SF Hep B Free—Bay Area HBV ECHO Didactic

Perinatal Hepatitis B Management

To Prevent Mother-to-Child Transmission

Amy Tang, MD
Director of Immigrant Health
North East Medical Services, San Francisco, CA

2.16.2021

What mode of transmission is responsible for the majority of chronic hepatitis B virus (HBV) infections worldwide?

A. Blood transfusion
B. Sexual contact
C. Mother to child during childbirth
D. Sharing needles, syringes, or other drug-injection equipment

What mode of transmission is responsible for the majority of chronic hepatitis B virus (HBV) infections worldwide?

A. Blood transfusion
B. Sexual contact
C. Mother to child during childbirth
D. Sharing needles, syringes, or other drug-injection equipment

HBV infection during infancy is associated with a ___% chance of developing **chronic** HBV infection.

A. 10%
B. 30%
C. 60%
D. 90%

HBV infection during infancy is associated with a ___% chance of developing **chronic** HBV infection.

A. 10%
B. 30%
C. 60%
D. 90%...leading to premature death from liver cancer or other liver complications in up to 25% of those unmonitored and untreated

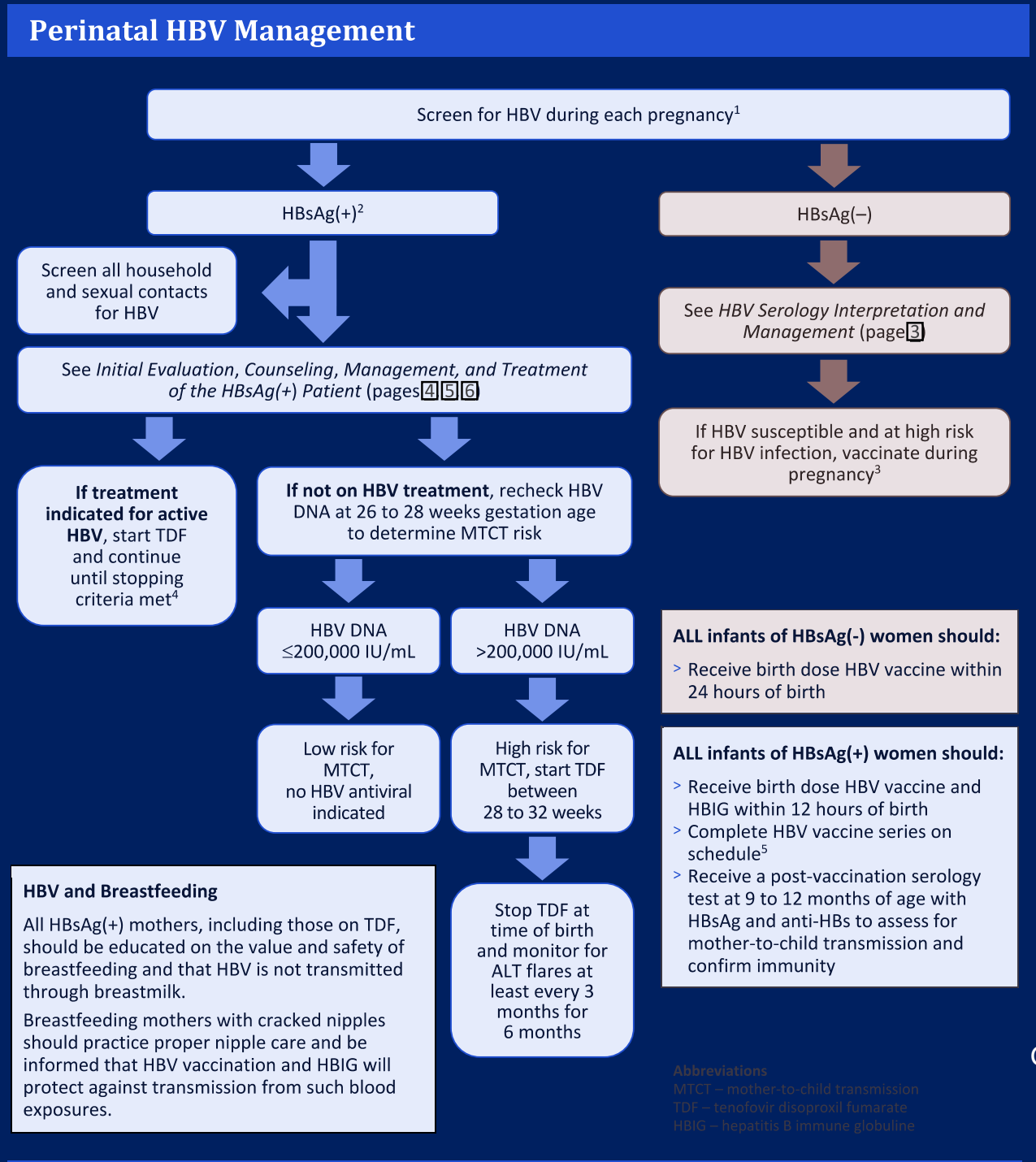
HBV Elimination Goal

Understand your roles as primary care providers in preventing new hepatitis B virus (HBV) infections for future generations through comprehensive perinatal management of women with HBV and their infants.

