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Hep B Moms

Prevention of Perinatal Transmission and Management of Hepatitis B in Pregnancy and Post Partum

Amy Tang, MD

Director of Immigrant Health

North East Medical Services, San Francisco, CA

05.24.2024

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

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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

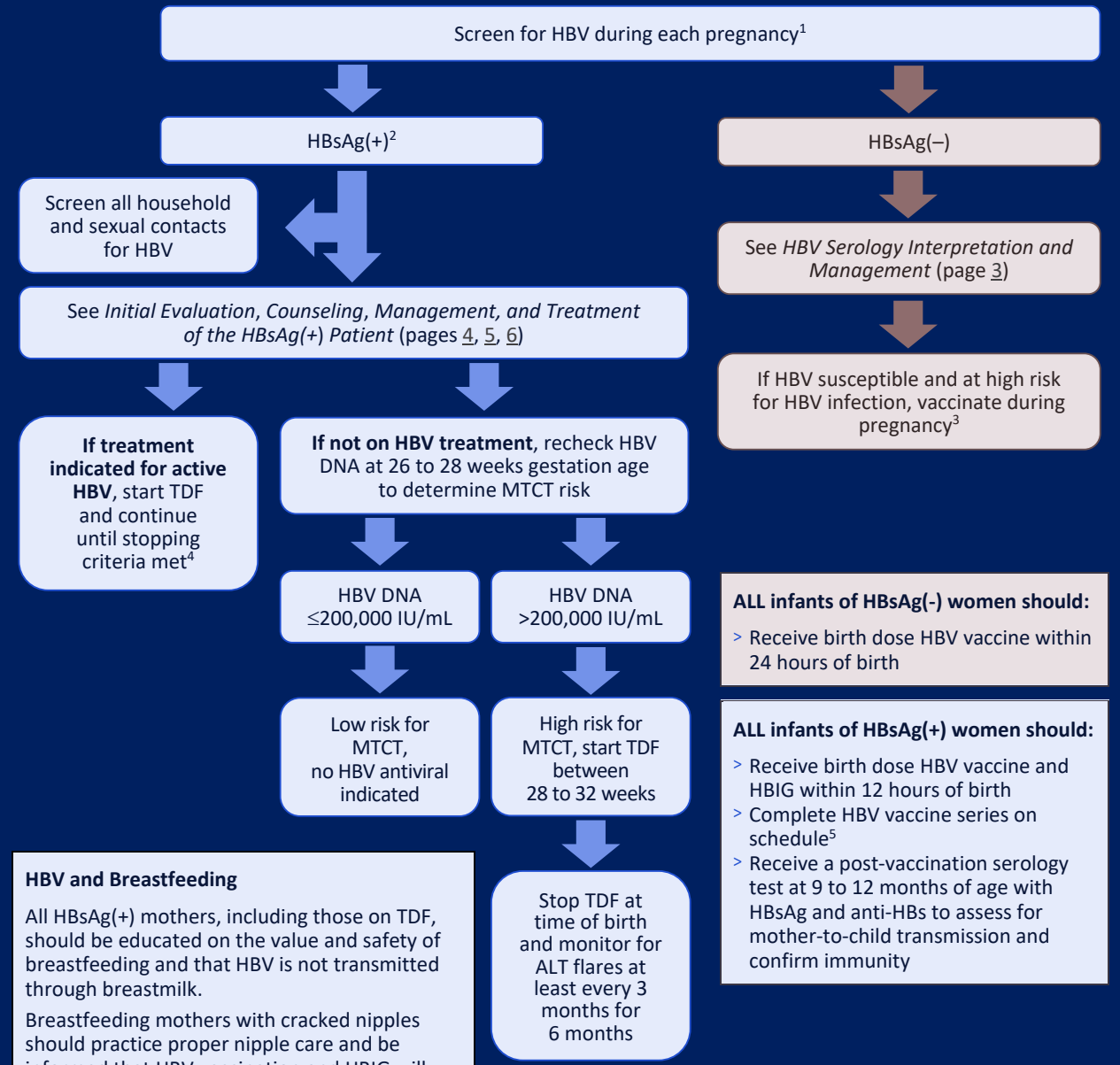
Understand your roles as health care and public health providers in preventing new hepatitis B virus (HBV) infections for future generations through comprehensive perinatal management of women with HBV and their infants.

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.
- Public Health: 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.

