Hepatitis B in Pregnancy: Update

ACP Rocky Mountain - Banff 2015

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Objectives

- Describe pregnancy outcomes
- Determine appropriate work-up
- Discuss indications and rationale for antiretroviral therapy
- Discuss importance of postpartum follow-up

Disclosure

- Medical Disorders in Pregnancy has received an unrestricted educational grant from Sanofi
- No conflict with any of the material I will be presenting

HBV Pregnancy Outcomes

- Major risk: mother to child transmission
- Acute or chronic HBV infection NOT associated with preterm birth, low birth weight, or gestational diabetes
- If cirrhosis: increased risk of maternal and perinatal death, gestational hypertension, abruption, preterm birth, and fetal growth restriction

HBV-related Cirrhosis Pregnancy Outcomes

- Unlikely to conceive: incidence of pregnancy in cirrhosis 1/5950
- High rates of spontaneous abortion, premature birth and perinatal death
- GI bleed: most common maternal complication

Aggarwal NAust N Z J Obstet Gynaecol 1999 39(4):503–506.

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cHBV Pregnancy Standard of Care

- Perform routine screening during pregnancy for cHBV infection with maternal HBsAg testing 1st TM **1A**
- Repeat screening if risk factors 3rd TM **2B***

* Society of Obstetricians and Gynaecologists of Canada
Society for Materno Fetal Medicine

cHBV Pregnancy Standard of Care

- Perform routine **screening during pregnancy** for HBV infection with maternal HBsAg testing **1A**
- Offer Neonatal Immunoprophylaxis: HBIG & hepatitis B vaccine first 12 hours of birth **1A**
  - All newborns of HBsAg-positive mothers
  - Unknown or undocumented maternal HBsAg status during pregnancy

Neonatal Immunoprophylaxis

Prevents 85-99% of all mother to child transmission cases

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Mrs. W

- 45yo G2P0 from China 16 weeks GA
- RFR: Abnormal ALT
  - G1 2010 HBsAg+ve HBeAg-ve normal ALT
  - G2 2015 HBsAg+ve HBeAg-ve ALT 100-200
- On HBV medications prior for “advanced fibrosis” in China: stopped upon recognition of pregnancy
- Wants to discuss risks of ammiocentesis
- Wants to go to Mexico

Mrs W

HBsAg+ve
HBeAg-ve
ALT 100-200

1. She's developed HCC and should be scheduled for a triple phase CT scan
2. She likely has a pre-core or core promoter mutant HBV: obtain a serum hepatitis B viral load
3. She is likely infected with a pre-core mutant HBV: obtain a hepatitis B genotype
4. Her liver enzyme elevation is probably unrelated to her cHBV infection. She may have fatty liver disease: obtain an ultrasound

Mrs. W

- USA: 27%-44% cHBV (all comers) carry a precore/core promoter mutants: do not synthesize HBeAg
- Precore and core-promoter mutations generally occur during spontaneous or treatment-induced clearance of HBeAg: usually seen after 4th decade