Objectives

- Obstetrics: Identify HBsAg(+) women through universal screening during pregnancy and link to care
- Adult Medicine: Identify HBsAg(+) women who need antiviral treatment during pregnancy and counsel women on HBV transmission and need for long-term monitoring
- Pediatrics: Ensure all infants born to HBsAg(+) women receive and complete hepatitis B immunizations/immune prophylaxis and post-vaccination serology testing in a timely manner.
- ALL: Ask about family history of HBV and liver cancer and recommend testing of all household contacts with unknown HBV status (and vaccination if susceptible)

Identification and **evaluation** of pregnant women with HBV infection and proper **vaccination** of infants are key steps to reducing MTCT.



Tang et al. Hepatitis B Management: Guidance for the Primary Care Provider. Feb 25, 2020. https//www.hepatitisB.uw.edu/hbv-pcw/guidance

Perinatal HBV References

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 67 / No. 1
January 12, 2018

Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices

New or Updated Recommendations

The following recommendations are new or updated:

- universal hepatitis B (HepB) vaccination within 24 hours of birth for medically stable infants weighing ≥2,000 grams;
- testing HBsAg-positive pregnant women for hepatitis B virus deoxyribonucleic acid (HBV DNA);
- postvaccination serologic testing for infants whose mother's HBsAg status remains unknown indefinitely (e.g., when a parent or person with lawful custody surrenders an infant confidentially shortly after birth);
- single-dose revaccination for infants born to HBsAg-positive women not responding to the initial vaccine series;
- vaccination for persons with chronic liver disease (including, but not limited to, those with hepatitis C virus [HCV] infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal); and
- removal of permissive language for delaying the birth dose until after hospital discharge.

HEPATOLOGY
AASLD
PRACTICE GUIDANCE | HEPATOLOGY, VOL. 67, NO. 4, 2018

Update on Prevention, Diagnosis, and Treatment of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance

Norah A. Terrault,[1] Anna S.F. Lok,[2] Brian J. McMahon,[3] Kyong-Mi Chang,[4] Jessica P. Hwang,[5] Maureen M. Jonas,[6] Robert S. Brown Jr.,[7] Natalie H. Bzowej,[8] and John B. Wong[9]

Guidance Statements on Counseling of Women in Pregnancy

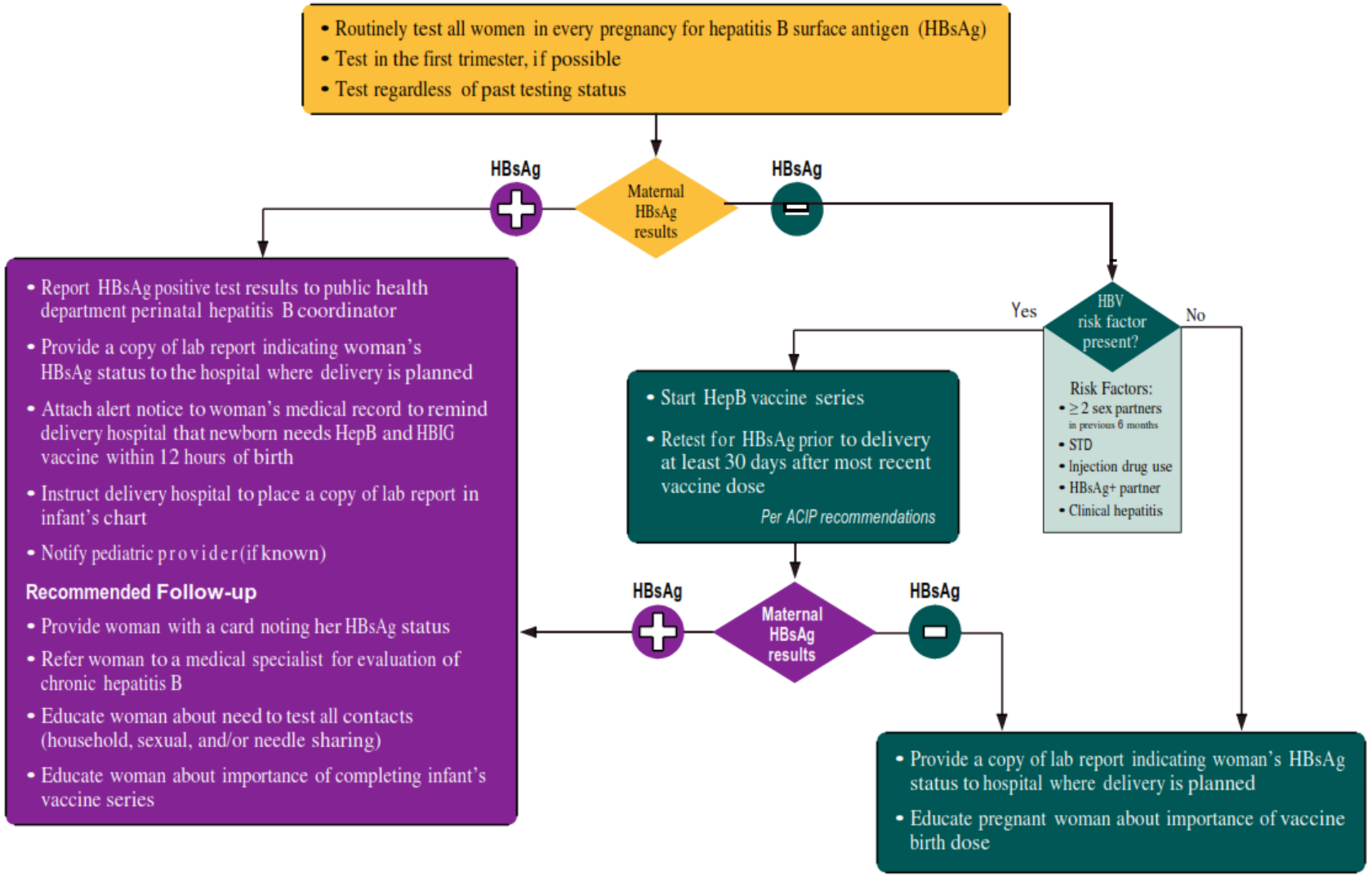
1. HBV vaccination is safe in pregnancy, and pregnant women who are not immune to or infected with HBV should receive this vaccine series.
2. Women identified as HBsAg positive during pregnancy should be linked to care for additional testing (ALT, HBV DNA, or imaging for HCC surveillance if indicated) and determination of need for antiviral therapy.
3. Women who meet standard indications for HBV therapy should be treated. Women without standard indications but who have HBV DNA >200,000 IU/mL in the second trimester should consider treatment to prevent mother-to-child transmission.(1)
4. HBV-infected pregnant women who are not on antiviral therapy as well as those who stop antiviral at or early after delivery should be monitored closely for up to 6 months after delivery for hepatitis flares and seroconversion. Long-term follow-up should be continued to assess need for future therapy.
5. The potential risk of mother-to-child transmission of HBV with amniocentesis should be included in the risk of harms versus benefits discussion in HBsAg-positive mothers with high-level viremia.
6. HBV-infected pregnant women with cirrhosis should be managed in high-risk obstetrical practices and treated with TDF to prevent decompensation.
7. Sexual partners of women identified as HBV-infected during pregnancy should be assessed for HBV infection or immunity and receive HBV vaccine if appropriate.
8. Breastfeeding is not prohibited.

