

# HEPATITIS B (Chronic, Acute, and Perinatal) AND HEPATITIS D

## ✓ DISEASE AND EPIDEMIOLOGY

### Clinical Description:

#### Hepatitis B infection:

There are generally three phases of hepatitis B symptoms.

#### Pre-icteric or prodromal phase:

The pre-icteric or prodromal phase is nonspecific and usually presents with malaise, anorexia, nausea, vomiting, right upper quadrant abdominal pain, fever, headache, myalgia, skin rashes, arthralgia and arthritis, and dark urine. It generally lasts for 3-10 days.

#### Icteric Phase:

The icteric phase occurs at the onset of jaundice, and is usually accompanied by light or gray stools, hepatic tenderness and hepatomegaly. This phase can last from 1-3 weeks.

#### Convalescent Phase:

The convalescent phase can last for weeks to months, and is characterized by malaise and fatigue.

Severity of the disease ranges from unapparent cases (detectable only by liver function tests) to fulminant, fatal disease. Asymptomatic infections are common in children <10 years of age, and occur in approximately 30–50% of older children, adolescents, and adults.

#### Acute infection:

Once a person is infected with the hepatitis B virus (HBV), they develop an acute infection. Symptoms may appear at this stage which can last for months. Persons with an acute infection can either make a complete recovery (which includes immunity to subsequent infection) or can become chronic carriers. Most acute HBV infections in adults result in complete recovery with elimination of HBsAg from the blood and the production of anti-HBs, creating immunity to future infection.

#### Chronic infection:

Approximately 5% of all acute HBV infections progress to chronic infection, with the risk of chronic HBV infection decreasing with age. As many as 90% of infants who acquire HBV infection from their mothers at birth become chronically infected. Of children who become infected with HBV between one and five years of age, 30% to 50% become chronically infected. By adulthood, the risk of acquiring chronic HBV infection is approximately 5%.

Persons with chronic infection are often asymptomatic and may not be aware that they are infected; however, they are capable of infecting others and have been referred to as carriers.

### **Perinatal infection:**

Perinatal transmission from mother to infant at birth is very efficient. If the mother is positive for both HBsAg and HBeAg, 70%–90% of infants will become infected in the absence of post-exposure prophylaxis. The risk of perinatal transmission is about 10% if the mother is positive only for HBsAg. Infants infected with HBV have a 90% chance of becoming chronic carriers.

Most persons acutely infected completely recover from the disease with no complications. However, 1-2% may develop fulminant hepatitis. The majority of complications occur with chronic infection. Chronic infection may result in chronic hepatitis, cirrhosis, liver failure, and hepatocellular carcinoma. Approximately 25% of persons with chronic HBV infection die prematurely from cirrhosis or liver cancer. Chronic active hepatitis develops in more than 25% of carriers and often results in cirrhosis.

### **Hepatitis D infection:**

#### **Co-infection with HBV**

A hepatitis D virus (HDV) co-infection occurs when the patient is suffering from both HBV and HDV acute infections. The onset of acute co-infection is typically abrupt and resembles the signs and symptoms of acute HBV infection, including anorexia, abdominal pain, nausea, vomiting, and jaundice. Acute co-infection is usually self-limited, although the likelihood of fulminant hepatitis can be as high as 5%.

#### **Super-infection**

A HDV super-infection occurs when a patient with chronic HBV becomes acutely infected with HDV. A super-infection can turn a mild or asymptomatic HBV chronic infection into a severe or fulminant case of hepatitis.

Like hepatitis B infections, hepatitis D infections can also be acute or chronic. Persons with HBV-HDV co-infections may have more severe acute disease and a higher risk (2%-20%) of developing acute liver failure compared with those infected with HBV alone. Persons with HBV-HDV superinfection will usually become chronic carriers of HDV. Progression to cirrhosis is believed to be more common with HBV-HDV chronic infections.

### **Causative Agent:**

Hepatitis B is caused by the hepatitis B virus, a DNA hepadnavirus. Important components of the viral particle include hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBcAg), and hepatitis B e antigen (HBeAg).

HDV is a single-stranded RNA virus that contains hepatitis B surface antigen (HBsAg) within its coat. HDV requires the hepatitis B virus as a “helper” virus, and it cannot produce infection in the absence of HBV infection. It is in the same viral family as Hepatitis B.

**Differential Diagnosis:**

Hepatitis has a variety of causes including, but not limited to: viral hepatitises (A, B, C, D, E, X), Epstein-Barr virus, cytomegalovirus, drug-induced hepatitis, toxin-induced hepatitis, auto-immune hepatitis, alcohol liver disease.

**Laboratory identification:**

**Hepatitis B:**

Hepatitis B cannot be definitively diagnosed without a blood test that measures various serologic markers for hepatitis B virus.

**Serology Panels:**

The following table displays the serologic tests available and what their results mean.

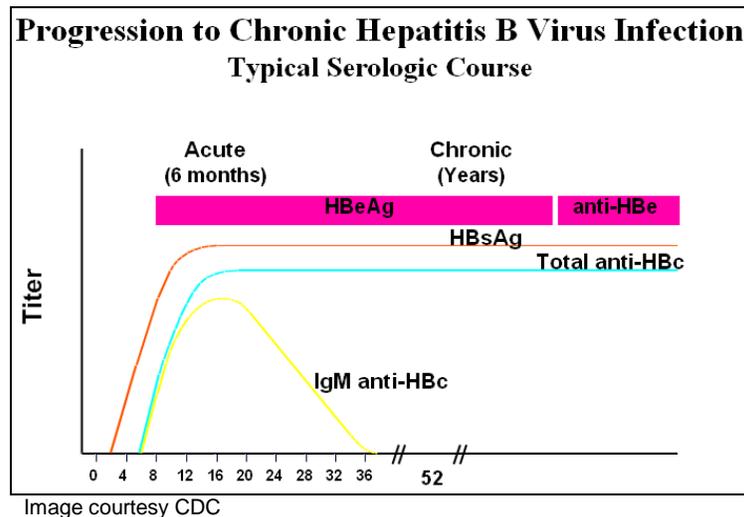
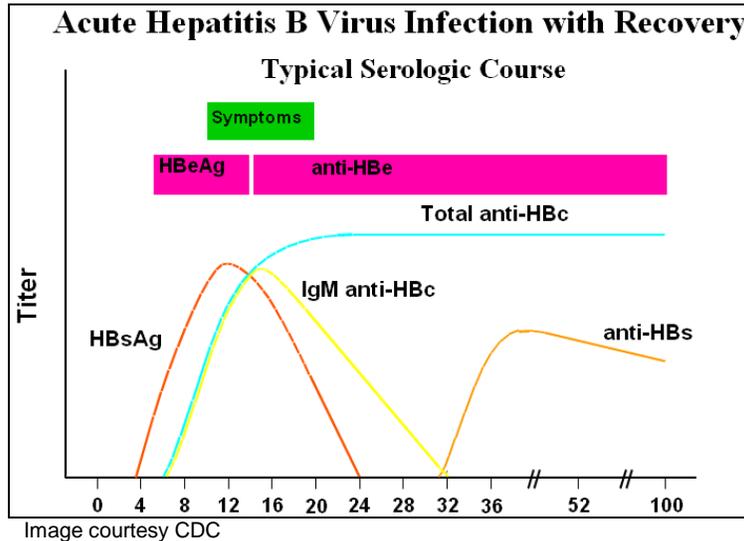
Serologic Test	Marker	Result
<b>HBsAg</b>	Viral particle	Tests for the presence of the virus; confirmatory testing needed to rule out false-positives
<b>HBcAb (anti-HBc)</b>	Viral antibody	Tests for past or present infection
<b>HBsAb (anti-HBs)</b>	Viral antibody	Tests for immunity to future infections
<b>IgM anti-HBc</b>	Viral antibody	Tests for recent infection; may reappear in persons who have a flare up
<b>HBeAg</b>	Viral particle	Tests for degree of infectivity (positive=high)
<b>Anti-HBe</b>	Viral antibody	Tests for degree of infectivity(positive=low)
<b>HBV DNA</b>	Viral DNA	Tests for viral replication