Neonatal Immunoprophylaxis

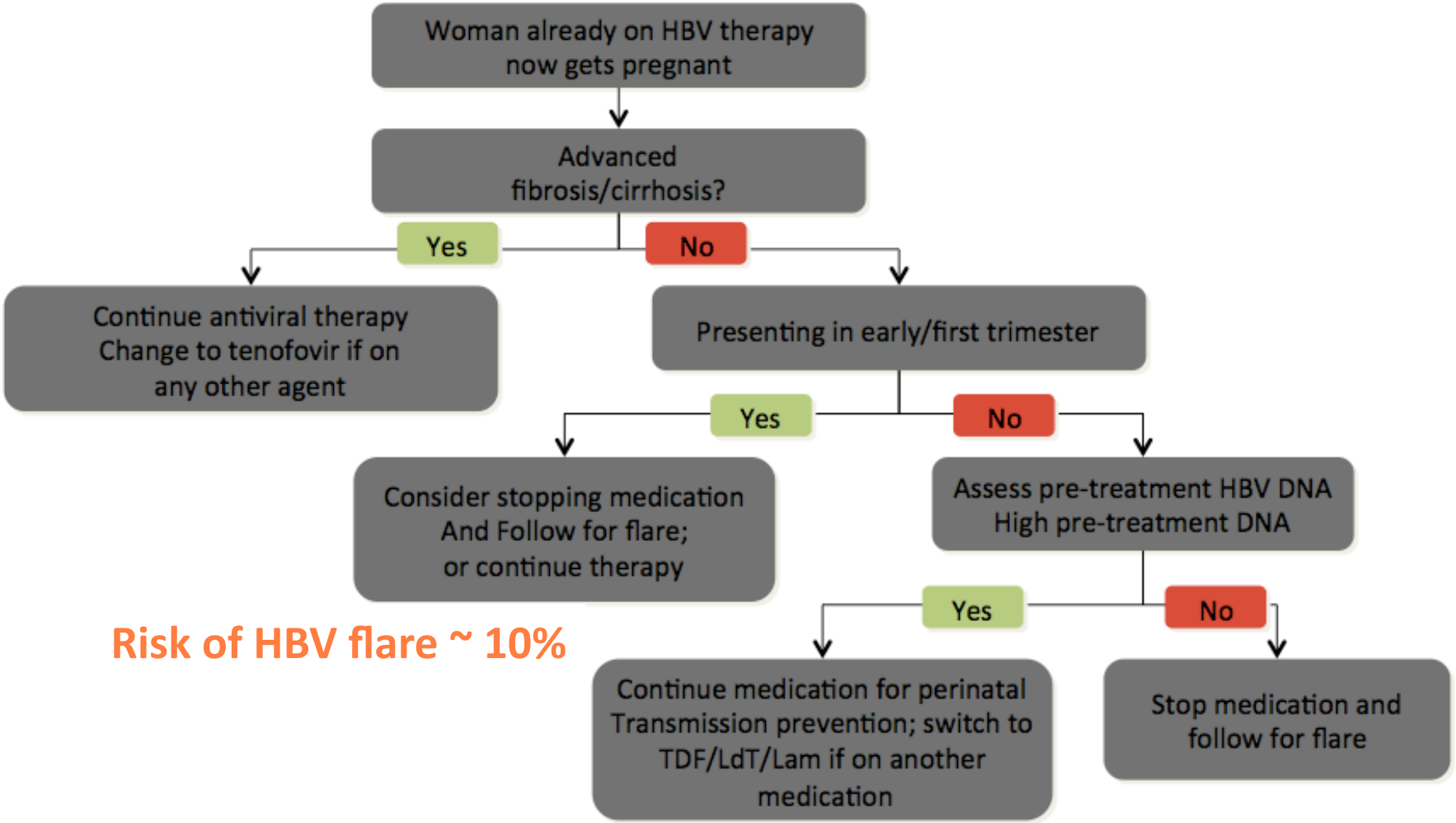
Neonatal immunoprophylaxis prevents 85-99% of all mother to child transmission cases

Mother		Infant	
HBeAg	HBsAg	No Vaccination	With Immunoprophylaxis
+	+	>90% chronic HBV	Vaccine + HBIG: 10% to 15% chronic HBV
-	+	<5% chronic HBV Risk of fulminant hepatitis, acute hepatitis	<1% chronic HBV and risk of fulminant hepatitis Reduced risk of acute hepatitis

Mrs. W

- HBsAg+ve HBeAg-ve ALT 100-200
- HBV DNA level of 130,000 IU/ml
  - Total HAV antibody negative
  - Liver U/S minimal fatty infiltration
  - Fibroscan: not done (no data in pregnancy) but "advanced fibrosis" on history

Mrs. W



Risk of HBV flare ~ 10%

Adapted from Dr. Tran AASLD CLD 2010

What about the Amnio?

- cHBV infected pregnant may require invasive testing (i.e. amniocentesis)
  - Risk for mother to child transmission increases HBV viral load >10^7 IU/mL **2C**

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Mrs. W

- Should to remain on HBV treatment for maternal benefit: has advanced fibrosis
- Ammiocentesis does not pose a major risk of mother to child transmission as HBV viral load $<10^7$ IU/mL
- Should receive HAV vaccination prior to travel to HAV endemic area (Mexico)