HBV Screening during pregnancy

Clinical guidelines (USPSTF, CDC, AASLD) recommend:

- Routinely test **all women in every pregnancy** for HBV
  - Not risk-based testing
- Test in the **first trimester,** if possible
  - Typically included in prenatal panel
  - Make sure to review document HBV status for late pregnancy transfers!
- Test **regardless of past testing status**
  - HBsAg negative > positive can occur if previously susceptible and unvaccinated
  - HBsAg positive > negative (HBsAg seroclearance) can occur spontaneously in 1-2% persons with chronic HBV

Testing for Hepatitis B Virus Infection During Pregnancy Flowchart for Prenatal Providers



Resources available at www.CDC.gov/hepatitis/perinatalHepB

Vaccinate* and re-test** during pregnancy if HBV risk factors present:

- **HBsAg+ partner**
- Clinical hepatitis (e.g. ALT elevated)
- STD
- IVDU
- >= 2 sex partners in past 6 months

Can vaccinate post-partum with if low-risk

**3-dose HBV vaccine (e.g. Engerix) is safe/FDA-approved for pregnancy. 2-dose Heplisav-B may be given postpartum.*
***Re-test at time of admission to hospital for delivery*

Why are infants born to HBsAg-negative women recommended HBV vaccine within 24 hours of birth?

A. To protect infant from HBV transmission by a caregiver/household member (e.g. father or grandparent)
B. Sometimes hospitals misidentify/misinterpret the mother's HBV lab results (e.g. mixing up HBsAg and HBsAb/anti-HBs results)
C. Some women do not get tested for HBV during pregnancy or their results were not properly reported to the hospital
D. All of the above

Why does the CDC/ACIP recommend that infants born to HBsAg-negative women recommended HBV vaccine within 24 hours of birth?

A. To protect infant from HBV transmission by a caregiver/household member (e.g. father or grandparent)

B. Sometimes hospitals misidentify/misinterpret the mother's HBV lab results (e.g. mixing up HBsAg and HBsAb/anti-HBs results)

C. Some women do not get tested for HBV during pregnancy or their results were not properly reported to the hospital

D. All of the above, universal HBV birth dose prior to hospital discharge serves as a safety net to prevent HBV transmission for infants.

Besides HBV vaccine birth dose, what else is given specifically to infants born to HBsAg(+) mothers within 12 hours of birth?

A. Hepatitis B Immune Globulin (HBIG)
B. A dose of injectable HBV antiviral medication
C. Hepatitis A vaccine birth dose
D. None of the above

Besides HBV vaccine birth dose, what else is given to infants born to HBsAg(+) mothers within 12 hours of birth?

A. Hepatitis B Immune Globulin (HBIG)
B. A dose of HBV antiviral medication
C. Hepatitis A vaccine birth dose
D. None of the above

HBV birth dose will prevention MTCT in 75% of infants

+ HBIG will prevent MTCT in 94% of infants

Postvaccination Serologic Testing (PVST)

Recommended for infants born to HBsAg-positive mothers

– AND— mothers whose HBsAg status remains unknown indefinitely (e.g. infants safely surrendered shortly after birth)

Performed at age 9 to 12 months (after completion of HBV vaccine series) and at least 1 month after last HBV vaccine dose (to avoid detecting HBsAg from vaccine)

- Do not perform before 9 months to avoid detection of anti-HBs from HBIG administered at birth and to maximize likelihood of detecting late HBV infection

PVST includes HBsAg and Anti-HBs only.