Several serologic tests are needed to determine the status of the patient’s immunity and/or infection. The three most commonly ordered tests that make up the basic hepatitis B testing panel are HBsAg, anti-HBc, and anti-HBs. The following table displays serologic test interpretations.

Immune and/or infection status	HBsAg	HBcAb (anti-HBc)	HBsAb (anti-HBs)	IgM anti-HBc	HBeAg	anti-HBe
susceptible	–	–	–			
immune due to natural infection	–	+	+			
immune due to hepatitis B vaccine	–	–	+			
acutely infected	+	+	–	+	+	+/-
chronically infected	+	+	–	–		
four interpretations possible*	–	+	–			

\*May be:

- Recovering from acute HBV infection.
- Distantly immune, test not sensitive enough to detect low levels of anti-HBs in serum.
- Susceptible with a false positive anti-HBc.
- Undetectable level of HBsAg present in the serum and person is actually a carrier.



**Chemistry Panels:**

Liver function tests, such as ALT and AST (aminotransferases) are sensitive for liver damage, but are not specific for Hepatitis B. In patients without jaundice, elevated serum aminotransferase levels are required to meet the clinical case definition. The normal value for ALT and AST is up to 50 mIU/mL, but reference ranges can be laboratory specific, so it is appropriate to ask the laboratory performing this test to provide their reference range.

**USLPH:** The Unified State Laboratory: Public Health performs HBsAg (including confirmatory testing), and anti-HBs testing. Testing is done twice a week, once on Monday and Thursday.

## Hepatitis D:

Laboratory tests for hepatitis D virus include IgM anti-HDV, IgG anti-HDV, HDAG, and HDAb (anti-HDV). A person infected with HDV will always be IgM anti-HDV positive. However, for a co-infection, they will also be IgM anti-HBV positive, whereas for a super-infection they will be IgM anti-HBV negative.

In about 15% of patients the only evidence of HDV infection may be the detection of either IgM anti-HDV alone during the early acute period of illness or IgG anti-HDV alone during convalescence. Anti-HDV generally declines to sub-detectable levels after the infection resolves and there is no serologic marker that persists to indicate that the patient was ever infected with HDV. HDAG can be detected in serum in only about 25% of patients with HBV-HDV co-infection. When HDAG is detectable it generally disappears as HBsAg disappears and most patients do not develop chronic infection. Tests for IgG anti-HDV are commercially available in the United States.

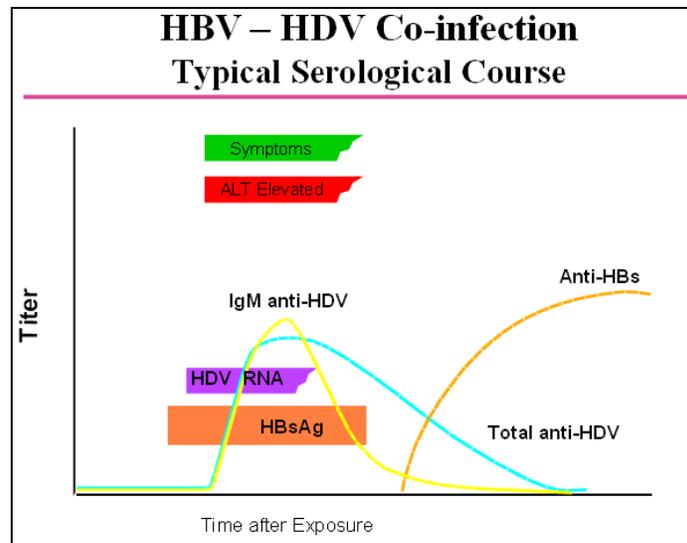


Image courtesy CDC

In patients with chronic HBV infection who are super-infected with HDV several characteristic serologic features generally occur, including: 1) the titer of HBsAg declines at the time HDAG appears in the serum, 2) HDAG and HDV RNA remain detectable in the serum because chronic HDV infection generally occurs in most patients with HDV superinfection, unlike the case with co-infection, 3) high titers of both IgM and IgG anti-HDV are detectable, which persist indefinitely.

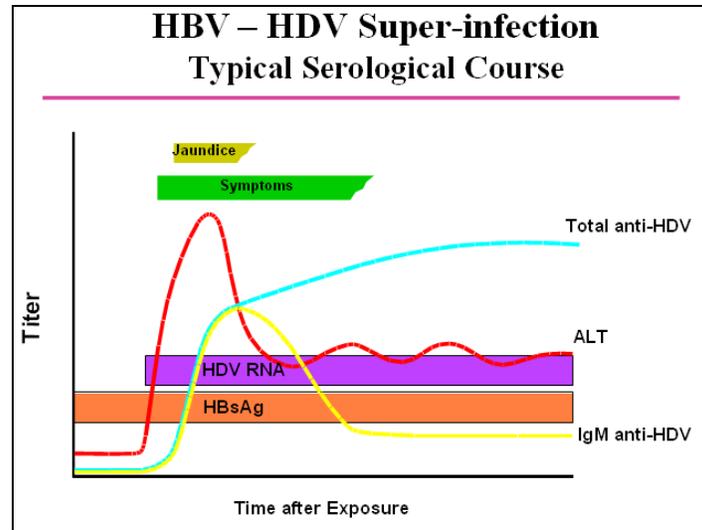


Image courtesy CDC

**Treatment:**

Treatment for acute hepatitis B and D is mainly supportive. Interferon is the most effective treatment for chronic hepatitis B and D carriers and is successful in 25-50% of cases.