Ms. C

- 23 yo G1P0 from Korea
- HBsAg+ve ALT 20 U/L
- Asymptomatic, normal examination

Neonatal Immunoprophylaxis

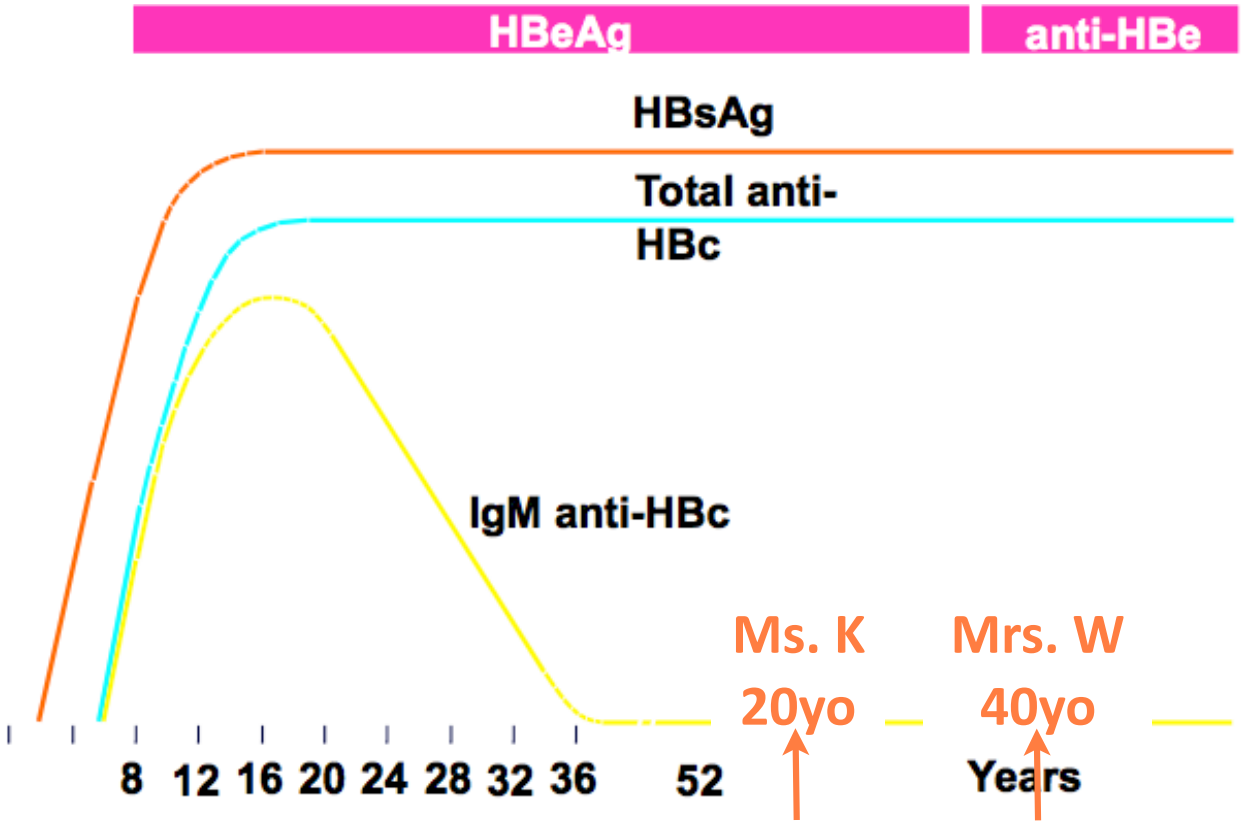
Neonatal immunoprophylaxis prevents 85-99% of all mother to child transmission cases

Mother		Infant	
HBeAg	HBsAg	No Vaccination	With Immunoprophylaxis
+	+	>90% chronic HBV	Vaccine + HBIG: 10% to 15% chronic HBV
-	+	<5% chronic HBV Risk of fulminant hepatitis, acute hepatitis	<1% chronic HBV and risk of fulminant hepatitis Reduced risk of acute hepatitis