- Anti-HBc not recommended due to possible false positive from passively acquired maternal anti-HBc detected in infants up to age 24 months

PVST Interpretation

- HBsAg-negative infants
  - Anti-HBs >= 10mIU/mL: protected; no further medical management for HBV
    - Immunocompetent persons remain protected, even if anti-HBs later declines to < 10 mL=IU/mL
  - Anti-HBs < 10mIU/mL: Revaccinate and re-test 1-2 months after the final dose
    - Option for single-dose revaccination with 1 month f/u PVST and additional 2 more doses if anti-HBs < 10mIU/mL
- HBsAg-positive infants:
  - Should receive appropriate clinical follow-up

HBV Immunoprophylaxis Failures

Timely HBV immunoprophylaxis of neonates has reduced MTCT worldwide; however, immunoprophylaxis failures still occur in approximately 8%-32% of infants born to mothers with high levels of HBV viremia.

Pregnant women with a HBV DNA greater than _____ are recommended HBV antiviral to prevent transmission to their infant(s)

A. 2000 IU/mL
B. 20,000 IU/mL
C. 200,000 IU/mL
D. 1 million IU/mL

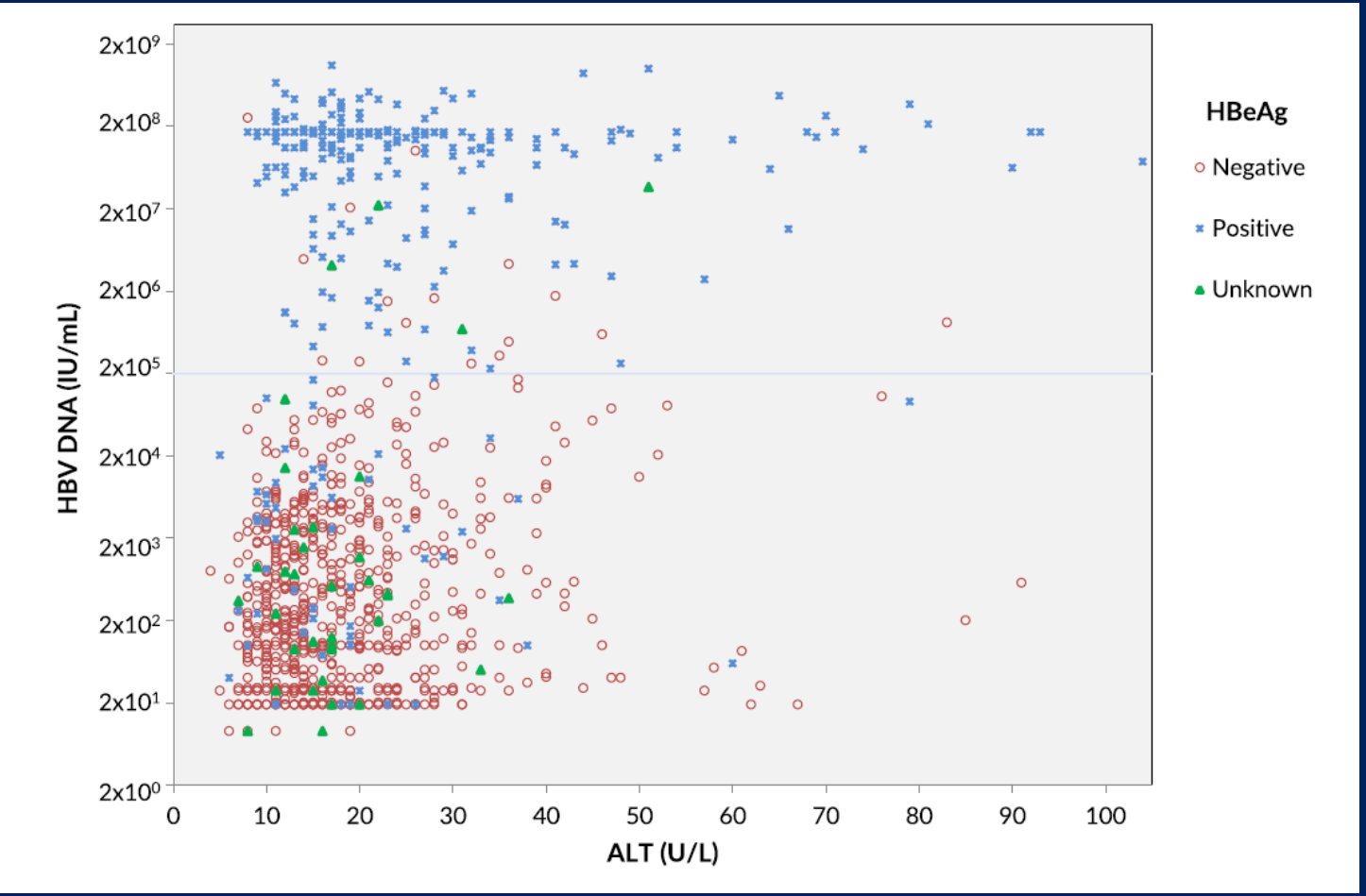
Pregnant women with a HBV DNA greater than _____ are recommended HBV antiviral to prevent transmission to their infant(s)

A. 2000 IU/mL
B. 20,000 IU/mL
C. 200,000 IU/mL
D. 1 million IU/mL

A large retrospective, study in 2012 of 869 Chinese mother-infant pairs observed that immunoprophyalxis failure occurred in infants born to mothers with an HBV DNA as low as 10^6 copies/mL (200,000 IU/mL).