Currently, at the University of Utah trials for a new treatment for hepatitis B are being conducted. To enroll in these trials, contact UDOH epidemiology (801) 538-6191 who can give you information for who to contact about arranging clinic visits or inclusion in clinical trials that use hepatitis B or C medications.

**Case fatality:**

More than 250,000 persons die worldwide each year of hepatitis B-associated acute and chronic liver disease. The case-fatality rate in hospitalized patients is about 1%. Disease tends to be worse and mortality higher in those over 40 years of age.

**Reservoir:**

Humans are the only natural host for HBV and HDV.

**Transmission:**

**Hepatitis B:**

HBV is transmitted through blood or body fluids, including wound exudates, semen, vaginal secretions, and saliva. Blood and serum contain the highest concentrations of the virus; saliva contains the lowest. Common modes of transmission include sexual contact, contact with contaminated blood, or perinatally – from a mother to child at birth. Contact with contaminated blood can occur through needle sticks, sharing or reusing non-sterile needles or syringes, transfusion of blood and blood products (rare in the U.S. due to current blood donor screening and testing protocols), hemodialysis, and tattooing.

Person-to-person spread of HBV can occur in settings involving interpersonal contact over extended periods, such as when a chronically infected person resides in a household. In household settings, nonsexual transmission occurs primarily from child to child, and

young children are at highest risk for infection. The precise mechanisms of transmission from child to child are unknown; however, frequent interpersonal contact of non-intact skin or mucous membranes with blood-containing secretions or saliva are the most likely means of transmission. Sharing of personal items such as washcloths, towels, razors, or toothbrushes, are behaviors that can facilitate transmission. Fecal-oral transmission does not appear to occur. Approximately one-third of infected persons do not have a readily identifiable risk factor.

**Hepatitis D:**

HDV can be transmitted through blood or blood products, injection drug use, or sexual contact, as long as HBV is also present in the patient.

**Susceptibility:**

Once infected with the hepatitis B virus, a person cannot get the disease again. However, hepatitis B infection does not protect against other types of hepatitis.

**Incubation period:**

**Hepatitis B:**

Symptoms of HBV develop slowly and on average appear 12 weeks after exposure, with a range of 9-21 weeks. Symptoms only occur in 70% of cases, and are more likely to occur in adults than children.

**Hepatitis D:**

The incubation period for HDV super-infection is about 2–8 weeks. With acute co-infection of HBV and HDV, the incubation period is similar to that of HBV.

**Period of communicability:**

A person with HBV infection is considered infectious as long as HBsAg is detectable in the blood. An infected person can spread the virus to others starting a few weeks before symptoms appear and as long as they are infected. Persons chronically infected remain infectious for the rest of their lives. HDV is likely transmissible during all phases of infection. The period of time just prior to the onset of acute illness is likely the most infectious period.

**Epidemiology:**

**Hepatitis B:**

Worldwide, HBV is a major cause of chronic liver disease and liver cancer. The frequency of HBV infection and patterns of transmission vary greatly throughout the world.

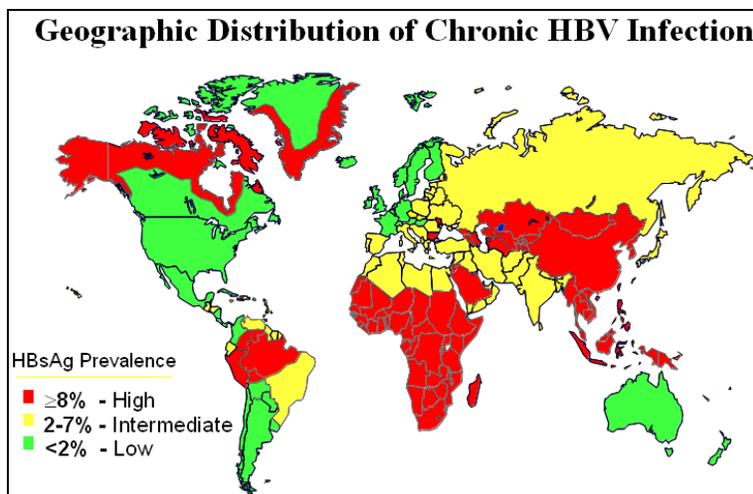


Image courtesy CDC (2006)

Within the US, there are pockets of high endemicity, including first-generation immigrants from areas where HBV is endemic, Alaskan Natives, and some inner city populations. The highest risk of early childhood infection is among children born to mothers from HBV endemic countries. Other persons at risk of infection include:

- household contacts of people with chronic HBV infection
- residents of institutions for the developmentally disabled
- patients undergoing hemodialysis
- patients with clotting disorders and others repeatedly receiving blood products

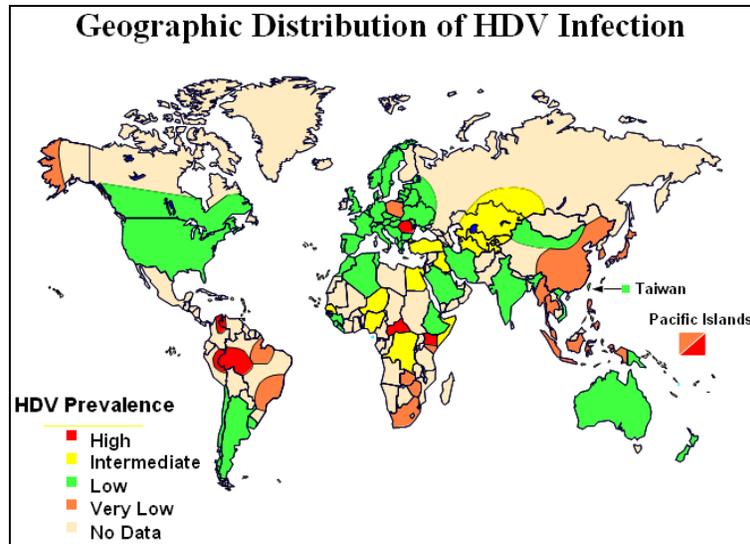
Although fewer than 10% of new HBV infections in the US occur in children, approximately one third of the estimated 1.25 million Americans with chronic HBV acquired the infection as infants or young children.

