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## Hepatitis B Serology

Hepatitis B virus (HBV) is a small double stranded DNA virus composed of an outer envelope containing hepatitis B surface antigen (HBsAg) and an inner nucleocapsid consisting of hepatitis B envelope antigen (HBeAg) and hepatitis B core antigen (HBcAg). The viral core also contains a double stranded DNA genome and DNA polymerase.

HBV infection can result in both acute and chronic hepatitis. Approximately 90% of adults who are infected will resolve the infection without permanent organ damage, while 10% become carriers and 6% progress to chronic disease. Infected newborns and children have a much worse outcome. Chronic infection occurs in 90% of infants infected at birth and in 30% of children infected between ages 1 and 5 years.

After exposure to HBV, there is an incubation period ranging from 1 to 4 months, during which the patient may not exhibit symptoms or positive serologic results. Symptoms, if they appear, usually occur within 4 to 6 weeks after exposure. The most common symptoms include nausea, anorexia, malaise and jaundice. The stage of the infection can be monitored with tests for HBV antigens and antibodies.

HBsAg is the first serologic marker, developing between 1 week and 6 months following infection, but prior to onset of symptoms. Presence of HBsAg in serum may indicate acute HBV infection, chronic HBV infection, or asymptomatic carrier state. In acute infection, HBsAg becomes undetectable within 4 to 6 months after onset of symptoms. HBsAg persists in patients with chronic hepatitis. The significance of a positive test for HBsAg is determined by evaluating it in relationship to the presence or absence of the other HBV markers and the clinical presentation and history of the patient.

Antibody to HBsAg (Anti-HBs) becomes detectable several weeks after HBsAg has disappeared. The interval between disappearance of HBsAg and

appearance of anti-HBs is known as the window period and may last as long as 6 months. Detection of anti-HBs usually indicates clinical recovery and subsequent immunity to HBV. Anti-HBs may persist after resolution of the infection. Therefore, the detection of anti-HBs does not discriminate between current or previous infection. Anti-HBs may fall below detectable levels with time.

Successful vaccination results in detectable anti-HBs. Levels of 10 mIU/mL or greater indicate protection against HBV infection. Anti-HBs quantitation is a useful tool to monitor vaccinees who are likely to have a blunted response including:

- >30 years of age at the time of first vaccination
- Immunocompromised patients
- Obese individuals
- Patients undergoing dialysis
- Patients with protein losing nephropathies
- Individuals working in high risk endemic areas.

HBeAg develops one week after HBsAg is detectable, but before symptoms appear. The presence of HBeAg correlates with the level of infectivity; a patient is most likely to transmit the virus when HBeAg is present. HBeAg usually disappears about 3 weeks before HBsAg disappears. Persistence of HBeAg beyond 12 weeks may indicate progression to a chronic carrier state. Pregnant women who are positive for HBeAg have a high risk (90%) of HBV transmission to the fetus.

Antibody to HBeAg (anti-HBe) is usually detectable between 12 and 16 weeks, when HBeAg disappears. When a patient is positive for HBsAg and anti-HBe, but negative for HBeAg, there is reduced infectivity and a probable likelihood of resolving the infection. Anti-HBe may be detectable in a chronic carrier. The presence of anti-HBe does not imply immunity to HBV.

Antibody to hepatitis B core antigen (anti-HBc) appears during the first few weeks after infection, shortly after the onset of symptoms and rises to high levels during convalescence. IgM anti-HBc

develops in the acute phase of HBV infection, indicating an infection in the past 3 to 6 months. It is detectable during prodromal, acute, and early convalescent phases. IgM anti-HBc may be the only antibody detectable during the window period when HBsAg has disappeared and before anti-HBs becomes detectable. In this situation, it is considered to be a reliable indicator of ongoing infection. Prenatally acquired anti-HBc gradually disappears in the first 2 to 4 months of life.

IgG anti-HBc develops in the late acute phase of infection. It is measured as part of total anti-HBc and may be the only serologic marker remaining following recovery from infection. It is an accurate serological marker of previous HBV infection, as it appears in all patients infected with the hepatitis B virus and may persist in individuals at low titer long after HBV exposure. In some cases, total anti-HBc titers may fall into the undetectable range along with total anti-HBs.

<b>Summary of Hepatitis B Serology</b>	
Surface Antigen (HBsAg)	Earliest marker of acute infection; persists in carriers/chronic infection
Surface Antibody (HBsAb)	Indicates acute infection has resolved, also indicates immunity after vaccine
Core IgM (HBcIgM)	Acute infection marker, appears later than HBsAg
Core Total Antibody (HBcTotal)	Includes IgM & IgG, most reliable marker for previous hep B infection, NOT positive after vaccine
e Antigen (HBeAg)	Acute infection marker, highly infectious when present
e Antibody (HBeAb)	Marker of previous infection
HBV DNA	Molecular viral load test

In subclinical asymptomatic hepatitis B virus infection, HBsAg and HBeAg are present for a brief period or may not be detectable and are followed by the appearance of anti-HBc and anti-HBs. In these patients, detection of anti-HBs and total anti-HBc must be relied on as evidence of previous HBV infection.

Chronic infection is defined as persistence of HBsAg for more than 6 months. In chronic hepatitis B infection, HBsAg appears during the incubation phase of the disease and may persist for years and possibly for life. All HBsAg-positive persons are considered infectious. Additional tests for HBV replication, including HBeAg and HBV DNA should be performed in those with chronic hepatitis B. In addition to HBsAg, serologic testing for hepatitis B surface antibody (anti-HBs) and total core antibody (anti-HBc) is advised for immuno-suppressed patients.

The presence of HBV DNA in the plasma is an accurate indicator of viral replication. HBV DNA levels that persist longer than 8 weeks may indicate progression to chronic HBV infection.

HBsAg and anti-HBc IgM are included in the Acute Hepatitis Panel. All other hepatitis tests must be ordered individually. Effective July 15, Hepatitis B core antibody total is performed at Saint Luke's Hospital laboratory. Specimen requirement for all hepatitis antigen and antibody tests is a red top tube of blood.

### **Reflex Testing**

Federal regulations require that laboratories inform physicians of their reflex test policy. Reflex testing refers to those situations where an initial test result is abnormal and the laboratory automatically performs follow-up testing when medically appropriate. Saint Luke's Regional Laboratories' (SLRL) clients should familiarize themselves with these tests by utilizing the [SLRL Services Directory](#) and make note of tests that prompt reflexive testing. In addition, some testing is sent out to specialty laboratories that perform medically appropriate reflex testing as necessary to provide information that would be essential to treat or diagnosis the patient. If additional help is needed choosing appropriate testing, please contact our Client Services department at 816-932-3850.

### **Protein C Change**

The reference range for Protein C Activity has changed from 70 – 140% to 70 – 210%.