Therefore, the CDC/AASLD recommend that women with HBV DNA level > 200,000 IU/mL should initiate antiviral treatment between 28 and 32 weeks of pregnancy to decrease HBV DNA levels before delivery.

1 in 5 pregnancies among Asian American women with chronic HBV considered high risk for MTCT and met criteria for antiviral therapy



Retrospective cross-sectional analysis of 1012 mostly (98%) China-born women with chronic HBV (and 1298 pregnancies) evaluated with HBV DNA during prenatal care at community health center in NYC from 2007 to 2017.

Approximately 1 in 5 pregnancies (22.4%) with HBV DNA > 200,000 IU/mL and high risk for MTCT

- 92% HBeAg-positive
- 7% HBeAg-negative

Tang et al. J Viral Hepatitis 2019

Indications for Antiviral Treatment to Prevent HBV Vertical Transmission

- Women with viral loads of >200,000 IU/ml are recommended for antiviral treatment to decrease the risk of transmission to the baby; however, there must be a discussion on the risks and benefits of antiviral treatment.

- Tenofovir DF/Viread is Pregnancy Category B and the recommended drug due to efficacy to reduce viral load and decreased likelihood of resistance (tenofovir AF/Vemlidy has insufficient evidence of safety to recommend during pregnancy)

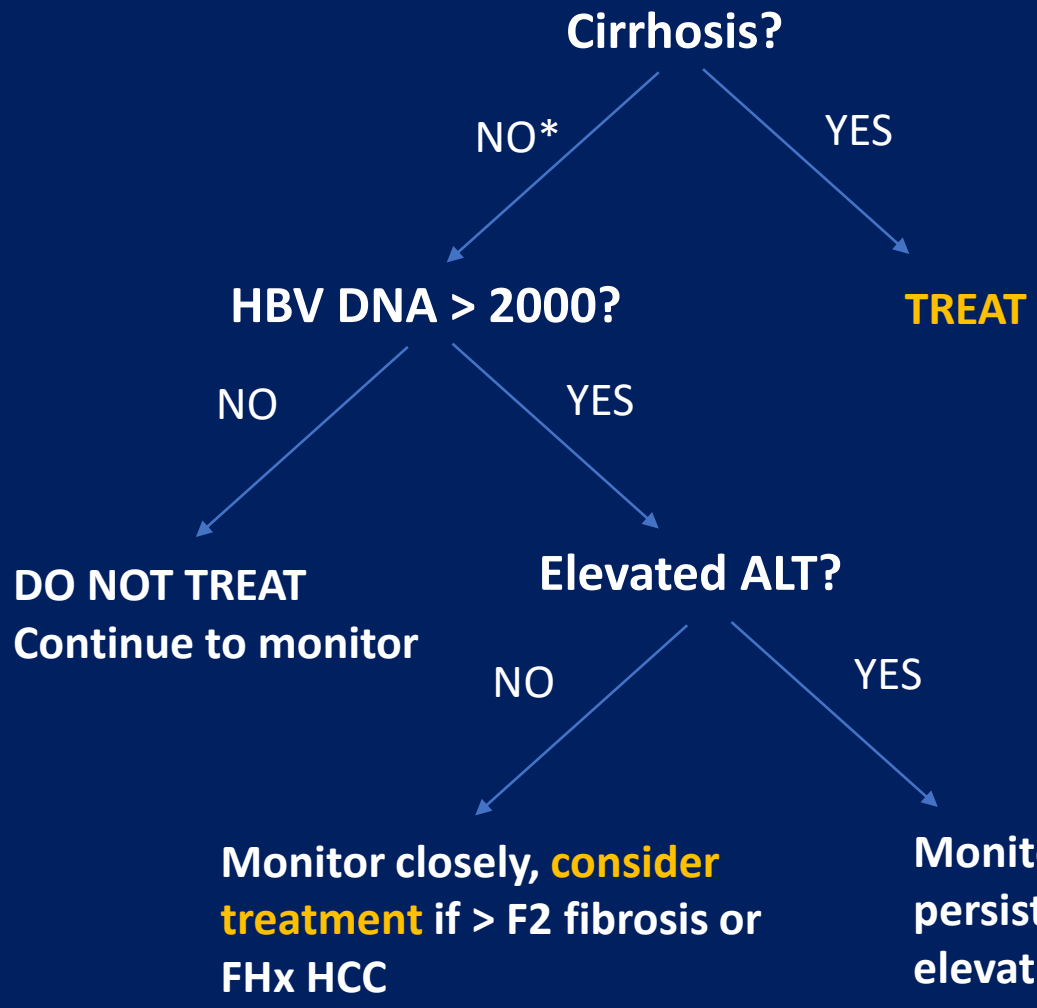
- **Antiviral treatment is recommended to be initiated at least 10 weeks prior to delivery**
  - Singleton pregnancy: 28-30 weeks GA
  - Twin pregnancy: 24-26 weeks GA
  - Triplet pregnancy: 20-22 weeks GA

- If the sole goal is to prevent vertical transmission, then antiviral therapy in most cases is discontinued postpartum at birth. When treatment is discontinued, women should be monitored at least every 3 months for 6 months for hepatitis flares.