In the U.S., the most common risk factors for HBV infection are sexual contact, injection drug use, and household contact with a chronic carrier, respectively. Acute HBV infection occurs most commonly among adolescents and adults. Groups at highest risk include:

- Men who have sex with other men
- Heterosexuals with multiple sex partners
- Persons diagnosed with a recently acquired sexually transmitted disease
- Prostitutes
- Injection-drug users who share needles
- Inmates of long-term correctional facilities
- Persons undergoing hemodialysis
- Healthcare workers (depends on how often they are exposed to blood or blood products through percutaneous and permucosal exposures)

### **Hepatitis D:**

An estimated ten million people worldwide are co-infected with HDV and HBV. In the U.S., the incidence of HDV cannot be directly calculated from national surveillance data because HDV is not currently nationally reportable. However, in prevalence studies among patients with acute HBV infection, 1.5–7.2% had serologic evidence of HBV-HDV co-infection.



In general, the global pattern of HDV infection corresponds to the prevalence of chronic HBV infection; however, several distinct features of the distribution of HDV infection have been identified. In countries with a low prevalence of chronic HBV infection, HDV prevalence is generally low among both asymptomatic HBV carriers (<10%) and among patients with chronic HBV-related liver disease (<25%). HDV infection in these countries occurs most commonly among injecting drug users and persons with hemophilia. In countries with moderate and high levels of chronic HBV prevalence, the prevalence of HDV infection is highly variable. In southern Italy and in parts of Russia and Romania, the prevalence of HDV infection is very high among both asymptomatic HBV carriers (>20%) and among patients with HBV-related chronic liver disease HBV (>60%). Other countries, including northern Italy, Spain, Turkey, and Egypt, have a moderate prevalence of HDV infection among asymptomatic HBV carriers (10%-19%) and among patients with chronic HBV-related liver disease (30%-50%). However, in most of Southeast Asia and China, where the prevalence of chronic HBV infection is very high, HDV infection is uncommon. In some South American countries in the Amazon River Basin, periodic epidemics of HDV infection have occurred among chronic HBV carriers in relatively isolated regions. Disease related to HDV infection in these outbreaks has been very severe, with rapid progression to fulminant hepatitis and case-fatality rates of 10%-20%. The cause of the atypical course of HDV infection in these populations is unknown.

## ✓ PUBLIC HEALTH CONTROL MEASURES

### Public health responsibility:

- Investigate suspect cases of disease for the following groups and enter data into NEDSS:
  - Women of childbearing age (12-50 years)
  - Co-infected individuals (with Hepatitis C, D or HIV/AIDS)
  - Suspected acute cases

- Provide education to the general public and clinicians regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.
- Identify sources of exposure and stop further transmission.
- Ensure identification of infected pregnant women, and prevent perinatal transmission to their babies.
- Collect surveillance data in order to assess groups and areas where public health intervention may be needed.

### **Prevention:**

Persons with acute or chronic HBV and/or HDV infections should prevent their blood and other potentially infective body fluids from contacting other persons. They should not donate blood or share toothbrushes or razors with household members. Testing all pregnant women for HBsAg is recommended because measures can be implemented to prevent spread from infected mothers to their infants. Donated blood should be tested for HBsAg, and rejected if positive. Syringes, acupuncture and tattooing needles should never be reused. Household contacts of infected persons should be vaccinated. Vaccination is highly effective in preventing hepatitis B. Since HDV cannot be transmitted in the absence of HBV infection, the prevention of HBV infection through immunization is the best way to prevent HDV infection. However, no products exist to prevent HDV super-infection of persons with chronic HBV infection. Thus, prevention of HDV super-infection depends primarily on education to reduce risk behaviors.

### **Chemoprophylaxis:**

When indicated, hepatitis B immune globulin (HBIG) should be given as soon after exposure as possible. Hepatitis B vaccine is also recommended for people at high risk of additional exposure. Depending on the exposure circumstance, the hepatitis B vaccine series may be started at the same time as treatment with HBIG. For infants born to infected mothers, the combination of HBIG and vaccine is effective at preventing infection. Hepatitis B vaccination and one dose of HBIG administered within 24 hours after birth are 85%–95% effective in preventing both acute HBV infection and chronic infection in the infant. Vaccination against hepatitis B will prevent HDV co-infection.

### **Vaccine:**

The hepatitis B vaccine is both safe and effective. After three intramuscular doses of hepatitis B vaccine, more than 90% of healthy adults and more than 95% of infants, children, and adolescents (from birth to 19 years of age) develop adequate antibody responses. The vaccine is 80% to 100% effective in preventing infection or clinical hepatitis in those who receive the complete course of vaccine. Immune memory remains intact for more than 15 years following immunization, and both adults and children with declining antibody levels are still protected against significant HBV infection. Chronic HBV infection has only rarely been documented among vaccine responders.

#### **Routine Infant Vaccination**

Hepatitis B vaccination is recommended for all infants. The first dose should be given shortly after birth and before hospital discharge. The second dose should be given at 1-2 months, with the third dose given at 6-18 months. Combination vaccines that

include hepatitis B are also available. The hepatitis B-DTaP-IPV combination (Pediatrix) should be given on the same schedule as the hepatitis B vaccination. The hepatitis B-Hib combination (Comvax) should be given at 2, 4, and 12 through 15 months of age.

### **Routine Childhood and Adolescent Vaccination**

Routine hepatitis B vaccination is also recommended for all children and adolescents through age 18 years. Three doses should be administered. The first two doses should be separated by no less than four weeks, and a third dose 4–6 months after the second dose. A combination hepatitis A/B vaccine (Twinrix) is available for persons 18 years and older. Three doses of the hepatitis A/B vaccine should be administered, on the same schedule as the hepatitis B vaccinations. A four dose accelerated hepatitis A/B vaccination schedule is also approved, with doses given at 0, 7, and 21 through 30 days and a booster dose 12 months after the first dose.

