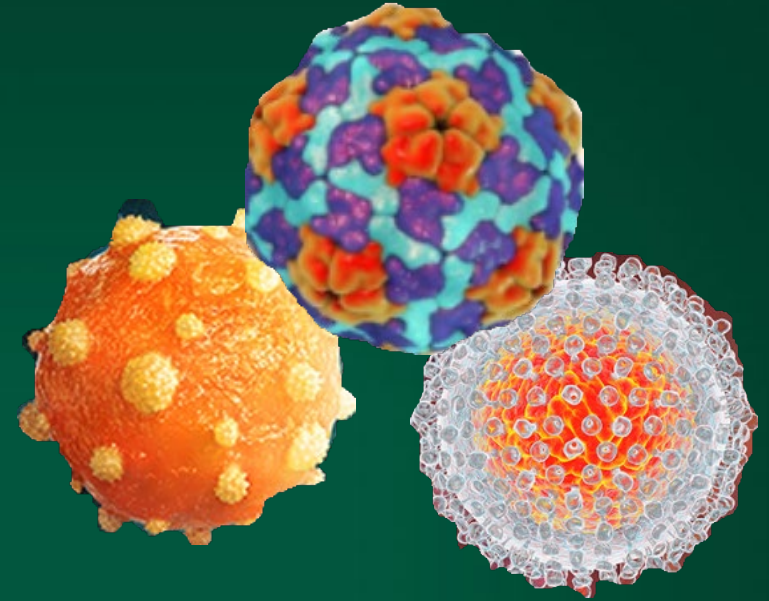




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# ABC's of Hepatitis in Pregnancy

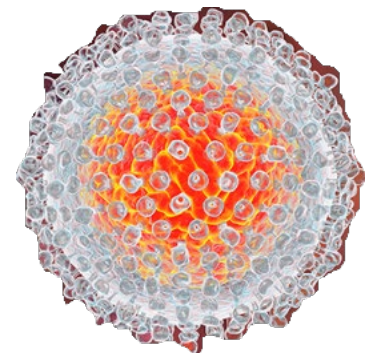
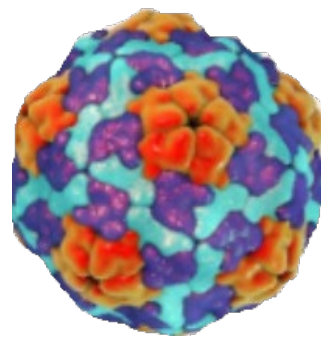
Kerri Brackney, MD  
UTHSC Maternal Fetal Medicine

# Disclosures

I have no disclosures relevant to this talk.