Perinatal HBV Management



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

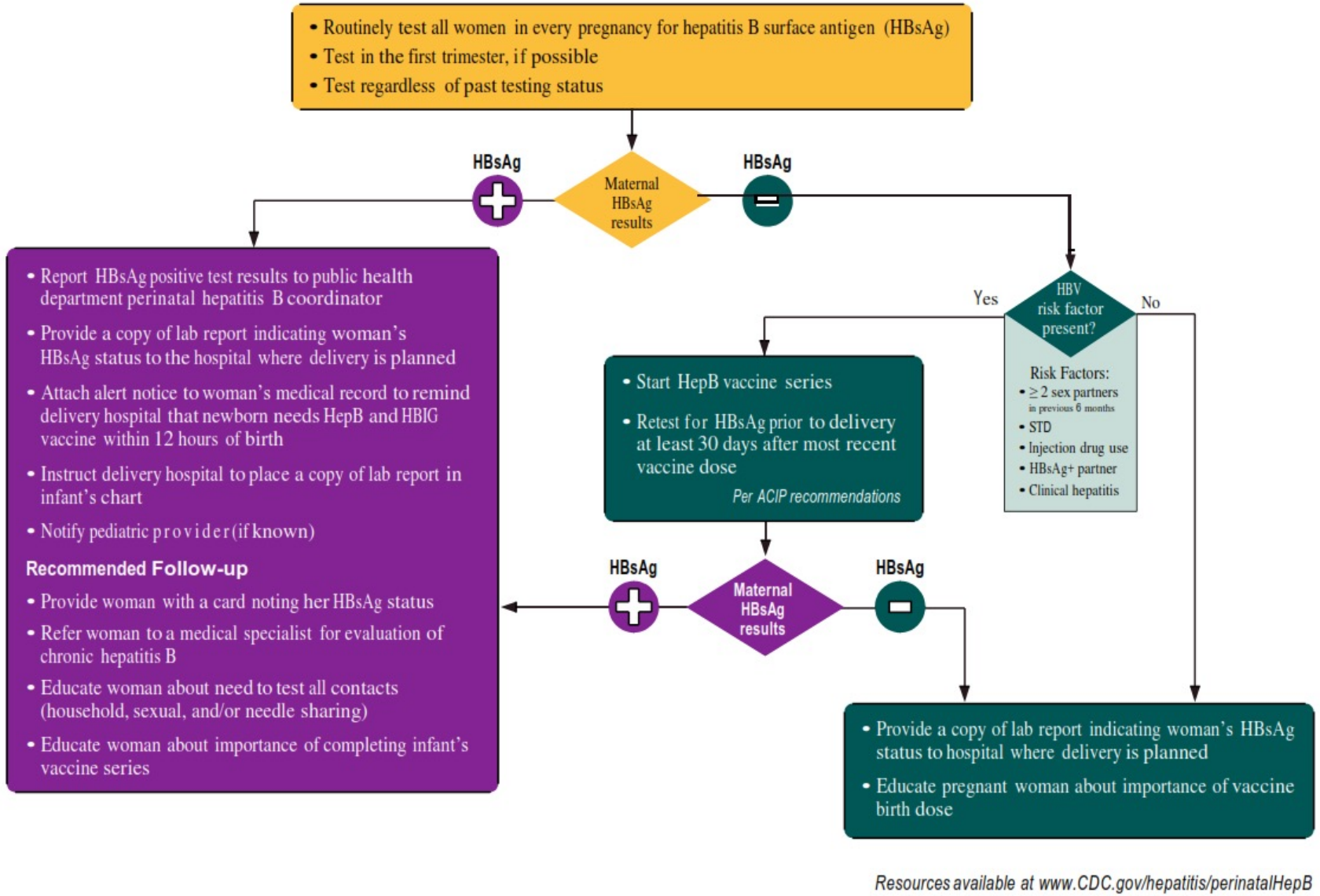
1. HBV vaccination is safe in pregnancy, and pregnant women who are not immune to or infected with HBV should receive this vaccine series.
2. Women identified as HBsAg positive during pregnancy should be linked to care for additional testing (ALT, HBV DNA, or imaging for HCC surveillance if indicated) 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



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

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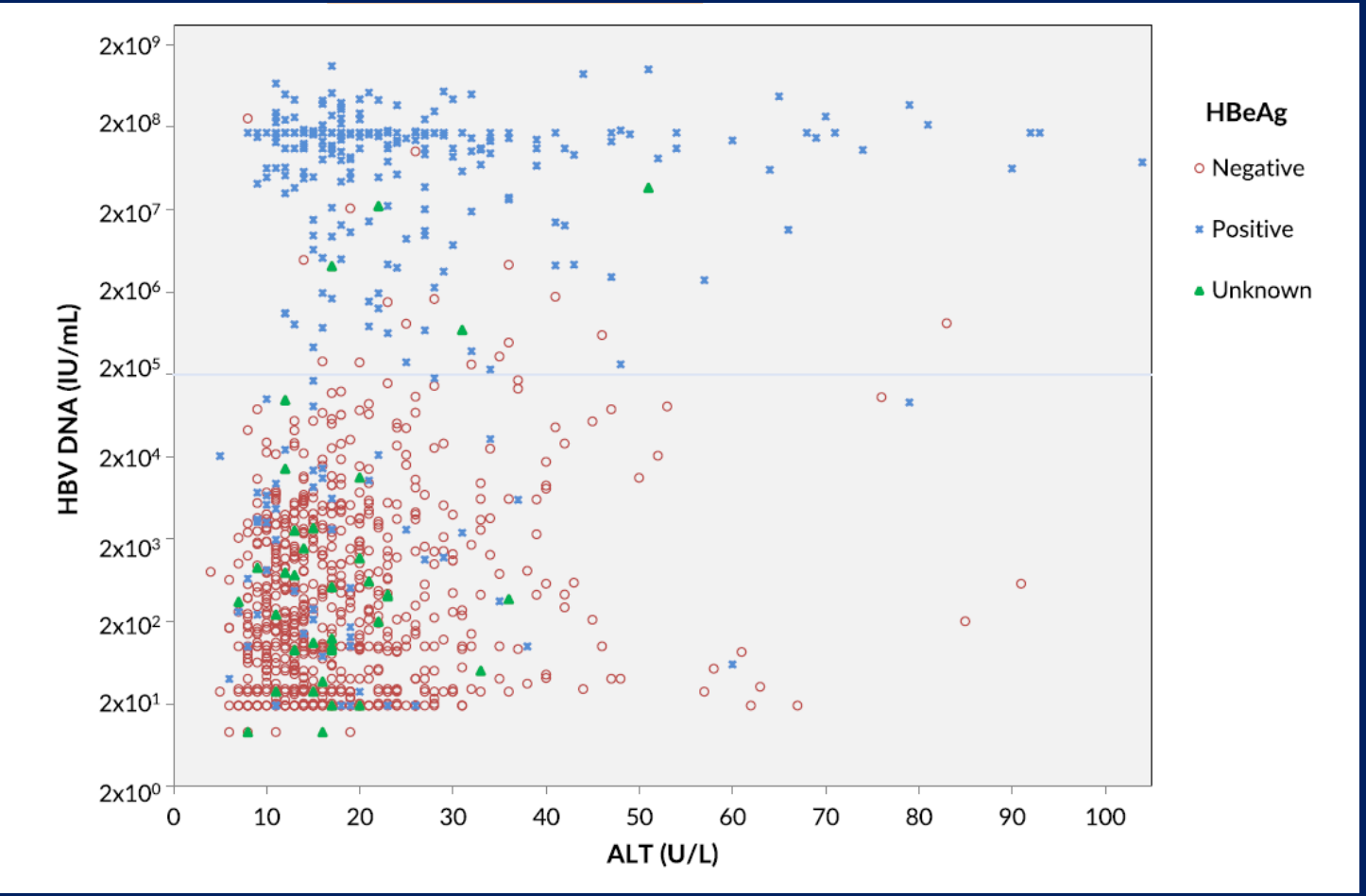
A large retrospective, study in 2012 of 869 Chinese mother-infant pairs observed that immunoprophyalxis failure occurred in infants born to mothers with an HBV DNA as low as 10^6 copies/mL (200,000 IU/mL).