### **Adults at High Risk**

Vaccination is also recommended for adults at increased risk of HBV infection. The schedule for adults should follow that for children and adolescents. Adults considered at increased risk for HBV infection include:

- Men who have sex with other men
- Heterosexuals with multiple sex partners
- Persons diagnosed with a recently acquired sexually transmitted disease
- Prostitutes
- Injection-drug users who share needles
- Inmates of long-term correctional facilities
- Persons undergoing hemodialysis
- Healthcare workers (depends on how often they are exposed to blood or blood products through percutaneous and permucosal exposures)

### **Other Populations**

Vaccination should also be considered for:

- Clients and staff of institutions for the developmentally disabled
- Household members and sex partners of HBV carriers
- Adults and children who plan to travel to areas outside the United States
- Recipients of certain blood products, such as persons with hemophilia, are at high risk of infection
- Pregnant women who are identified as being at risk for HBV infection during pregnancy – pregnancy is *not* a contraindication to vaccination
- Individuals with diabetes, as recommended by the ACIP in December 2011 should be considered for the vaccine under the following recommendations:
  - Hepatitis B vaccination should be administered to unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (recommendation category A; evidence type 2).
  - Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged  $\geq 60$  years (recommendation category B; evidence type 2).

### **Pre-Vaccination Serologic Testing**

Pre-vaccination serologic testing is not indicated before routine vaccination of children or adolescents. Pre-vaccination testing is recommended for:

- Foreign-born persons from endemic countries
- Children of immigrants from endemic countries
- Unvaccinated household, sexual, and needle-sharing contacts of HBV carriers
- HIV infected persons

Pre-vaccination testing should be considered for:

- Men who have sex with men
- Injection-drug users
- Incarcerated persons

### **Post-Vaccination Serologic Testing**

Post-vaccination serologic testing is not routinely recommended for most infants, children, adolescents, and adults. It should, however, be considered for persons whose subsequent management depends on knowing their immune status, including:

- Infants born to HBsAg-positive women
- Chronic hemodialysis patients
- Immunocompromised persons
- Persons with HIV
- Health care workers who have significant exposure to HBV
- Sex partners of HBsAg-positive persons

Post-vaccination testing should be performed 1-2 months after completion of the vaccine series. Children born to HBsAg-positive women should be tested at 9-18 months. Healthcare workers who have contact with patients or blood and are at ongoing risk for injuries with sharp instruments or needlesticks should be routinely tested for antibody after vaccination.

### **Management of Non-Response to Hepatitis B Vaccine**

Non-response to the hepatitis B vaccine is considered anti-HBs levels <10 mIU/mL when tested 1–2 months after completion of the vaccine series. If a person has had a non-response to the vaccine, then they should:

- Complete a second series of three doses of hepatitis B vaccine
- Retest 1–2 months after completing the second series

### **Booster Doses**

Booster doses are not recommended for persons with a normal immune status who were vaccinated as infants, children, or adolescents. However, booster doses are recommended for hemodialysis patients, if annual testing of anti-HBs levels decline to <10 mIU/mL.

For other immunocompromised persons (e.g., HIV-infected persons, hematopoietic stem cell transplant recipients, and persons receiving chemotherapy), the need for booster doses has not been determined. Annual anti-HBs testing and booster doses when anti-HBs levels decline to <10 mIU/mL should be considered in persons with an ongoing high risk for exposure.

### **Interruption in Schedule**

There are no maximum intervals and it is not necessary to restart the series of any vaccine due to extended intervals between doses.

**Isolation and quarantine requirements:**

**Isolation:** Staff and students ill with acute HBV and/or acute HDV should stay home until they feel well and until fever and jaundice are gone. Otherwise, no isolation measures are necessary.

**Hospital:** NA

**Quarantine:** NA

 **CASE INVESTIGATION**

**Reporting:**

All forms of Hepatitis B should be reported to the Utah Department of Health.

**CSTE Reporting Swimlanes, Chronic Hepatitis B Infection**

Criterion	Reporting
<i>Clinical and Administrative Data</i>	
Healthcare record contains a diagnosis of disease due to	S
Death certificate lists disease due to chronic hepatitis B as a cause of death or a significant condition contributing to death	S
<i>Laboratory Evidence</i>	
Hepatitis B surface antigen (HBsAg) positive	S
Hepatitis B e antigen (HBeAg) positive	S
Nucleic acid test for hepatitis B virus DNA (HBV DNA) positive	S

Notes:

S = This criterion alone is sufficient to report a case

**CSTE Reporting Swimlanes, Acute Hepatitis B Infection**

Criterion	Reporting			
<i>Clinical Evidence</i>				
Jaundice		N		N
Acute onset		N	N	N
Fever		O	O	O
Headache		O	O	O
Malaise		O	O	O
Anorexia		O	O	O
Nausea		O	O	O
Vomiting		O	O	O
Diarrhea		O	O	O
Abdominal Pain		O	O	O
<i>Clinical and Administrative Data</i>		O	O	O
Healthcare record contains a diagnosis of acute hepatitis B	S			
Death certificate lists acute hepatitis B as a cause of death or a significant condition contributing to death	S			

<i>Laboratory Evidence</i>					
Elevated serum aminotransferase (ALT or AST) levels			N		N
IgM antibody to hepatitis B core antigen (IgM antiHBc) positive	S	N	N		
Hepatitis B surface antigen (HBsAg) positive	S			N	N

Notes:

S = This criterion alone is sufficient to report a case

N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to report a case.

O = At least one of these “O” criteria in each category in the same column (e.g., clinical presentation and laboratory findings)—in conjunction with all other “N” criteria in the same column—is required to report a case.

## Hepatitis B, acute (2011): Case Definition

### Clinical Evidence

An acute illness with a discrete onset of any sign or symptom\* consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), and either a) jaundice, or b) elevated serum alanine aminotransferase (ALT) levels >100 IU/L.

\*A documented negative HBsAg laboratory test result within 6 months prior to a positive test(either HBsAg, HBeAg, or HBV NAT including genotype) result does not require an acute clinical presentation to meet the surveillance case definition.

### Laboratory criteria for diagnosis:

Hepatitis B surface antigen (HBsAg) positive and IgM antibody to hepatitis B core antigen (IgM anti-HBc) positive (if done)

### Case classification:

Confirmed: a case that meets the clinical case definition is laboratory confirmed, and is not known to have chronic hepatitis B

## Hepatitis B, chronic (2011): Case Definition

### Clinical evidence

No symptoms are required. Persons with chronic HBV infection may have no evidence of liver disease or may have a spectrum of disease ranging from chronic hepatitis to cirrhosis or liver cancer.