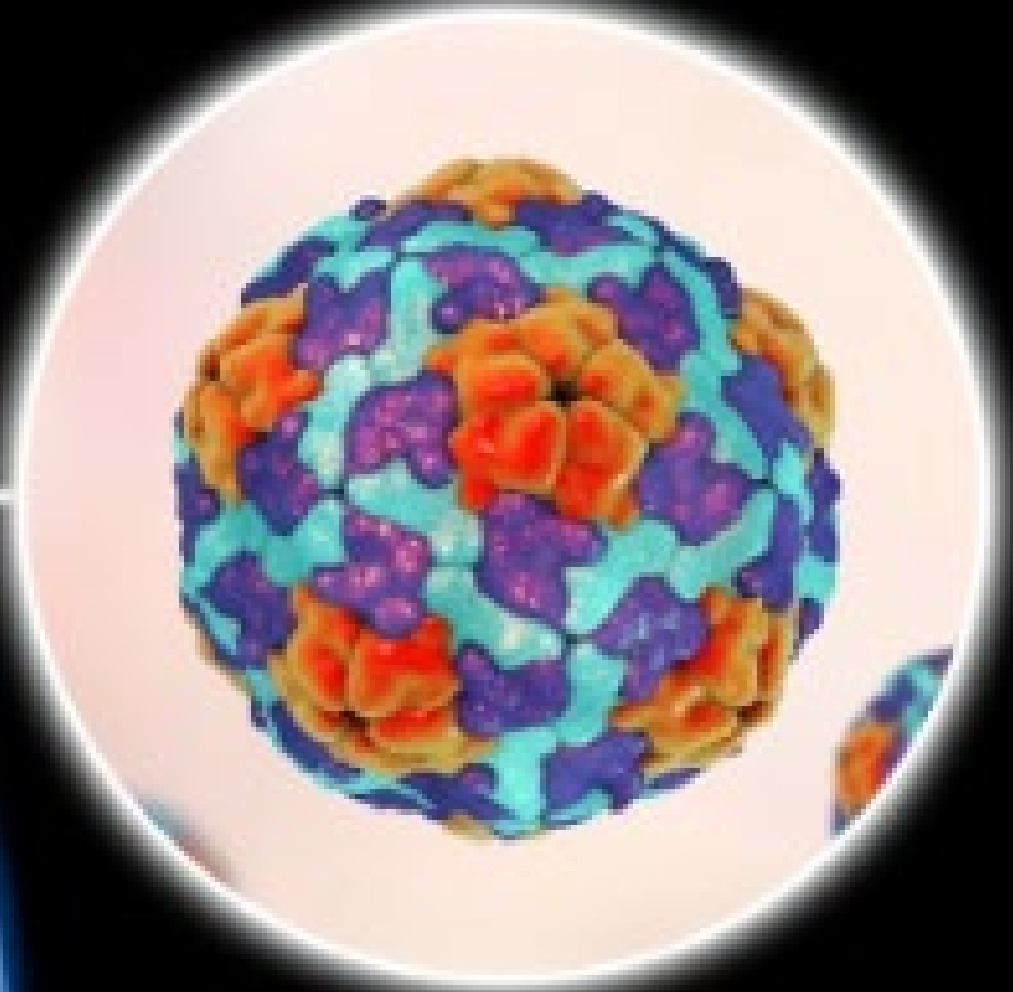
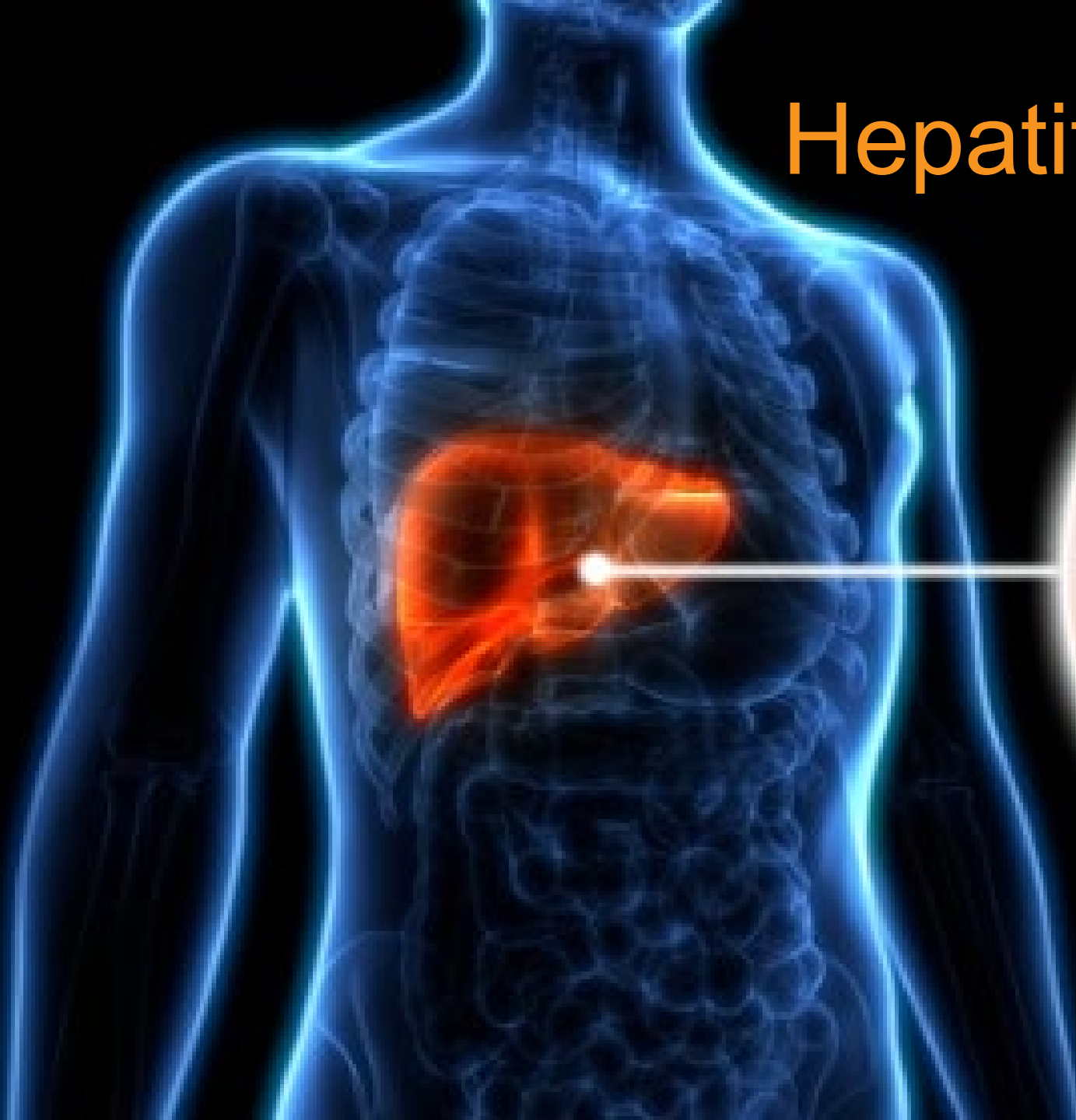


# Learning Objectives



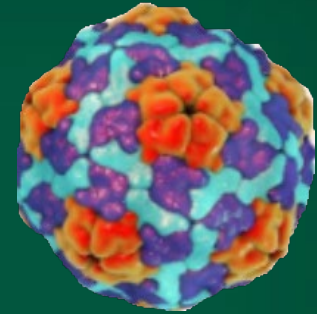
1. Review indications for Hepatitis A vaccination
2. Learn the new Hepatitis B screening guidelines for pregnant patients in the United States
3. Appropriately manage Hepatitis B and C screening results
4. Identify patients with Hepatitis B for whom medications will decrease the risk of vertical transmission
5. Minimize the risk of hepatitis vertical transmission
6. Improve long-term maternal outcomes after hepatitis infection

# Hepatitis A



# Hepatitis A: the basics

- A small RNA virus
- Infection can be symptomatic or asymptomatic
- Average incubation 28 days (range 15-50 days)
- Replicates in the liver; excreted in bile
- Highest fecal viral concentrations are late in the incubation period (greatest infectivity)



# Hepatitis A: symptoms



ABDOMINAL PAIN



FEVER



DARK URINE



NAUSEA



VOMITING



JAUNDICE  
(YELLOWING OF  
THE EYES)



PALE STOOLS  
(POOP)