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)

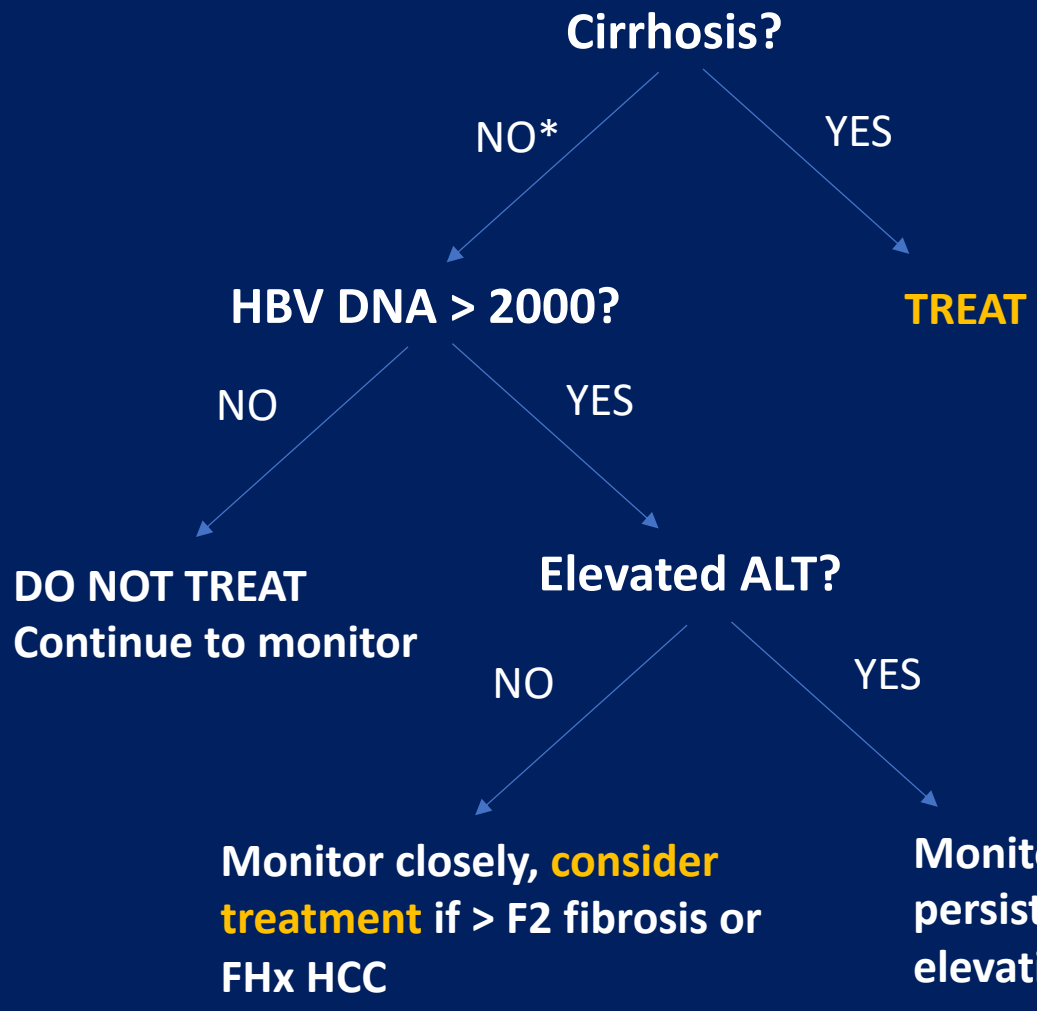
- **Antiviral treatment is recommended to be initiated at least 10 weeks prior to delivery**
  - Singleton pregnancy: 28-30 weeks GA
  - Twin pregnancy: 24-26 weeks GA
  - Triplet pregnancy: 20-22 weeks GA