### Laboratory evidence

IgM antibodies to hepatitis B core antigen (IgM anti-HBc) negative AND a positive result on one of the following tests: hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), or nucleic acid test for hepatitis B virus DNA (including qualitative, quantitative and genotype testing)

**OR**

HBsAg positive or nucleic acid test for HBV DNA positive (including qualitative, quantitative and genotype testing) or HBeAg positive two times at least six months apart (Any combination of these tests performed six months apart is acceptable)

**Case classification**

*Confirmed:* a person who meets either of the above laboratory criteria for diagnosis

*Probable:* a person with a single HBsAg positive or HBV DNA positive (including qualitative, quantitative and genotype testing) or HBeAg positive lab result and does not meet the case definition for acute hepatitis B.

**Comment**

Multiple laboratory tests indicative of chronic HBV infection may be performed simultaneously on the same patient specimen as part of a “hepatitis panel.” Testing performed in this manner may lead to seemingly discordant results, e.g., HBsAg-negative AND HBV DNA-positive. For the purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results. Negative HBeAg results and HBV DNA levels below positive cutoff level do not confirm the absence of HBV infection.

CSTE Case Classification Swimlanes, Chronic Hepatitis B Infection

Criterion	Case Definition		
	Confirmed		Probable
<i>Laboratory Evidence</i>			
Hepatitis B surface antigen (HBsAg) positive	O <sub>1</sub>	O <sub>2</sub>	O <sub>1</sub>
Hepatitis B e antigen (HBeAg) positive	O <sub>1</sub>	O <sub>2</sub>	O <sub>1</sub>
Nucleic acid test for hepatitis B virus (HBV) DNA positive	O <sub>1</sub>	O <sub>2</sub>	O <sub>1</sub>
Hepatitis B core antigen (anti-HBc) IgM negative	N		
Does not meet acute Hepatitis B definition			O

Notes:

N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to classify a case.

O = At least one of these “O” criteria in each category in the same column—in conjunction with all other “N” criteria in the same column—is required to classify a case.

Laboratory finding labeled O<sub>1</sub> are a single specimen.

Laboratory findings labeled O<sub>2</sub> are two positive specimens spaced at least six months apart. The O<sub>2</sub> laboratory tests may be used in any combination so long as there is a minimum interval of six months between specimens.

## **Hepatitis B, perinatal:**

### **Clinical Description**

Perinatal hepatitis B in the newborn may range from asymptomatic to fulminant hepatitis.

### **Laboratory Criteria**

Hepatitis B surface antigen (HBsAg) positive

### **Case Classification**

*Confirmed:* HBsAg positivity in any infant aged 1-24 months who was born in the United States or in US territories to an HBsAg-positive mother.

### **Comments**

If HBIG and the initial dose of vaccine are delayed for >1 month after birth, testing for HBsAg can determine if the infant is already infected. Children vaccinated on the recommended schedule should receive post-vaccination testing at 9-18 months for HBsAg and anti-HBs (antibody to HBsAg). If a child receives a second hepatitis B vaccine series, post-vaccination testing should be performed 1-2 months after completion of the series.

## **Hepatitis D, co-infection:**

### **Clinical Case Definition**

No clinical case definition is available.

### **Laboratory Criteria**

- IgM antibody to hepatitis D (anti-HDV) positive
- AND**
- IgM antibody to hepatitis B core antigen (anti-HBc) positive

### **Case Classification**

*Confirmed:* a case that meets the clinical case definition and is laboratory confirmed.

## **Hepatitis D, super-infection:**

### **Clinical Case Definition**

No clinical case definition is available.

### **Laboratory Criteria**

- IgM antibody to hepatitis D (anti-HDV) positive
- AND**
- IgM antibody to hepatitis B core antigen (anti-HBc) negative

### **Case Classification**

*Confirmed:* a case that meets the clinical case definition and is laboratory confirmed.

## **Case Investigation Process:**

- Enter a confidential morbidity report (CMR) into NEDSS as a 'Hepatitis B, Chronic' (investigation will determine if this needs to be changed later to an acute case classification).

- The following groups are to be investigated when a positive hepatitis B lab report or report of disease is given to public health:
  - Suspect acute cases
  - Individuals who are co-infected with one of the following: hepatitis C, hepatitis D, HIV or AIDS.
  - Women of child bearing age (12-50 years of age)
    - Women who are found to be pregnant should have a new CMR created in UT-NEDSS through a deep copy of the existing record and classified as a 'Hepatitis B Pregnancy Event' for perinatal case management and follow up
- Although rare, the following should also be investigated:
  - Infants born to HBsAg positive mothers who were not given prenatal care and/or no vaccine was administered to the infant.
  - Mothers with unknown HBsAg status, whose infant has been reported as receiving HBIG within 7 days of birth.
    - Mother would be investigated as a pregnancy event
- Assure that all case contacts of the above investigated groups are identified and appropriately managed.

### **Outbreaks:**

Hepatitis B and D do not typically cause outbreaks.

### **Identification of case contacts:**

Close contacts of persons diagnosed with HBV and/or HDV are household members and sex partners. Transmission of HBV in schools and childcare settings is most likely to occur through direct exposure to blood after an injury or from bites or scratches that break the skin and introduce blood or body secretions from an HBV carrier into another person. The risk of transmission of HBV and/or HDV in the school and childcare setting has always been low, and with universal vaccination, exposure in the school setting does not require contact notification. Currently there are no recommendations by CDC or the Committee on Infectious Disease (authors of the Red Book) to implement contact investigations in school or child care settings. Universal precautions should be followed by staff.

### **Case contact management:**

#### **Infants Born to HBsAg-Positive Mothers**

- Newborns born to HBsAg-positive mothers should receive HBIG (0.5 mL IM) and the first dose of hepatitis B vaccine within 12 hours of birth. The vaccination schedule is dependent on weight at birth.
  - Infants born that weigh  $\geq 2000$  grams should receive a three-dose vaccination series with doses administered at 0, 1-2, and 6 months of age.
  - Infants born that weigh  $< 2000$  grams should receive a four-dose vaccination series with doses administered at 0, 1-2, 2-3, and 6-7 months of age.
  - Hepatitis B containing combination vaccines may be used for perinatal children, but not as a birth dose. Perinatal children receiving combination

vaccines should have a hepatitis B birth dose then transition to the combination vaccine.