LOSS OF APPETITE



JOINT PAIN

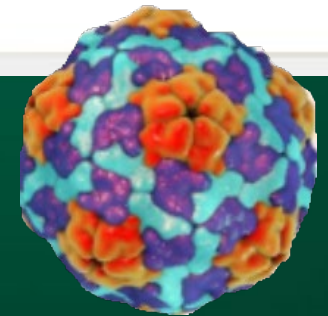


DIARRHEA



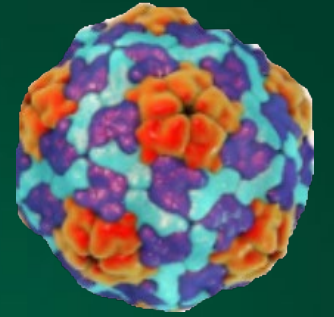
FATIGUE  
(EXTREME TIREDNESS)

Symptoms are more likely to occur in adults than in children. They usually last fewer than two months, but some people can be ill as long as six months.





# Hepatitis A: Transmission



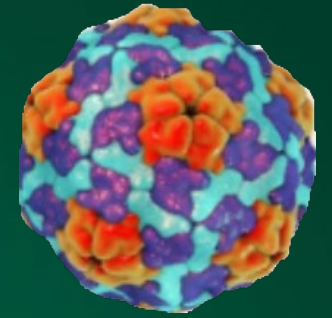
- Person-to-person through fecal-oral contamination
- Exposure to contaminated uncooked/undercooked food or water
- Perinatal transmission is uncommon, but reported

## PREVENTION

- Heat foods to 185° or higher
- Disinfect surfaces with dilute bleach
- Wash hands when caring for children <6 yrs old
- Vaccinate if high risk



# Hepatitis A: Vaccination



- All children ages 12-23 mos
- All children ages 2-18 not previously vaccinated
- All people, including pregnant, with risk factors



# Hepatitis A: Vaccination



- All children ages 12-23 mos
- All children ages 2-18 not previously vaccinated
- All people, including pregnant, with risk factors

**International travel**

**Men who have sex with men**

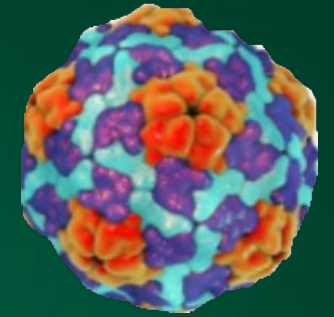
**Substance use disorder**

**Job-related exposure**

**Close personal contact with international adoptee**

**Homelessness**

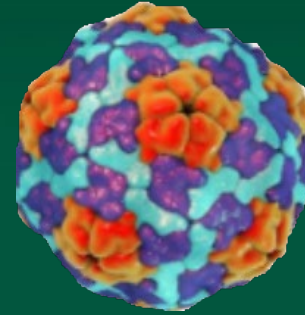
# Hepatitis A: Vaccination



- All children ages 12-23 mos
- All children ages 2-18 not previously vaccinated
- All people, including pregnant, with risk factors

**Patients with other types of hepatitis**

# Hepatitis A: Vaccination



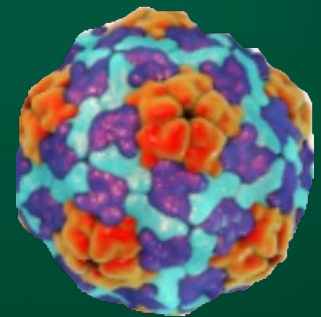
- All children ages 12-23 mos
- All children ages 2-18 not previously vaccinated
- All people, including pregnant, with risk factors