Ms. C

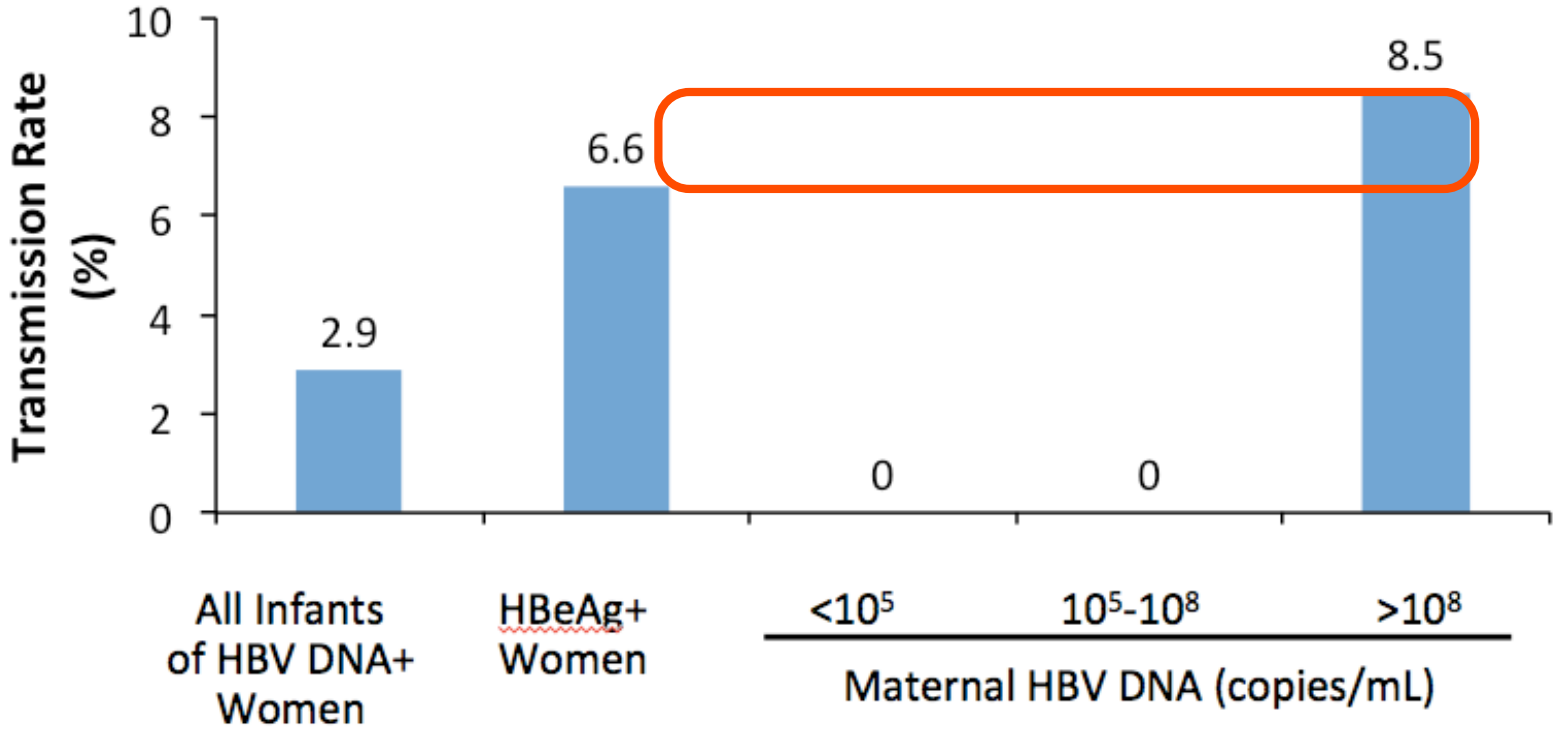
- 23 yo G1P0 from Korea
- HBsAg+ve ALT 20 U/L
- HBeAg+ve
- HBV DNA $3x10^{10}$ IU/ml

HBV Natural History



- Chronic infection occurs in about 90% of infected infants, 30% of infected children aged <5 years

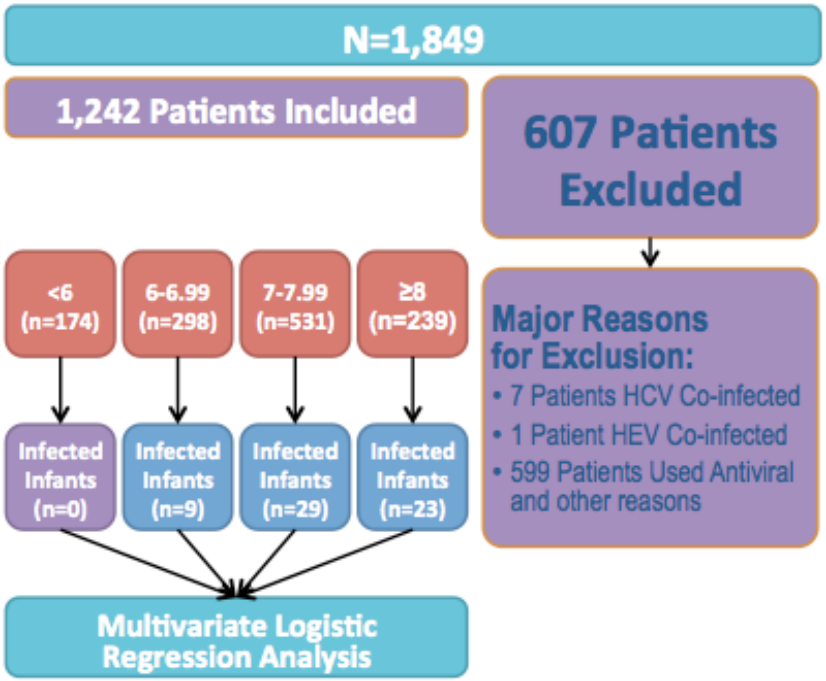
HBV DNA & MTCT Risk



Wiseman E et al. *Med J Aust.* 2009;190:489-492.