- The infant should be screened for HBsAg and anti-HBs after completion of the immunization series at 9–15 months of age, to monitor the success or failure of the immunization. Testing should not be performed before 9 months of age to avoid detection of anti-HBs from HBIG administered during infancy and to maximize the likelihood of detecting HBV infections. If HBsAg is not present and anti-HBs antibody is  $\geq 10$  mIU/mL, children can be considered protected.
- Infants with anti-HBs concentrations of  $< 10$  mIU/mL and who are HBsAg-negative should receive three additional doses of vaccine in a 0, 1, and 6-month schedule, followed by testing for anti-HBs 1–2 months after the sixth dose. No data suggest that children who have no detectable antibody after six doses of vaccine would benefit from any additional doses.
- Infants who become HBsAg-positive despite immunization (because of intrauterine infection or vaccine failure) should be referred to a pediatric hepatologist for follow-up, and the parents should be counseled.

### **Infants Born to Mothers Whose HBsAg Status is Unknown**

- Newborns born to mothers whose HBsAg status is not known should be given hepatitis B vaccine within 12 hours of birth while awaiting HBsAg test results on the mother.
- If the mother is determined to be positive, the infant should receive HBIG as soon as possible, within seven days of birth. This child should then complete the three-dose hepatitis B vaccination series according to birth weight. The child should then be screened for HBsAg and anti-HBs at 9–18 months of age.
- If the mother is determined to be HBsAg-negative, the infant should complete the three-dose hepatitis B vaccine series according to the schedule for infants born to HBsAg-negative mothers (0, 1–2, 6–18 months). If the mother's HBsAg status remains unknown, the infant should complete the vaccine series according to the recommended schedule for infants born to HBsAg-positive mothers (0, 1–2, 6 months). Administration of HBIG is not necessary.

### **Infants Exposed After Birth**

- Children younger than 12 months of age who have close contact with primary caregivers with acute infection require immunoprophylaxis.
- If at the time of exposure, the infant has been fully immunized or has received at least two doses of vaccine, the infant should be presumed protected, and HBIG is not required.
- If only one dose of vaccine has been administered, the second dose should be administered if the interval is appropriate, or HBIG should be administered if immunization is not due.
- If immunization has not been initiated, the infant should receive HBIG (0.5 mL) and should initiate and complete the three-dose hepatitis B vaccine series.

### **Sexual Exposure to HBV Infection**

- Sexual contacts of a person with HBV who is under investigation (women of childbearing age, suspect acute cases and co-infected individuals) if susceptible, should begin the hepatitis B vaccine series.
  - Contacts who are insured by a health insurance plan should use that for vaccine coverage
  - For un-insured adult contacts, LHDs or private providers can offer vaccine purchased privately or publicly (as available) and bill according to established billing policies
  - For children contacts <18 years of age, vaccine is available through the Vaccines for Children (VFC) Program for eligible children. Un-insured children would have access to VFC vaccine, but parents would be required to pay the administration fee to the provider.
- Pre-vaccination serologic testing can determine if the sexual contact is susceptible to HBV.
- If the sexual exposure is to a person with acute HBV infection, then the contact should receive a single dose of HBIG (0.06 mL/kg) with the first vaccine dose.
- HBIG administration is unlikely to be beneficial if given more than 14 days after exposure.

### **Household/Close Contact Exposure to HBV Infection**

- All susceptible household contacts, including infants, of persons who are under investigation (women of childbearing age, suspect acute cases and co-infected individuals) with hepatitis B should initiate and complete the three-dose series of hepatitis B vaccine according to age specifications.
  - Contacts who are insured by a health insurance plan should use that for vaccine coverage
  - For un-insured adult contacts, LHDs or private providers can offer vaccine purchased privately or publicly (as available) and bill according to established billing policies
  - For children contacts <18 years of age, vaccine is available through the Vaccines for Children (VFC) for children who are eligible for that program. Un-insured children would have access to VFC vaccine, but parents would be required to pay the administration fee to the provider.
- Susceptible nonsexual household contacts of a person with acute HBV who have had a blood exposure to a case (such as sharing toothbrushes or razors) should receive a single dose of HBIG (0.06 mL/kg) with the first vaccine dose.

### **Percutaneous and Mucosal Exposure to HBV Infection**

Appropriate post-exposure management depends on the HBsAg status of the source of the exposure and the hepatitis B vaccination status of the individual exposed.

#### **HBsAg-Positive Source**

- Unvaccinated persons or persons known not to have responded to a complete hepatitis B vaccine series should receive both HBIG and hepatitis B vaccine as soon as possible after exposure (preferably within 24 hours). The hepatitis B vaccine series should be completed using the age-appropriate vaccine dose and schedule.

- Persons who are in the process of being vaccinated but who have not completed the vaccine series should receive the appropriate dose of HBIG and should complete the vaccine series.
- Children and adolescents who have written documentation of a complete hepatitis B vaccine series and who did not receive post-vaccination testing should receive a single vaccine booster dose.

**Source with Unknown HBsAg Status**

- Unvaccinated persons should begin the hepatitis B vaccine series within 24 hours after exposure. The vaccine series should be completed using the age-appropriate dose and schedule.
- Persons who are not fully vaccinated should complete the vaccine series.
- Children and adolescents with written documentation of a complete hepatitis B vaccine series require no further treatment.

**TABLE. Guidelines for postexposure prophylaxis\* of persons with nonoccupational exposures† to blood or body fluids that contain blood, by exposure type and vaccination status**

Exposure	Treatment	
	Unvaccinated person‡	Previously vaccinated person¶
<b>HBsAg**‑positive source</b>		
Percutaneous (e.g., bite or needlestick) or mucosal exposure to HBsAg‑positive blood or body fluids	Administer hepatitis B vaccine series and hepatitis B immune globulin (HBIG)	Administer hepatitis B vaccine booster dose
Sex or needle-sharing contact of an HBsAg‑positive person	Administer hepatitis B vaccine series and HBIG	Administer hepatitis B vaccine booster dose
Victim of sexual assault/abuse by a perpetrator who is HBsAg positive	Administer hepatitis B vaccine series and HBIG	Administer hepatitis B vaccine booster dose
<b>Source with unknown HBsAg status</b>		
Victim of sexual assault/abuse by a perpetrator with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment
Percutaneous (e.g., bite or needlestick) or mucosal exposure to potentially infectious blood or body fluids from a source with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment
Sex or needle-sharing contact of person with unknown HBsAg status	Administer hepatitis B vaccine series	No treatment

\* When indicated, immunoprophylaxis should be initiated as soon as possible, preferably within 24 hours. Studies are limited on the maximum interval after exposure during which postexposure prophylaxis is effective, but the interval is unlikely to exceed 7 days for percutaneous exposures or 14 days for sexual exposures. The hepatitis B vaccine series should be completed.