**Patients with other types of hepatitis**



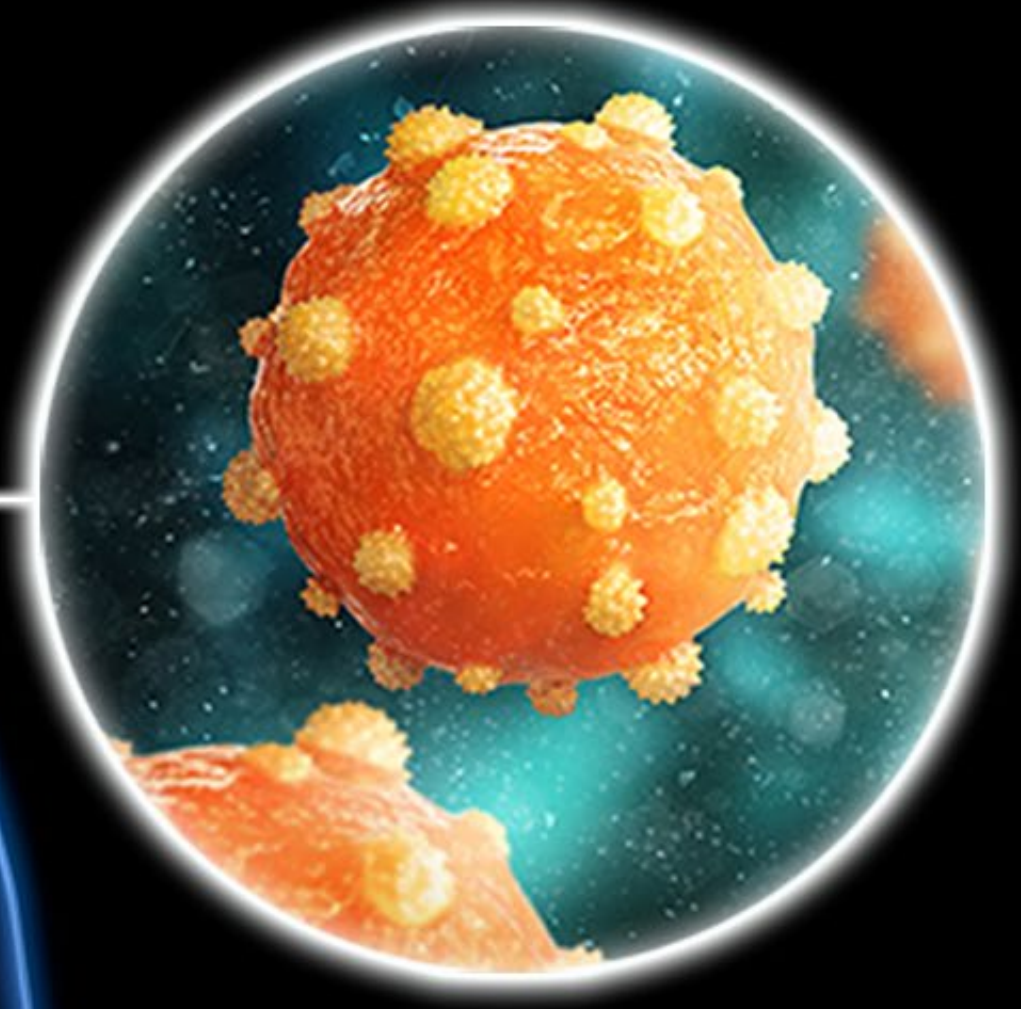
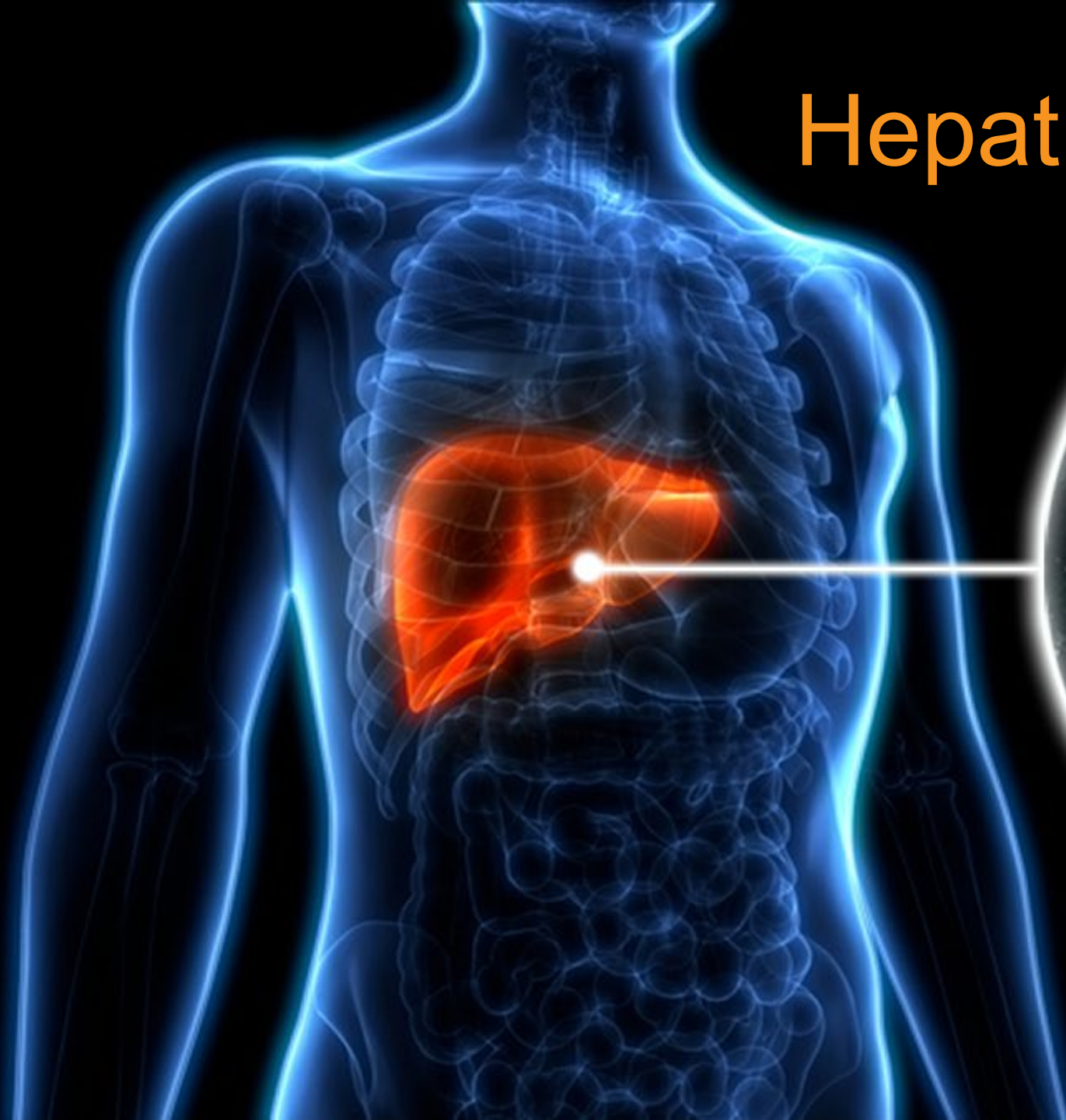
# Hepatitis A: Sequelae

- Serious complications are uncommon
- Case-fatality ratio <1%
- 10-15% with prolonged or relapsing disease up to 6 months
- 2nd/3rd tri infection increases risks of PTD (median 34 weeks)
- Perinatal transmission is rare