- 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.
- 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.
- Tenofovir and breastfeeding:
  - 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

Hep B Moms Program Essentials

- 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

NEMS Hep B Moms Program

Prevent

Prevent HBV perinatal transmission

Departmental HBV Champions
Amy Tang, MD, Adult Medicine
Rena Hu, MD, Ob/Gyn
Stanley Ng, MD, Pediatrics

HBV Provider Site Champions
Lauren Quan, MD, Eastmoor Clinic
Joann Lin, NP, Stockton Clinic
Connie Tran, NP, San Bruno Clinic
Lydia Chan, MD, San Bruno Clinic
TBD, Noriega Clinic

Perinatal HBV Care Management Specialist
Lixin Zhang, CPSP Provider & GI/UM Specialist

Perinatal HBV education and care coordination

Household contacts testing for HBV

Linkage to care with a NEMS HBV provider before and after pregnancy and HBV antiviral treatment to prevent mother-to-child transmission of HBV

Timely HBV immunoprophylaxis, complete HBV vaccinations, and post-vaccination serology testing for infants born to Hep B Moms.

Hepatitis B/C Microelimination at NEMS

Screen	Vaccinate	Prevent	Mitigate
Screen all adult patients for HBV and HCV status	Vaccinate all HBV susceptible patients	Prevent HBV perinatal transmission	Minimize/prevent liver complications through routine monitoring, liver cancer surveillance, liver fibrosis staging, and treatment of patients with chronic HBV and HCV infection

Educate

Educate providers on HBV/HCV care and patients about HBV/HCV transmission and risk factors

Advocate

Advocate for policies to increase screening, vaccination and affordable treatment

Hepatitis B at NEMS

1 in 3 adult patients at NEMS were infected with hepatitis B in their lifetime and are at risk for hepatitis B reactivation and liver complications if immunosuppressed

1 in 12 of adult patients at NEMS have chronic hepatitis B infection

- Many did not know they were infected until tested by NEMS provider
- Globally, only 1 in 3 persons with chronic hepatitis B are aware of their diagnosis

1 in 4 persons with chronic hepatitis B will suffer liver complications such as liver cancer or cirrhosis if unmonitored or untreated

1 in 4 pregnant women with hepatitis B in San Francisco receive their prenatal care at NEMS

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.

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NEMS - Rev. 12/2020

Comprehensive Perinatal Services Program (CPSP)

- **Medi-Cal program** that provides enhanced services for eligible low-income pregnant and postpartum women
- Enhanced services include nutrition, psychosocial, **health education**, in addition to routine obstetric care

CPSP Providers

- MD/DO, NP, PA, RN, LVN, SW, RD, etc.
- Comprehensive Perinatal Health Worker (**CPHW**)
  - Age 18+
  - High School Graduate
  - 1 Year of Paid Perinatal Experience
- Must complete (online) orientation to become certified provider
- Application approval by county DPH

Services

- Initial assessments
- Trimester reassessments
- Postpartum assessments
- **Intervention/follow-up**

Timeframe to Receive Services

- From conception to two months postpartum

Billing

- CPSP support services are billed per 15-min units
- **Perinatal Education** has max of 16 billable units

NEMS Hep B Moms Program

- Enrolled Hep B Moms care manager as CPSP provider to provide Hep B perinatal education to pregnant patients with HBV infection
- Services > 15 min. for eligible patients (Medi-Cal, pregnant or postpartum < 2 months) can be billed using Perinatal Education code

HBV Next Gen EHR Template (1)

EDD: [redacted] Gestation Age: [redacted] Grav: [redacted] Para: [redacted] ☐ Follow-Up Note

Lab Results

	Last Date	Last Value		Last Date	Last Value		Last Date	Last Value
HBsAg:	[redacted]		HBeAg:	[redacted]		ALT:	[redacted]	
Anti-Hbs:	[redacted]		Anti-Hbe:	[redacted]		AST:	[redacted]	
Anti-HBc:	[redacted]		HBV DNA:	[redacted]		Platelet:	[redacted]	

Assessments

When were you first aware of having HBV? (check all that apply)

☐ Current pregnancy ☐ Past pregnancy ☐ >=18 years old ☑ < 18 years old ☐ Unsure

Seen a medical provider for HBV before? ◉ Yes ○ No

If yes, ◉ at NEMS ○ other

If yes, HBV medication given? ○ Yes ◉ No

Details [redacted]

HBV Next Gen EHR Template (2)

HBV Family History ◉ Yes ○ No

Household Contact Screening

	HBV	HCC	Cirrhosis	Live in Same Household	Screened	Vaccinated	Not Sure	Refer for Screening
Spouse	☐	☐	☐	☑	☑	☑	☐	☐
Father	☐	☐	☐	☐	☐	☐	☐	☐
Mother	☐	☐	☐	☐	☐	☐	☐	☐
Brother	☐	☐	☐	☐	☐	☐	☐	☐
Sister	☑	☐	☐	☐	☐	☐	☐	☐
Son	☐	☐	☐	☐	☐	☐	☐	☐
Daughter	☐	☐	☐	☑	☑	☑	☐	☐
Other	☐	☐	☐	☐	☐	☐	☐	☐