Monitoring for post-treatment and post-partum hepatitis flare

- Hepatitis flare (increased ALT and HBV DNA) is common postpartum, especially in women who were on treatment during pregnancy and stopped at birth.
- Some experts recommend ALT monitoring at 1 month, 3 month, and 6 months (or more frequently if ALT elevated)
- If ALT increased > 100, also monitor direct bilirubin, INR, platelets, AST for evidence of liver decompensation and consider consultation with HBV specialist.
- Antiviral should be restarted if ALT > 10XULN (>250 for women)

New HBsAg(+) patients need an initial HBV evaluation to identify if HBV antiviral needed for immune active CHB



*Need to actively rule out cirrhosis in all patients with a baseline fibrosis assessment, e.g. *Fibroscan, FibroSure*

Treatment Endpoints for Women on HBV Antiviral Therapy for Immune Active CHB

Assessing Treatment Response and Endpoints for Antiviral Discontinuation

After initiation of HBV antiviral, recheck HBV DNA every 3 months until undetectable, then every 6 months once undetectable. If the patient does not achieve undetectable HBV DNA after 1 year of antiviral therapy and the HBV DNA levels are not downtrending, obtain expert consultation or refer to a specialist.

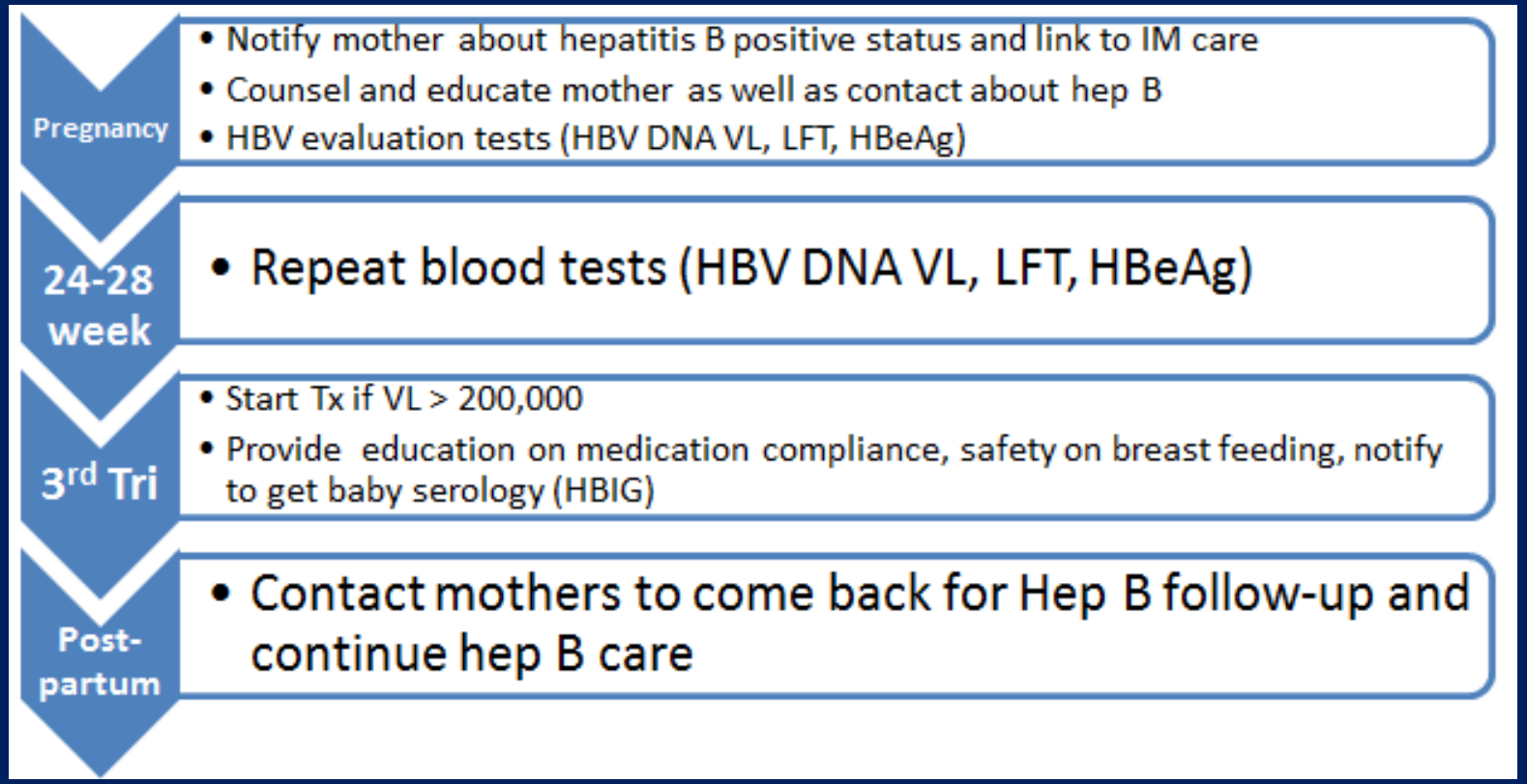
- Persons with cirrhosis: Do not stop antiviral treatment, unless guided by expert consultation.
- Persons without cirrhosis and HBeAg(+) at baseline: Patients with persistent undetectable HBV DNA, normal ALT, and persistent HBeAg(-) and anti-HBe(+) 1 year after HBeAg seroconversion [from HBeAg(+)/anti-HBe(-) to HBeAg(-)/anti-HBe(+)] may trial off antiviral treatment.
- Persons without cirrhosis and HBeAg(-) at baseline: Continue antiviral treatment until HBsAg clearance.