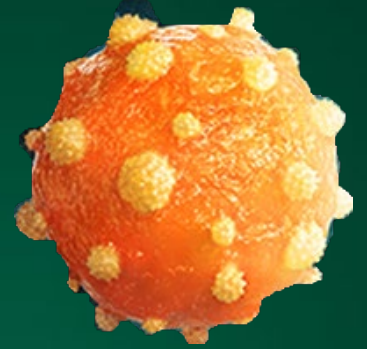




# Hepatitis B



# Hepatitis B: the basics



- A small DNA virus
- Highly pathogenic & infectious
- Perinatal transmission is largest cause of chronic infection worldwide
- 3.5% prevalence among foreign-born persons



Chronic hepatitis B is  
vaccine-preventable



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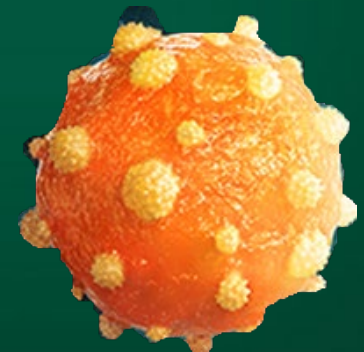


20% of people with chronic HBV  
infection will die of complications,  
including cirrhosis, end-stage liver  
disease, and hepatocellular carcinoma