Household Contact Note:

Caretaker plan for baby (first 6 months of age):

☑ Self ☐ Family Member / Relative ☐ Nanny / Babysitter ☐ Other (Remind to have screening done)

Additional Notes:

Pediatrician: ◉ NEMS ○ Other ○ Undecided

HBV Next Gen EHR Template (3)

Education

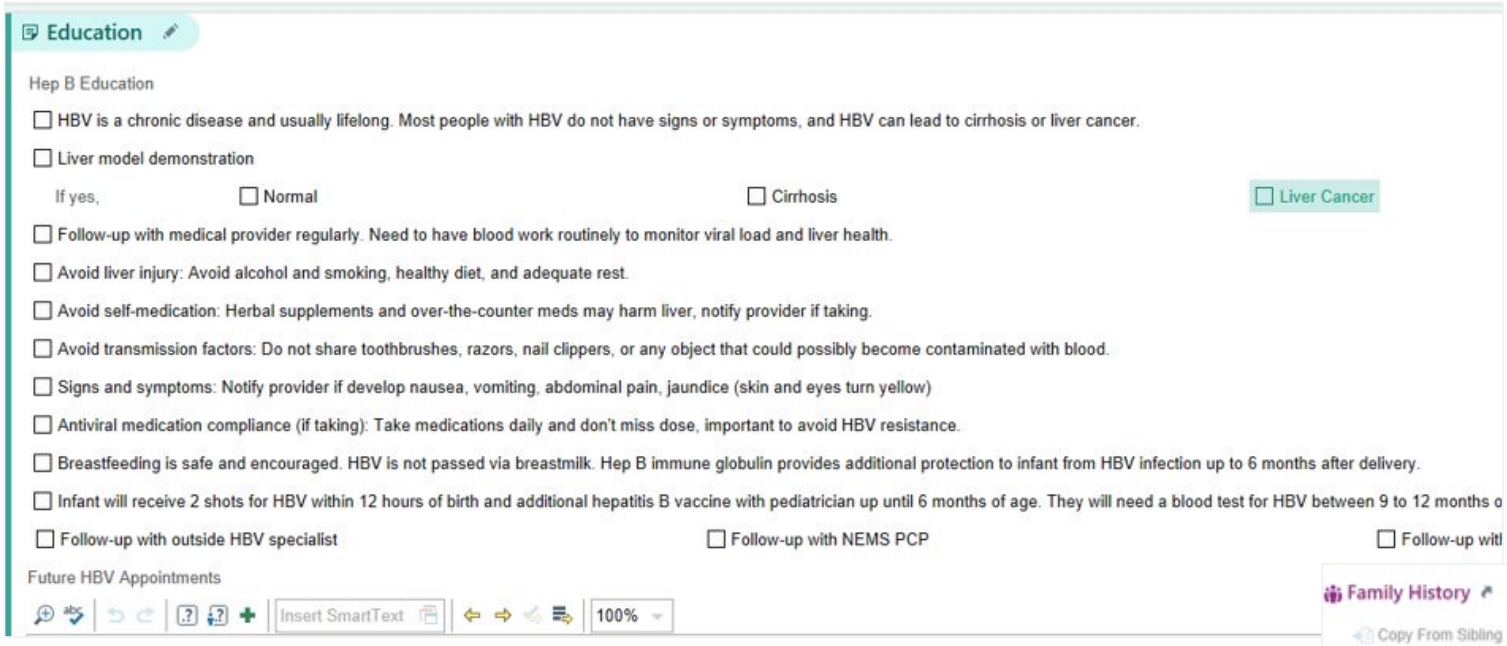
- [x] HBV is a chronic disease and usually lifelong. Most people with HBV do not have signs or symptoms, and HBV can lead to cirrhosis or liver cancer.
- [ ] Liver model demonstration: ○ Normal ○ Cirrhosis ○ Liver Cancer
- [x] Follow-up with medical provider regularly. Need to have blood work routinely to monitor viral load and liver health
- [x] Avoid liver injury: Avoid alcohol and smoking, healthy diet, and adequate rest
- [x] Avoid self-medication: Herbal supplements and over-the-counter meds may harm liver, notify provider if taking
- [x] Avoid transmission factors: Do not share toothbrushes, razors, nail clippers, or any object that could possibly become contaminated with blood
- [x] Signs and symptoms: Notify provider if develop nausea, vomiting, abdominal pain, jaundice (skin and eyes turn yellow)
- [x] Antiviral medication compliance (if taking): Take medications daily and don't miss dose, important to avoid HBV resistance
- [x] Breastfeeding is safe and encouraged. HBV is not passed via breastmilk. Hep B immune globulin provides additional protection to infant from HBV infection up to 6 months after delivery.
- [x] Infant will receive 2 shots for HBV within 12 hours of birth and additional hepatitis B vaccine with pediatrician up until 6 months of age. They will need a blood test for HBV between 9 to 12 months of age to see if infant has immunity to HBV or is infected.
- [ ] Follow-up with outside HBV specialist
- [x] Follow-up with NEMS PCP
- [x] Follow-up with a NEMS HBV provider