Hepatitis B and Breastfeeding

- Although HBsAg can be detected in breast milk, there is no evidence that HBV can be transmitted by breastfeeding. Per WHO and CDC recommendations, breastfeeding is acceptable and encouraged, even if the mother is HBsAg-positive.
- Among infants receiving post-exposure prophylaxis to prevent perinatal HBV infection, there is no known increased risk of infection among breastfed infants.
- Immunization of the baby at birth should protect the infant from modes of postnatal HBV transmission, including possible exposure to HBV from cracked or bleeding nipples during breastfeeding. To prevent cracked and bleeding nipples, all mothers who breastfeed should be instructed on proper nipple care.
- Although no adverse effects have been linked to infants breastfed while the mother was on antiviral therapy, providers may consider stopping anti-viral treatment after delivery if the mother wishes to breastfeed in order to minimize exposure of the medication through breast milk.

Wong VC, et al. BrJ OB Gyn1980:87:958-65
Hill JB et al, Obstet Gynecol. 2002. 99:1049-1052
Wang JS Int J. Clin Prac 2003:57:100

Summary of Peripartum HBV Surveillance



Hep B Moms Program

- HBV care manager provides perinatal HBV education and coordinates household contact screening for all Hep B Moms
- Collaboration between Adult Medicine, Ob/Gyn, Pediatrics
  - Link all moms to HBV care with NEMS adult medicine provider/HBV site champion during and after pregnancy
- EHR report allows care manager to track perinatal HBV patients, facilitate linkage to care, ensure labs done and high risk started on HBV antiviral

If you are pregnant and have hepatitis B, the virus can easily infect your newborn through your blood at birth. The baby can then carry this serious disease for a lifetime. To prevent infection to your baby and damage to your liver, make sure you see your doctor for hepatitis B and your baby is protected with immunizations.

If You Have Hepatitis B
Protect Your Baby & Your Health

Use this chart to track your care and your baby's care!

For Mom

1st Trimester & 2nd Trimester

- ☐ See a doctor for hepatitis B care and get blood tests to check your hepatitis B virus level and other liver tests.
- ☐ If needed, your doctor may talk to you about taking hepatitis B medication.

3rd Trimester

- ☐ Your doctor will check your hepatitis B virus level before or at 28 weeks to decide if you need to start hepatitis B medication to prevent infection of your baby.

At Birth

- ☐ Tell the staff at the hospital you have hepatitis B.

1-2 Months

- ☐ Follow-up with your doctor for hepatitis B care if you were started on treatment during pregnancy.
- ☐ Tell the doctor who will care for your baby that you have hepatitis B.

6 Months

- ☐ Follow-up with your doctor for hepatitis B monitoring at least every 6 months.

>>>>>> DURING PREGNANCY >>>>>>>>>>>>>>>>>>>>>>>>>>>> AT BIRTH >>>>>>>>>>>>>>>> AFTER DELIVERY >>>>>>>>>>>>>>>>>

For Baby

At Birth

- ☐ Baby must receive 2 shots within 12 hours of birth to protect from infection.
  - One shot of hepatitis B immunoglobulin (HBIG)
  - 1st shot of the hepatitis B vaccine
- ☐ Once your baby gets the HBIG shot and hepatitis B vaccine, it is safe to breastfeed. You cannot give your baby hepatitis B from breast milk. Ask your doctor if you should still breastfeed if you have cracked nipples or open sores on your breast.
- ☐ Hospital staff will give you an immunization card to track baby's shots. Bring this card to all of your baby's doctor visits.

1-2 Months

- ☐ Your baby is due for their 2nd hepatitis B vaccine.

2nd shot of the hepatitis B vaccine

6 Months

- ☐ Your baby is due for their 3rd hepatitis B vaccine.

3rd shot of the hepatitis B vaccine

9-12 Months

- ☐ Your baby needs a blood test to check their hepatitis B status.

  This is special for babies born to mothers with hepatitis B.

- ☐ **Make sure your spouse and those living with you are tested for hepatitis B during your pregnancy.**

Acknowledgements: The creation of this material was funded by the Prevent Cancer Foundation and modeled after Charles B. Wang Community Health Center's Hep B Roadmap.