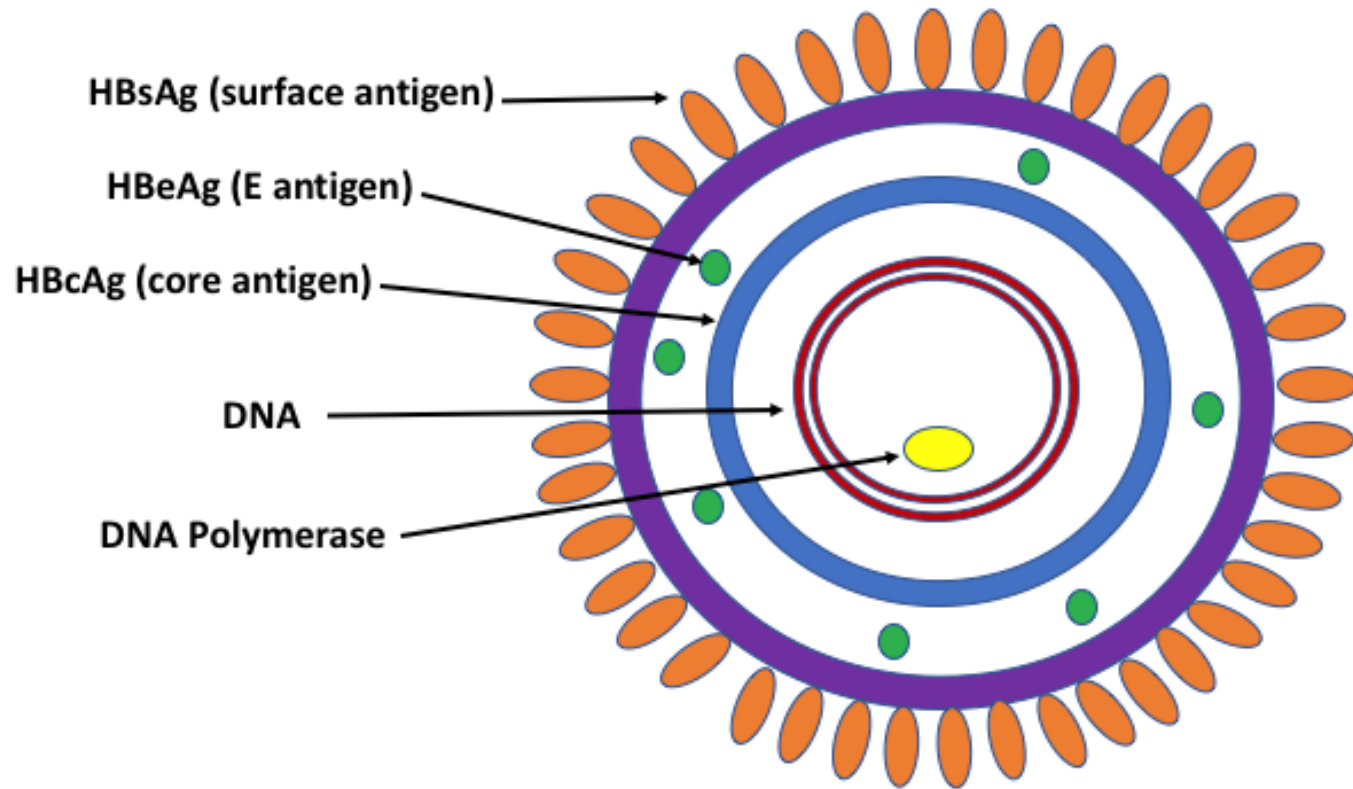


# Hepatitis B: the basics

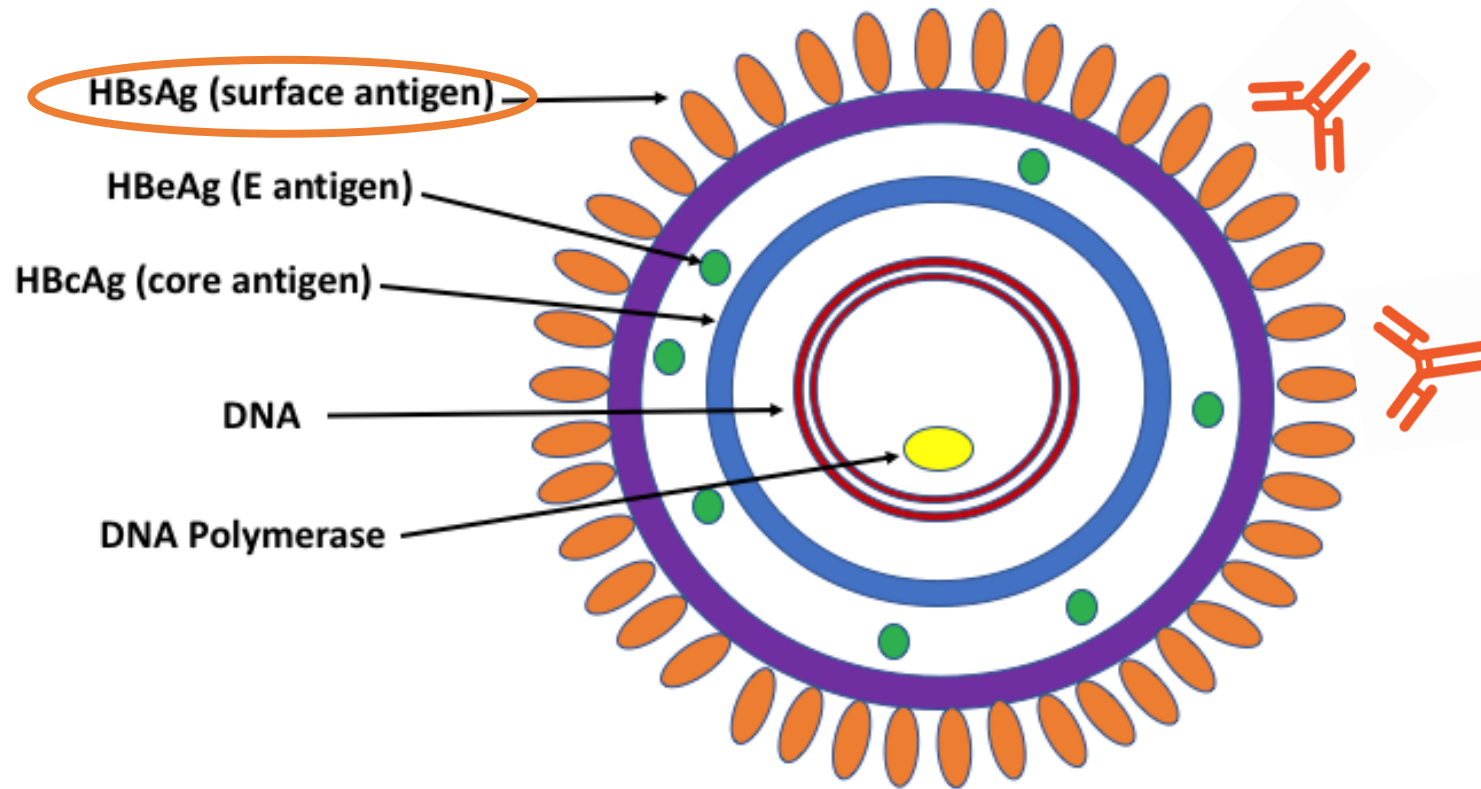
- There is a vaccine, but...
- Only 25-30% of adults are adequately vaccinated
- Only 15% of adolescents demonstrate serologic immunity



# Hepatitis B Virus Structure



# Hepatitis B Virus Structure



## Surface Antigen

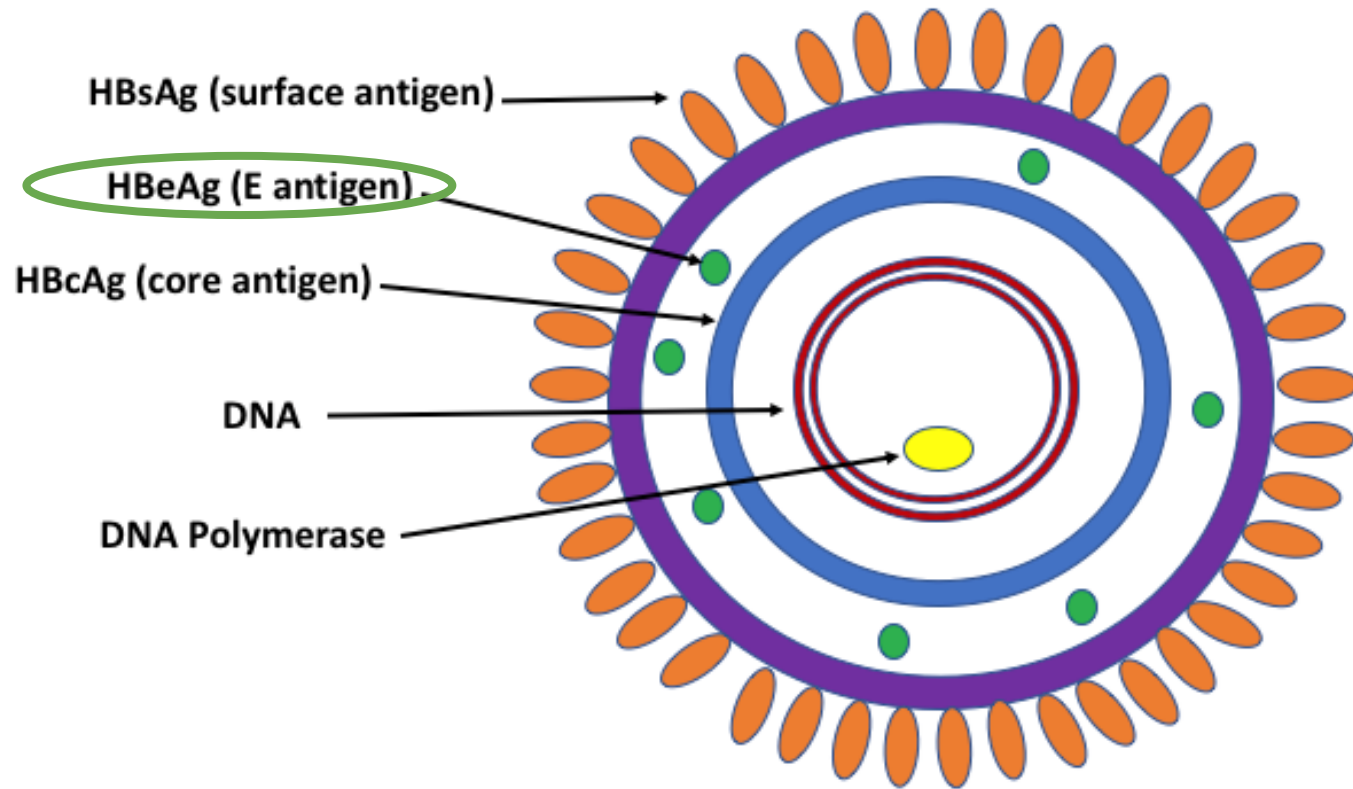
- Present in acute and chronic infection
- Absent in resolved infection