Future HBV Appointments

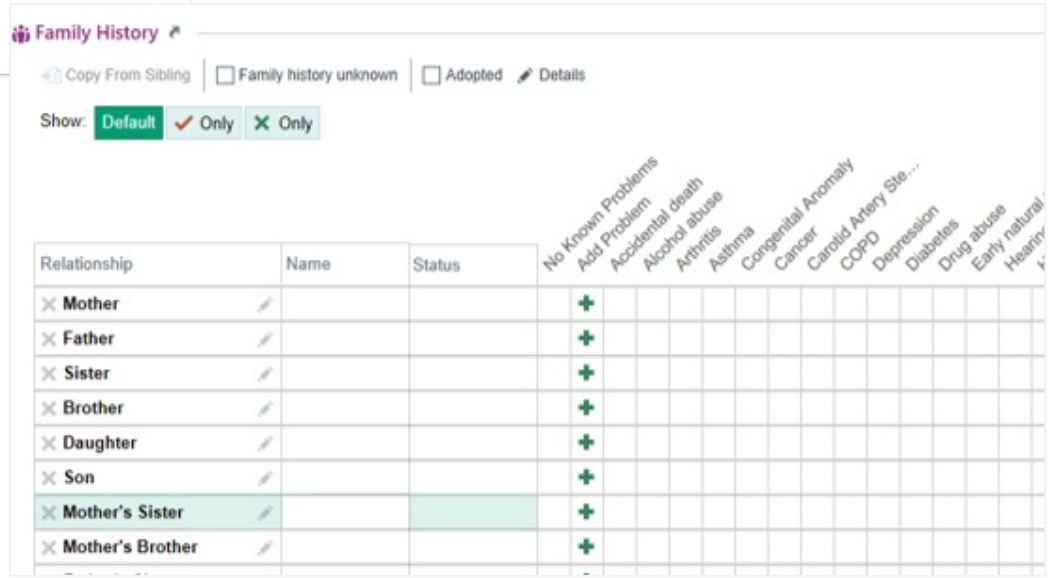
Notes:

I will schedule her to see a Hep b champion at 28 weeks.

Perinatal care management for Hep B Moms Program using Compass Rose



NEMS HBV Perinatal Manager has customized fields to complete for pregnant patients with hepatitis B



The HBV Perinatal Manager is able to document family history of hepatitis infection or liver disease

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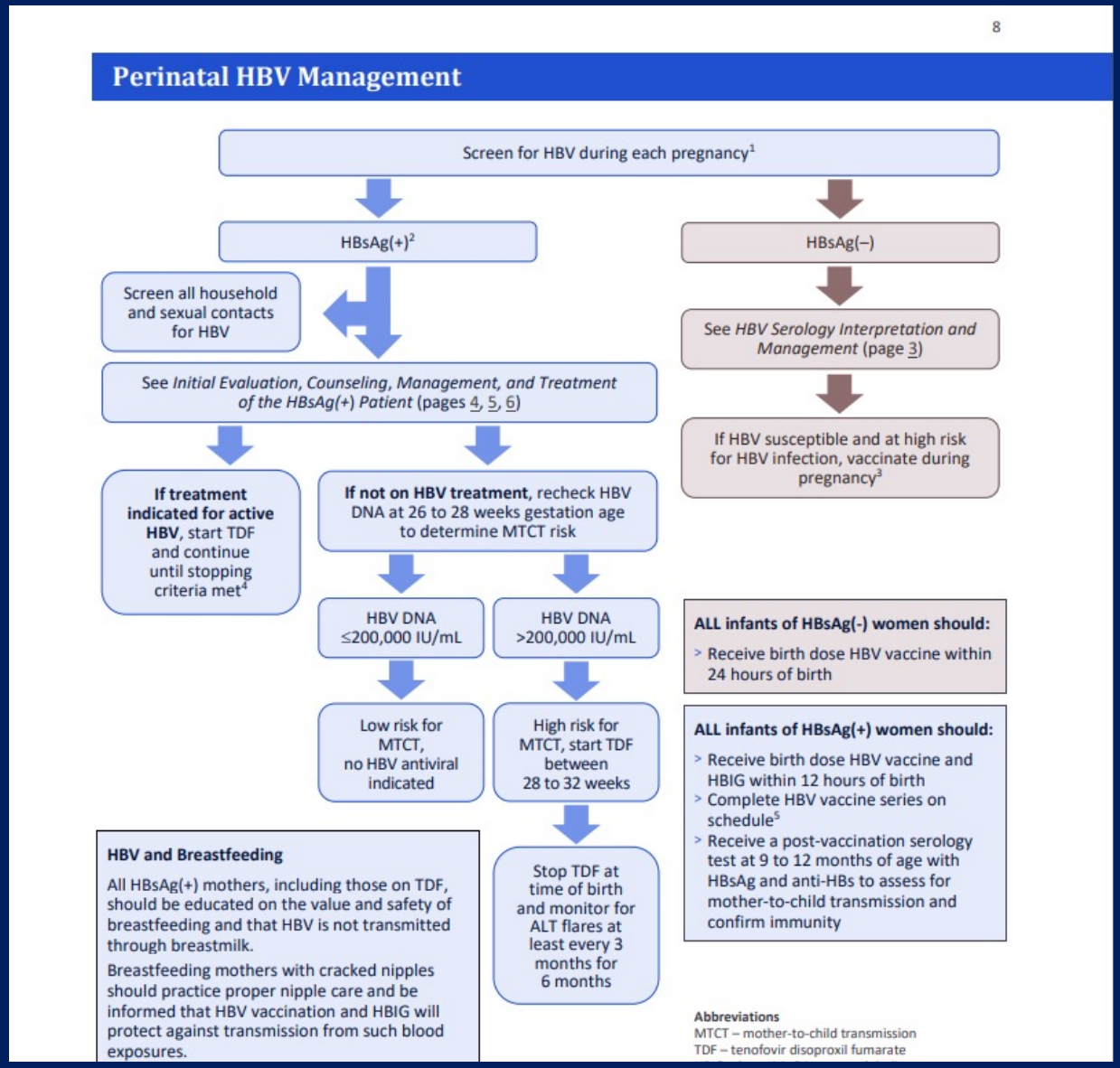
Take home points

