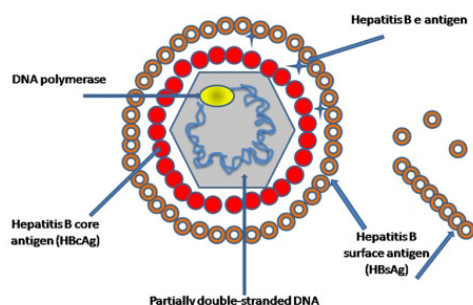
## CHRONIC HEPATITIS B DIAGNOSIS, TREATMENT AND MONITORING INFECTION: DIAGNOSIS, TREATMENT AND MONITORING

Chronic Hepatitis B remains a challenging worldwide health problem despite the availability of Hepatitis B (HBV) vaccine. Between 350 and 400 million people are chronically infected with this virus and develop the complications of liver failure, cirrhosis and hepatocellular carcinoma (HCC).



Of most interest in this map is that the infection rate in Sub-Saharan Africa is >8% - and, in fact, up to 20%, among the highest in the world.

An improved understanding of the virology, genotypes, pathogenetic mechanisms and the key role that the HBV replication together with the immune-mediated liver injury play, has altered the diagnosis and therapy of this serious disease. This newsletter will focus on the diagnosis and treatment of chronic HBV infections. The virological features of HBV are illustrated in the figure below. The virus belongs to the hepadnaviridae family, with an envelope and core which contains the partially double-stranded DNA genome.



After HBV entry into the hepatocyte nucleus, the relaxed circular DNA changes to covalently-closed-circular DNA (cccDNA) which plays a pivotal role in the maintenance of chronic HBV infection.

The virus has at least 8 major genotypes named A-H. The importance of the specific genotypes is that it is linked geographically and also linked with progression of disease as well as treatment response. A is found in northwestern Europe and the USA, B and C in Asia, D in the Mediterranean, Middle East and India. Genotype E occurs in West Africa, F in South and Central America, G in the USA and France and H in Mexico and South America.

Diagnosis and monitoring  
Acute HBV infection is diagnosed by the appearance of HBsAg and IgM antiHBc, which usually disappear when the ALT peaks and antiHBs appears. HBeAg and HBV DNA are also present early during acute infection.

Persistence of HBeAg for > 10 weeks indicates a high possibility of transition to persistent infection. Persistence of S-HBsAg for more than 6 months implies the progression to chronic infection. High levels of HBV DNA are found in HBeAg positive patients. HBV DNA assay is a direct measurement of viral load. The viral load is useful for assessment of disease progression, treatment and treatment monitoring. HBV replication with immunemediated liver damage is the main driver for disease progression. This disease progression should be monitored for a lifelong period, including serum ALT and alpha-fetoprotein measurements, and liver biopsies. Other risk factors for the development of cirrhosis include being male, increasing age, HBeAg positivity and HBV genotype C. Assays for viral load, genotypes and mutations have become increasingly important in the clinical management of the chronically HBV infected patient.

The treatment of chronic HBV infection has evolved greatly since 1998. Interferon and pegylated interferon alpha as well as nucleoside analogues (lamivudine, entecavir, telbivudine, emtricitabine) and nucleotide analogues (adefovir dipivoxil) are widely used. Drug therapy should be selected to suit the patient's individual requirements and is based on the condition, the drug's mechanism of action, potency, rapidity of action, adverse effects and cost. In HIV/HBV co-infected individuals who do not need HIV treatment but who need to be treated for chronic hepatitis B, monotherapy with an agent that is active against both HIV and HBV (such as lamivudine, emtricitabine, entecavir, or tenofovir disoproxil fumarate) should not be used because of the rapid development of drug-resistant HIV. HBV is, however, rarely eliminated and drug resistance comes into play during long term therapy and occurs most frequently with lamivudine and in decreasing mode with telbivudine, adefovir, tenofovir and least of all with entecavir.

HBV Specific Laboratory Monitoring of Chronic HBV Infection

1. S-HBsAg for > 6 months (viral mutants exist that do not produce detectable HBsAg).
2. S-HBeAg (viral mutants exist that do not produce detectable HBeAg).
3. HBV viral load directly detects circulating HBV genomes.
4. HBV genotyping assists not only for geographic distribution as mentioned earlier, but is also linked to pre-core mutations (D followed by C and B and least frequent with genotype A). This means that genotype D is HBeAg negative and is found in 80-90% of Mediterranean areas and 30-50% in Southeast Asia. Genotype C and D have faster disease progression and poorer treatment response.
5. Line probe assays are now available to detect not only genotypes A-H and, therefore, mixed infections but also mutations of the Basal Core Promoter (BCP) and precore region which impact on the pathogenesis and treatment. HBV Wild-type motif and lamivudine, telbivudine, adefovir and emtricitabine resistance mutations are also done concurrently. These molecular tests will certainly enhance the therapeutic management of the chronically HBV infected patient. Please contact the Molecular Laboratory at Lancet for further information and advice on the best suited tests.

### References

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