HBV DNA & MTCT Risk

- Retrospective N=1,068 infants HBsAg(+) and HBeAg(+) mothers with appropriate prophylaxis: HBIG/HBV vaccine
- No transmission occurred <10^6 copies/mL (<200,000 IU/mL) viremia
- **Maternal HBV viral load: most important factor for MTCT transmission**



G. Han W. Zhao C. Xu C. Ge3 H. Jiang C. Pan Risk Factors Associated with Perinatal Infection of HBV in Infants Who Born to HBsAg and HBeAg Positive Mothers

Treating cHBV in Pregnancy: 2 aspects

1. Treatment for maternal benefit

2. Treatment to prevent transmission to the infant

Rx: Ms. C

AASLD 2015 SOGC 2016

- Pregnant women with HBV infection and viral load >log10^6 copies/mL or >200,000 IU/mL should receive HBV-antiviral therapy to decrease the risk of intrauterine fetal infection **2B**
- If so, Tenofovir is first-line agent **2B**

Tenofovir

- Antiretroviral Pregnancy Registry (1989-2012)
- Data on exposure in HBV-mono infected mothers since 1/2003
- Overall birth defects: 2.72% (95% CI: 2.68-2.76)

Antiretroviral Pregnancy Registry. December 2012. 7. Correa A, et al. Birth Defects Res A Clin Mol Teratol. 2007;79:65-186.

Regimen Containing	First Trimester		Second or Third Trimester	
	Exposed, n	Birth Defects, % (95% CI)	Exposed, n	Birth Defects, % (95% CI)
Lamivudine	4185	3.2 (2.7-3.8)	6843	2.8 (2.4-3.2)
Tenofovir	1612	2.4 (1.7-3.3)	838	2.3 (1.4-3.5)

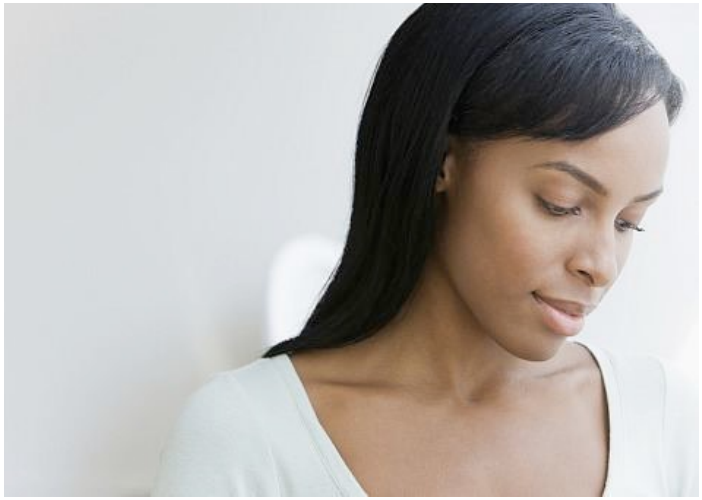
Treating cHBV in Pregnancy: 2 aspects

1. Treatment for maternal benefit

   Maternal cirrhosis or advanced fibrosis

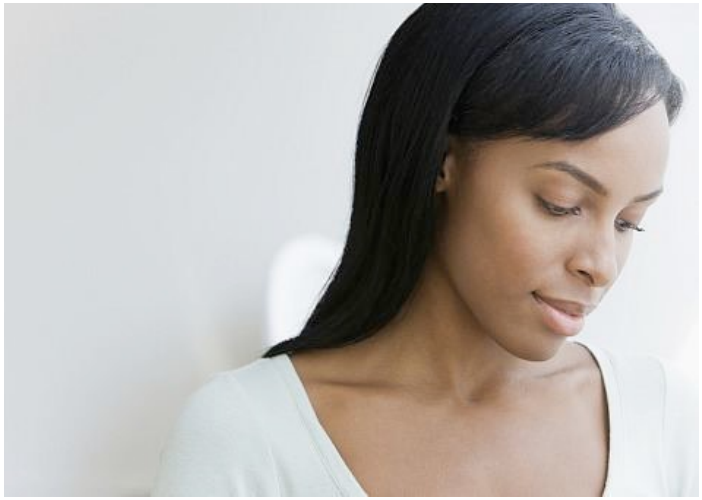
2. Treatment to prevent transmission to the infant