## Surface Antibody

- Present with resolved infection or immunity



# Hepatitis B Virus Structure

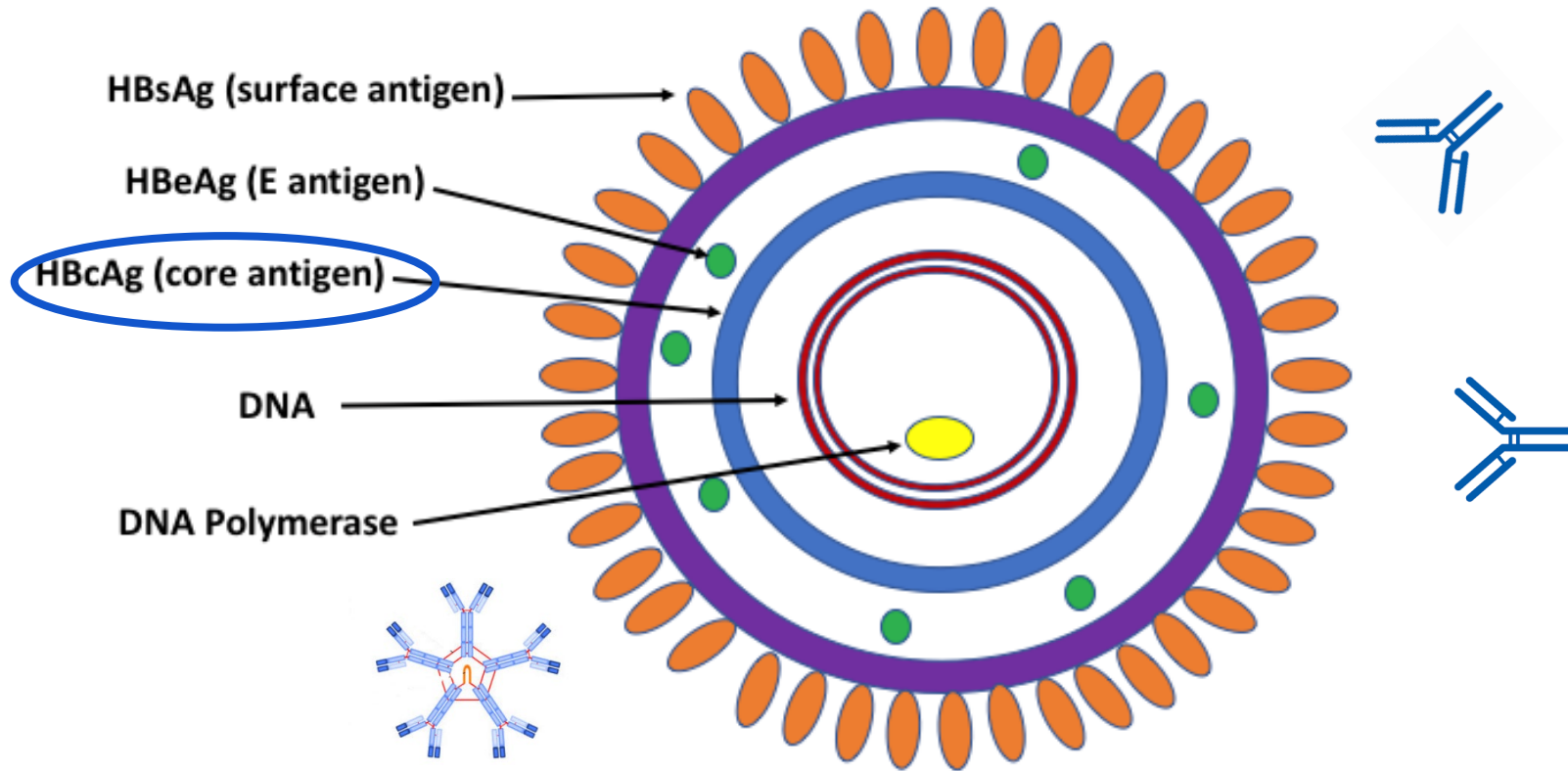


## E Antigen

- Encoded by the same portion of viral genome that codes for core antigen
- Presence indicates extremely high viral load and active replication



# Hepatitis B Virus Structure



## Core Antigen

- Only present in hepatocytes
- No serum circulation

## Total Core Antibody

- Present in acute/chronic infection, resolved infection, passive transfer to infant, false positive or mutant HBsAg strain not detectable by lab assay