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.
- Public Health: 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.

Questions?

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Hepatitis B Management: Guidance for the Primary Care Provider

The purpose of this document is to provide simplified, up-to-date, and readily accessible guidance for primary care medical providers related to the prevention, diagnosis, and management of hepatitis B virus (HBV) infection, including hepatocellular carcinoma surveillance.

About the HBV Primary Care Workgroup

This guidance was developed by the Hepatitis B Primary Care Workgroup, a multidisciplinary panel of national experts in the field of viral hepatitis B, including representation from hepatology, infectious diseases, pharmacy, primary care, public health, and other national organizations. The workgroup was organized by the National Taskforce on Hepatitis B in partnership with the San Francisco Hep B Free — Bay Area and Project ECHO™ and did not receive any outside funding.

Collaboration with University of Washington

This guidance was produced in collaboration with the University of Washington's National Hepatitis Training Center (HTC). The UW HTC will host and feature the most current version of these guidelines on the free *Hepatitis B Online* website (hepatitisB.uw.edu). The UW HTC is funded by the Centers for Disease Control and Prevention (CDC).

Suggested citation. Tang AS, Thornton K, and HBV Primary Care Workgroup. Hepatitis B Management: Guidance for the Primary Care Provider. February 25, 2020. [https://www.hepatitisB.uw.edu/hbv-pcw/guidance]

HBV Primary Care Workgroup

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Hepatitis B Virus (HBV) Serology Interpretation and Management

HBsAg	Anti-HBc (Total or IgG)	Anti-HBs	Interpretation	Management
+	+	−/+	Current infection	> See *Evaluation*, *Counseling*, *Management*, *Treatment*, and *HCC Surveillance* (pages 4, 5, 6, 7) > Refer household and sexual contacts for HBV screening; if susceptible, vaccinate
−	+	+	Prior infection with immune control	> No transmission risk; HBV dormant in liver > Reactivation risk if on immunosuppressive medications
−	+	−	Prior infection or occult infection[1]	> If immunocompetent[2], counsel as prior infection above > Reactivation risk if on immunosuppressive medications > If immunocompromised, check HBV DNA for occult infection[1]
−	−	+	Immune from prior vaccination	Protected for life. No need for booster vaccine
−	−	−	Susceptible	VACCINATE[3]

Post-Vaccination Serologic Testing

Assessment of the response to HBV vaccination with a post-vaccination serologic test of anti-HBs between 1 and 2 months after the final dose of vaccine should be obtained in all of the following adult groups at high risk for HBV:

- Health care personnel and public safety workers
- Sexual and household contacts of HBsAg(+) persons
- Hemodialysis patients
- Persons who inject drugs
- Persons with HIV and other immunocompromising conditions

Initial Evaluation of the HBsAg(+) Patient

History/Examination

- ☐ Symptoms/signs of cirrhosis
- ☐ Alcohol and metabolic risk factors
- ☐ Family history of hepatocellular carcinoma (HCC)
- ☐ Hepatitis A vaccination status

Routine Laboratory Tests

- ☐ CBC comprehensive
- ☐ Comprehensive metabolic panel including:
  - AST/ALT
  - Total bilirubin
  - Alkaline phosphatase
  - Albumin
  - Creatinine
- ☐ INR

Serology/Virology

- ☐ HBeAg/anti-HBe
- ☐ HBV DNA
- ☐ Anti-HAV (total or IgG) to determine need for vaccination if none documented
- ☐ Anti-HCV
- ☐ Anti-HDV
- ☐ Anti-HIV

Imaging/Staging Studies

- ☐ Abdominal ultrasound
- ☐ Elastography (e.g. FibroScan)
  or
  Serum fibrosis assessment[1] (e.g. APRI, FibroSure, FIB-4)

[1] APRI and FIB-4 scores can be calculated using platelet count and AST and ALT from routine labs. Calculators with score interpretation are available. See *Hepatitis B Online* APRI calculator and FIB-4 calculator. FibroSure and FibroTest are commercially available blood tests that can be ordered as well.