   If maternal HBV viral load >10^6 copies/mL or 200,000 IU/mL



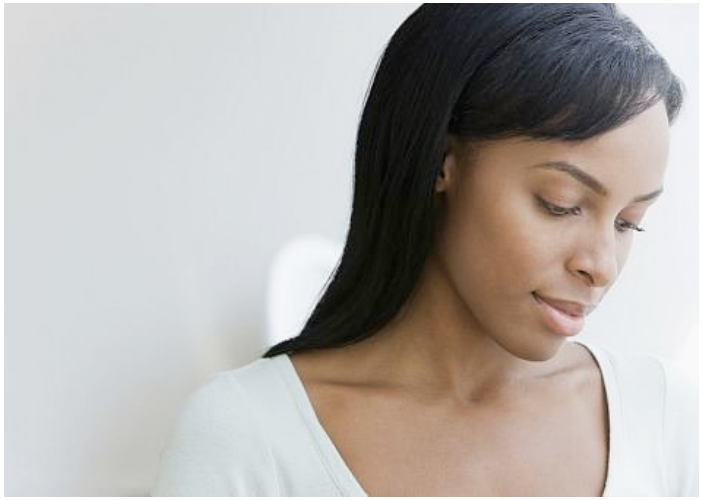
Mrs. M

- 37 yo G4L2 25w GA
- Rwanda
- HBsAg +ve HBeAg+ve ALT 30
- HBV DNA $3x10^3$ IU/ml
- No Comorbidities



Mrs. M

- 37 yo G4L2 25w GA
- Rwanda
- HBsAg +ve HBeAg+ve ALT 30
- HBV DNA $3x10^3$ IU/ml
- Doesn't need antiretrovirals
- Anything else?



Mrs. M: Risk HCC

- African women risk of HCC higher and earlier: can see on 4th decade
- Mrs. M should be considered for yearly HCC surveillance with alpha-fetoprotein & ultrasound

Other Maternal Care

- Avoid further liver injury
  - Offered vaccination if not immune for HAV
  - Avoid exposures to potentially hepatotoxic medications, herbals, TCM and alcohol even when not pregnant!

Mode of Delivery

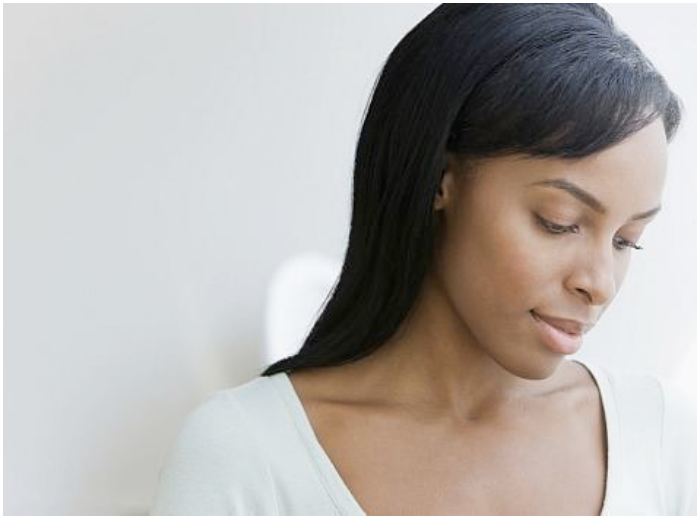
- SMFM, ACOG
- Cesarean delivery not be performed solely for reduction of vertical HBV/ HCV transmission **2C**
- Precautions: avoid fetal scalp sampling, fetal scalp electrodes

Breastfeeding

- No problem! As long as the infant receives immunoprophylaxis at birth (HBV vaccination and hepatitis B immunoglobulin) **IC**

Take home messages

- For both maternal and MTCT risk stratification HBV there is more than HBeAg
- Treat the Mom if you gotta treat her: baby will be grateful
- cHBV infection: risk factor for HCC (Black African Women)



- Questions