† These guidelines apply to nonoccupational exposures. Guidelines for management of occupational exposures have been published separately (7) and also can be used for management of nonoccupational exposures, if feasible.

‡ A person who is in the process of being vaccinated but who has not completed the vaccine series should complete the series and receive treatment as indicated.

¶ A person who has written documentation of a complete hepatitis B vaccine series and who did not receive postvaccination testing.

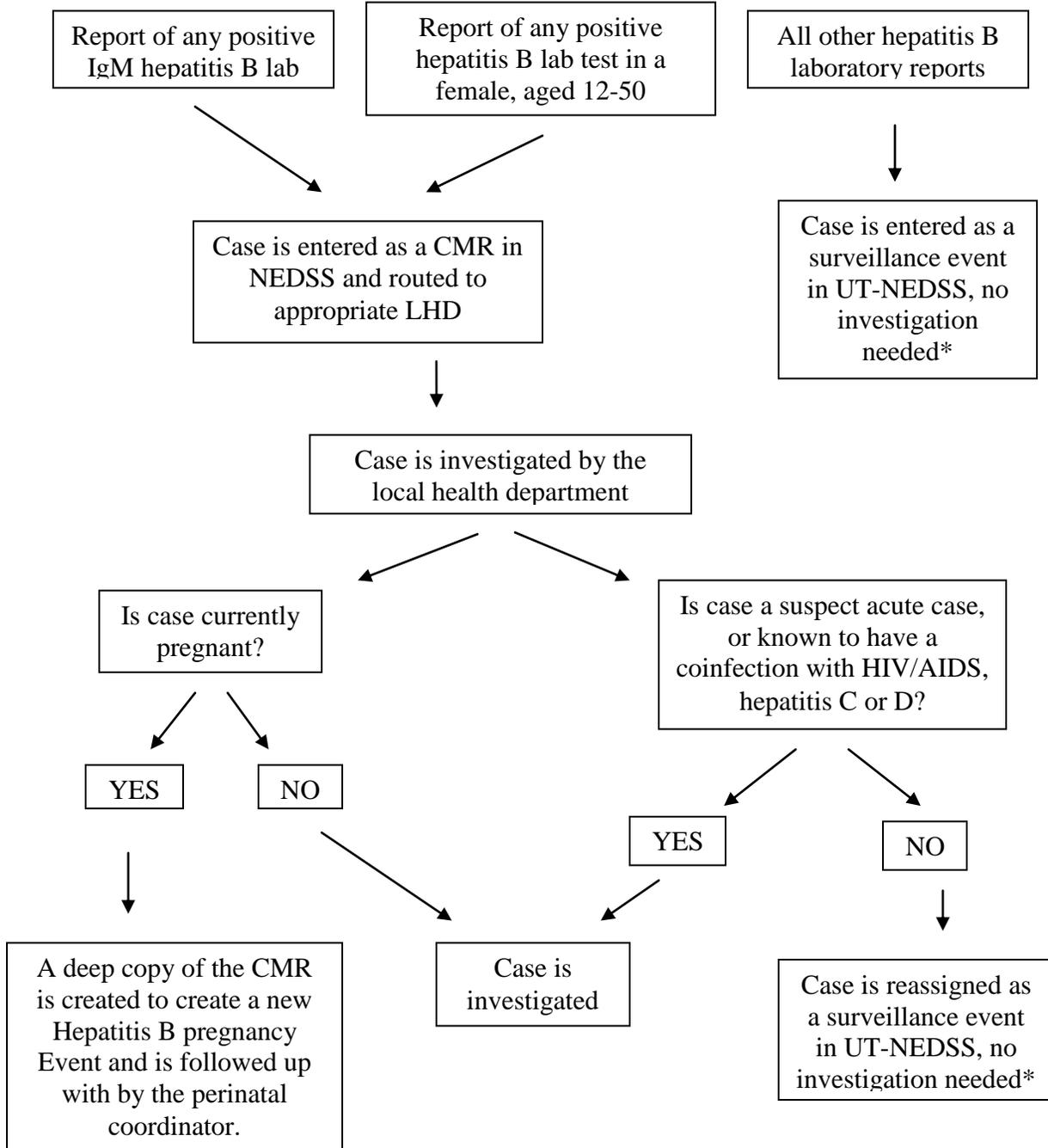
\*\* Hepatitis B surface antigen.

Table from CDC MMWR 55 (RR-16) 2006: Post Exposure Prophylaxis to Prevent Hepatitis B Infection, Appendix B

## ✓ SURVEILLANCE PARAMETERS FOR HEPATITIS B

Surveillance event data, combined with CMR data for hepatitis B cases will be analyzed by geographic location to determine areas of greatest prevalence in order to target public health intervention strategies. These data will be shared with public health partners in order to focus prevention efforts to areas and specific populations to assist in decreasing the hepatitis B disease burden in Utah.

All cases/positive laboratory results reported to public health will follow the following algorithm:



**\*NOTE:** A monthly export of hepatitis cases will be done by UDOH and matched to any currently known cases of HIV/AIDS, Hepatitis D and C and will be opened as CMRs and routed to LHDs for further investigation.

## ✓ REFERENCES

Council of State and Territorial Epidemiologists, *Hepatitis B, Chronic Position Statement 2011*. Retrieved on 12/15/2014 from:

<http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/11-ID-04.pdf>

Council of State and Territorial Epidemiologists, *Hepatitis B, Acute Position Statement 2011*. Retrieved on 12/15/2014 from:

<http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/11-ID-03.pdf>

Control of Communicable Diseases Manual (18<sup>th</sup> Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26<sup>th</sup> Edition), Larry K. Pickering MD, Ed; 2003.

Massachusetts Department of Public Health, Guide to Surveillance, Reporting and Control, 2006.

ARUP Labs; Physician's Guide to Laboratory Test Selection and Interpretation

Centers for Disease Control, Post Exposure Prophylaxis to Prevent Hepatitis B Infection. MMWR 55(RR16);30-31 Appendix B 2006

[http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a3.htm?s\\_cid=rr5516a3\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5516a3.htm?s_cid=rr5516a3_e)  
(accessed on 2/8/2012)

Centers for Disease Control, Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. MMWR57(RR-7) 2008. <http://www.cdc.gov/mmwr/pdf/rr/rr5708.pdf> accessed on 2/8/2012

Centers for Disease Control, Use of Hepatitis B Vaccination for Adults with Diabetes Mellitus: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 60(50);1709-1711 2011