Counseling of the HBsAg(+) Patient

1. Give a plan for follow-up care. Patients will need regular (minimum every 6 months) follow-up and monitoring for disease progression.
2. Educate and counsel on the long-term implications of chronic HBV infection (e.g., cirrhosis and hepatocellular carcinoma).
3. Advise patient to inform all current and future medical providers of their HBsAg-positive status, especially if they ever need treatment for cancer or any immunologic condition such as rheumatoid arthritis or other immune disorders.
4. Counsel to avoid or limit alcohol use.
5. Advise to optimize body weight and address metabolic complications, including control of diabetes and dyslipidemia (to prevent concurrent development of metabolic syndrome and fatty liver).
6. Provide education on how to prevent transmission of HBV to others.

Persons with chronic HBV:

Should:	> Verify that sexual contacts, household contacts, family members, or injection partners are screened and vaccinated > Cover open cuts and scratches > Clean blood spills with diluted bleach (1:10)	> Use condoms to prevent HBV transmission during sexual intercourse with partners who are susceptible to HBV infection.
Should NOT:	> Share toothbrushes, razors, nail clippers, or earrings > Share injection equipment	> Share glucose testing equipment > Donate blood, organs, or sperm
Can:	> Participate in all activities, including contact sports > Share food and utensils, or kiss others	> Pursue educational or career opportunities without limitations, including work as a health care professional

Management of the HBsAg(+) Patient[1]

Cirrhosis	HBV DNA (IU/mL)	ALT (U/L)	Management
YES	Any	Any	> TREAT with antiviral medication (page 6) > Monitor HBV DNA and ALT every 6 months > Refer to specialist for screening endoscopy and, if needed, for other cirrhosis-related complications > HCC surveillance, including in persons who become HBsAg(-) (page 7) > All patients with decompensated cirrhosis[2] should be promptly referred to a hepatologist
NO	>2,000	Elevated[3]	> TREAT with antiviral medication (page 6) > Monitor HBV DNA and ALT every 6 months > Monitor HBeAg and anti-HBe every 6 months in patients who are HBeAg+ at time of treatment initiation to evaluate for seroconversion from HBeAg(+)/anti-HBe(-) to HBeAg(-)/anti-HBe(+) > Check HBsAg annually if/when HBeAg negative
		Normal	> Monitor HBV DNA and ALT every 6 months > Liver fibrosis assessment every 2 to 3 years
	≤2,000	Elevated[3]	> Evaluate other etiologies for elevated ALT > Monitor HBV DNA and ALT every 6 months
		Normal	> Monitor HBV DNA and ALT every 6 months and HBsAg every 1 year for seroclearance

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.

Preferred Antiviral Treatment of the HBsAg(+) Patient

Drug	Adult dose	Pregnancy category[1]	Side effects	Monitoring on treatment
Entecavir *Baraclude*	Standard: 0.5 mg by mouth daily Decompensated liver disease: 1 mg by mouth daily Take 2 hours before or after food	Formerly FDA category C Limited pregnancy exposure, pregnancy exposure registry available Insufficient human data to assess risk of major birth defects No adverse effects observed in animal studies	Headache, fatigue, dizziness, nausea reported in ≥3% Post-marketing surveillance include infrequent reports of: > lactic acidosis > severe hepatomegaly	Adjust dose with CrCl <50 mL/min Avoid in pregnant patients Avoid in patients with prior exposure to lamivudine or known lamivudine resistance Lactic acid levels if clinical concern
Tenofovir disoproxil fumarate (TDF) *Viread*	300 mg by mouth daily Take without regard to food	Formerly FDA category B Pregnancy exposure registry available Extensive data from pregnant women with HIV or HBV infections indicate no increase in pregnancy complications or major birth defects	Nausea (9%) Post-marketing surveillance include infrequent reports of: > nephropathy > Fanconi syndrome > osteomalacia > lactic acidosis	Adjust dose with CrCl <50 mL/min Serum creatinine at baseline; if at risk for renal impairment, serum creatinine and phosphorus, and urine glucose and protein at least annually Consider bone density study at baseline and during treatment in persons with history of fracture or risks for osteopenia Lactic acid levels if clinical concern
Tenofovir alafenamide (TAF) *Vemlidy*	25 mg by mouth daily Take with food	No human data in pregnancy No adverse effects observed in animal studies	Headache (12%) Lactic acidosis/ severe hepatomegaly with steatosis is a warning for tenofovir AF due to rare reports with use of tenofovir DF	Avoid with CrCl <15 mL/min if not receiving hemodialysis Dose after HD in those on HD If at risk for renal impairment, serum creatinine and phosphorus, and urine glucose and protein as clinically indicated. Lactic acid levels if clinical concern

Hepatocellular Carcinoma (HCC) Surveillance

Indications for HCC Surveillance

Persons with chronic HBV at increased risk for hepatocellular carcinoma (HCC) who require routine surveillance include:

- All persons with cirrhosis, including persons who become HBsAg(-)
- The following populations, even in the absence of cirrhosis:
  - Asian or black/African[1] males older than 40 years of age
  - Asian females older than 50 years of age
  - Persons with a family history of HCC
  - Persons with hepatitis D virus coinfection

Recommended HCC Surveillance Method

HCC surveillance should be performed in the primary care setting with liver ultrasound with or without serum alpha-fetoprotein (AFP)[2] every 6 months. More frequent monitoring or other imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI), with and without contrast, may be indicated to further evaluate new liver lesions.

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[1] More recent African immigrants may be at increased risk for HCC and some experts begin HCC surveillance at age <40 years.

[2] Wait at least 6 months after pregnancy before using AFP for HCC surveillance.

Perinatal HBV Management