NEMS NORTH EAST MEDICAL SERVICES 東北醫療中心
a california health center

NEMS - Rev. 12/2020

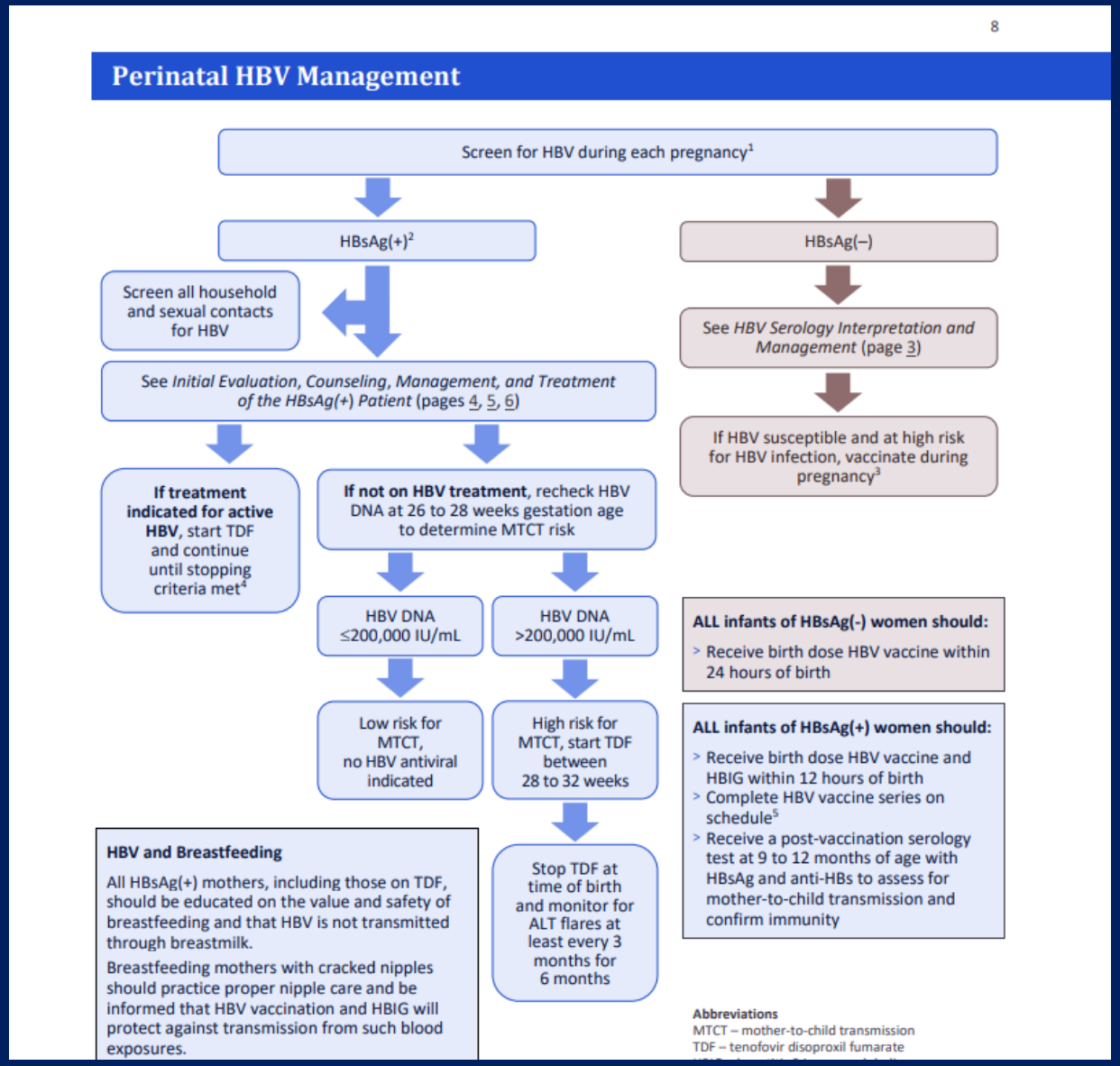
Take home points

Comprehensive management of HBV+ pregnancies involves coordination between obstetrics, HBV provider, delivery hospital, pediatrics and local department of health and accurate information exchange amongst all providers is crucial

- Obstetrics: Identify HBsAg(+) women through universal screening during pregnancy and link to care
- Adult Medicine: Identify HBsAg(+) women who need antiviral treatment during pregnancy and counsel women on HBV transmission and need for long-term monitoring
- Pediatrics: Ensure all infants born to HBsAg(+) women receive and complete hepatitis B immunizations/immune prophylaxis and post-vaccination serology testing in a timely manner.
- ALL: Ask about family history of HBV and liver cancer and recommend testing of all household contacts with unknown HBV status (and vaccination if susceptible)

Hepatitis B Online (www.hepatitisb.uw.edu)

- A CDC-funded viral hepatitis training resource
- Free, up-to-date educational website for diagnosing, monitoring, managing, and preventing hepatitis B virus (HBV) infection
- Free CME credits and CNE contact hours
- Sections on HBV medications and vaccinations, nine clinical calculators
- Simplified clinical guidance for primary care providers developed in collaboration with the multi-disciplinary HBV Primary Care Workgroup



Hepatitis B Online is funded through CDC Cooperative Agreement PS16-1608 and developed by the University of Washington (UW) National Hepatitis Training Center.