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The Interpretation of Diagnostic Blood Tests for Hepatitis B Virus (HBV)

HBsAg - Hepatitis B surface antigen

- Presence indicates infection with HBV
- Is **DETECTED** in both acute cases and in HBV carriers
- Persistence for six months defines carrier status
- Levels may reflect the amount of virus in the liver and may provide useful information during treatment monitoring
- A decline in levels may predict eventual clearance of HBsAg

HBeAg - Hepatitis B e antigen

- Can be **DETECTED** in the early phase of HBV infection (usually short lived, 3-6 weeks)
- Becomes **UNDETECTABLE** in acute HBV as the virus clears and HBeAb is **DETECTED**
- Can persist in carriers and is usually associated with **DETECTABLE** HBV DNA
- During the immune-active phase in HBV carriers a seroconversion occurs when HBeAg becomes **NOT DETECTED** as HBeAb becomes **DETECTED**
- It is possible for HBeAg and HBeAb to be both **DETECTED** at the same time or both **NOT DETECTED** but this is uncommon
- **NB:** Presence of HBeAg is not required for infectivity or replication. It is not part of the structure of the virus. Some patients with active viral replication do not produce HBeAg due to the presence of HBV variants

HBeAb - Hepatitis B e antibody - anti-HBe

- Appearance in acute cases likely to be indicative of spontaneous resolution
- Carriers who are HBeAg **NOT DETECTED**, HBeAb **DETECTED** and HBV DNA **NOT DETECTED** are considered to be in the inactive phase. Liver function tests are usually normal in these cases and they are of low infectivity
- Carriers who are HBeAg **NOT DETECTED**, HBeAb **DETECTED** and HBV DNA **DETECTED** usually have abnormal liver function tests and are an infection risk

HBV DNA - Hepatitis B virus DNA

- Presence indicates infectivity and active viral replication
- HBV DNA levels in the blood are essential for the diagnosis, decision to treat and monitoring of patients
- $<10^3$ IU/ml is likely to be associated with disease resolution
- High levels may be present in carriers with no evidence of liver damage
- May be **NOT DETECTED** in blood but **DETECTABLE** in the liver

- Presence in the liver of individuals with **UNDETECTABLE** HBsAg in blood defines Occult HBV

HBV genotype and subtypes

- Eight genotypes defined, designated A,B,C,D,E and F with a number of subtypes
- Associated with distinct geographical areas
- Different genotypes may respond differently to anti-viral treatment
- May influence the severity of liver disease, disease progression and clinical outcome

HBsAb - Hepatitis B surface antibody - anti-HBs

- Is usually, but not always, **DETECTED** after the disappearance of HBsAg in acute infection
- Is sometimes **DETECTED** in HBV carriers
- Is the **ONLY** antibody produced by successful vaccination

HBcAb - Hepatitis B core antibody - anti-HBc

- **DETECTED** in anyone who has been previously exposed or is currently, infected with HBV
- In acute infection appears after the appearance of HBsAg and usually before a rise in liver enzymes
- Its persistence in all those who have been exposed to HBV makes it a useful epidemiological marker
- Is **NOT DETECTED** in those who have been vaccinated against HBV and have never been infected with the virus

HBcAb IgM - IgM anti-HBc

- Routinely used to confirm the diagnosis of acute HBV infection
- May be the only marker present in cases of acute liver failure where HBsAg has already become **NOT DETECTABLE** and anti-HBc is not yet **DETECTED** but this is uncommon
- Levels may be elevated in HBV carriers with an active immune response to the virus such as those undergoing seroconversion

Note:

- Transfused blood or transplanted organs of people who are HBsAg **NOT DETECTED**, HBcAb **DETECTED** may transmit HBV to the recipients
- People who are HBsAg **NOT DETECTED**, HBcAb **DETECTED** may reactivate and become HBsAg **DETECTED** again if they become immune compromised
- HBcAg - Hepatitis B core antigen cannot be **DETECTED** in the blood but can be **DETECTED** in the liver

Phases of HBV infection:

Phase 1: immune-tolerant or replicative phase. In the initial phase of infection there is little or no immune recognition of HBV. Inflammatory activity is low, liver enzymes are normal or of low levels, levels of HBV DNA are high, HBeAg is positive and there is no or minimal pathology on liver biopsy. During this phase the rate of spontaneous HBeAg loss is very low. This phase is more frequent and more prolonged in those infected perinatally or in the first years of life. These carriers are highly infectious.

Phase 2: immune-reactive phase. During this phase the immune system recognizes the virus and tries to eradicate it. There is moderate or severe liver necroinflammation and more rapid progression to fibrosis compared to the previous phase, liver enzymes are elevated or fluctuating and HBV DNA and HBeAg levels fall. Seroconversion occurs with loss of HBeAg, detection of HBeAb and lowering of HBV DNA levels to below 10^2 - 10^3 IU/ml. There is an increased rate of spontaneous HBeAg loss. This phase may last for several weeks to several years. Patients in this phase are infectious.

Phase 3: inactive-phase. This may follow seroconversion from HBeAg to HBeAb detection. HBV DNA levels are very low or undetectable and liver enzymes fall as inflammatory activity in the liver decreases. This state suggests a favourable long-term outcome with a very low risk of cirrhosis or HCC in the majority of patients. HBsAg loss and seroconversion to HBsAb may occur spontaneously in ~1.5% of cases per year, usually following several years of undetectable HBV DNA. Patients remain infectious but at a lower level.

Phase 4: HBeAg negative chronic HBV may follow seroconversion. This is characterised by periodic reactivation with fluctuating levels of HBV DNA and aminotransferases and active hepatitis. These patients harbour HBV variants with nucleotide substitutions in the precore and/or basal core promoter regions and are either unable to express HBeAg or express low levels. Patients in this phase are infectious.

Phase 5: HBsAg negative phase. In this phase HBV DNA is generally undetectable in serum while anti-HBc with or without anti-HBs is detectable. HBsAg loss is associated with a reduced risk of cirrhosis, decompensation and HCC. The clinical relevance of Occult HBV where HBV DNA continues to be detectable in the liver in such patients is unclear. Immunosuppression may lead to reactivation in these patients. Patients are considered non-infectious.