## IgM Core Antibody

- Only present in acute infection

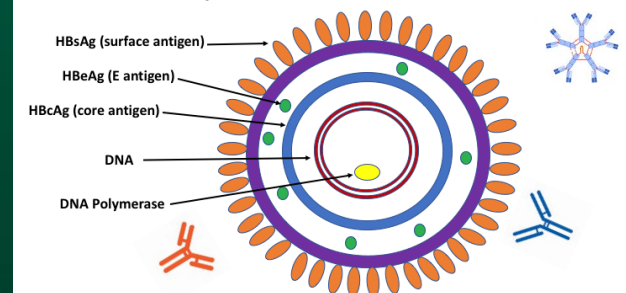




**Table 1. Interpretation of Screening Test Results for Hepatitis B Virus Infection and Recommended Actions**

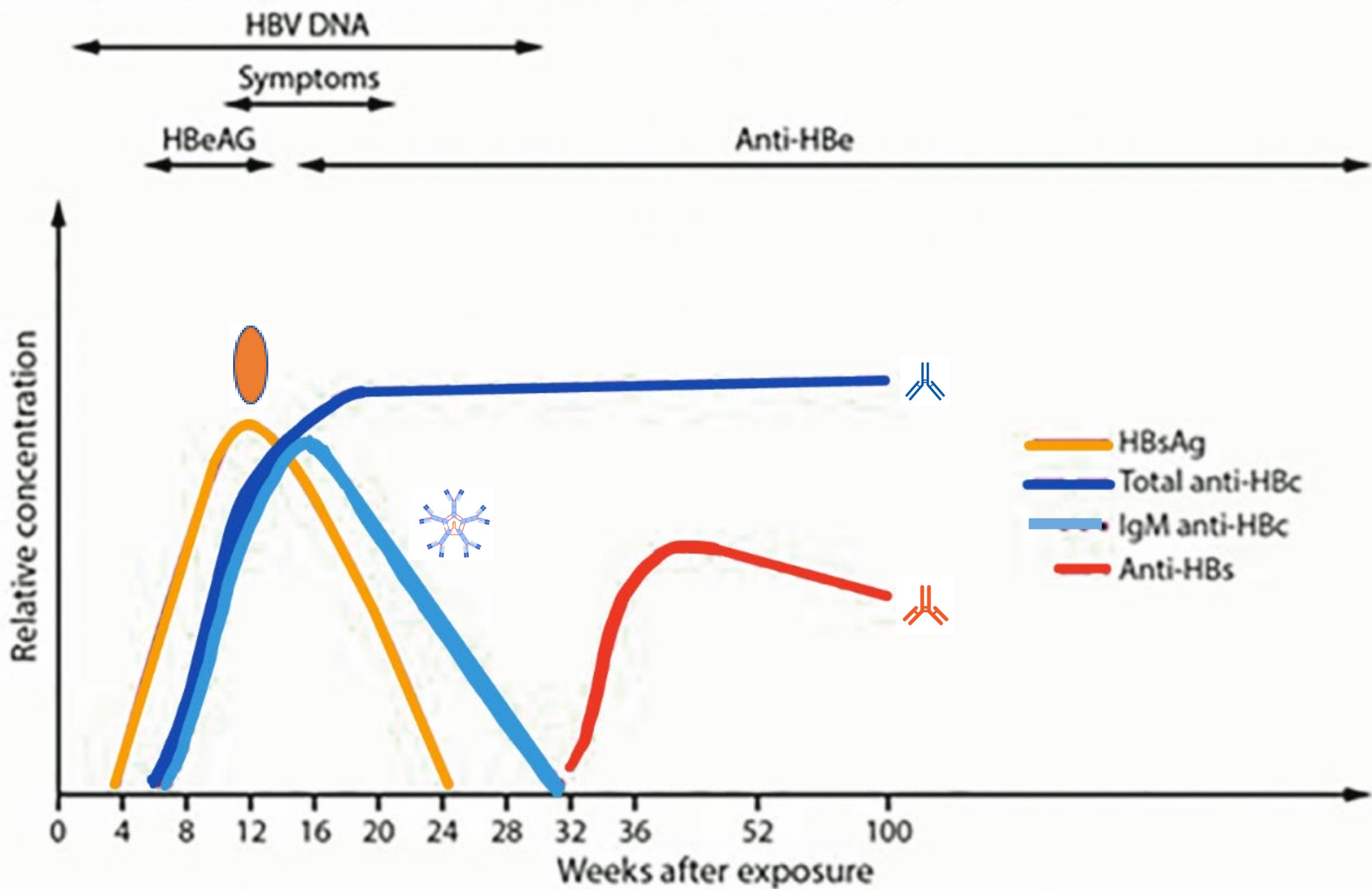
Clinical State	 HBsAg	 Anti-HBs	 Total anti-HBc*	 IgM anti-HBc	Action <sup>†</sup>
Acute infection	Positive	Negative	Positive	Positive	Link to HBV infection care
Chronic infection	Positive	Negative	Positive	Negative <sup>‡</sup>	Link to HBV infection care
Resolved infection	Negative	Positive	Positive	Negative	Counsel about HBV infection reactivation risk
Immune (immunity inferred from receipt of previous vaccination)	Negative	Positive <sup>§</sup>	Negative	Negative	Reassure if history of HepB vaccine series completion; if partially vaccinated, complete vaccine series per ACIP recommendations
Susceptible, never infected	Negative	Negative <sup>  </sup>	Negative	Negative	Offer HepB vaccine per ACIP recommendations
Isolated core antibody positive <sup>¶</sup>	Negative	Negative	Positive	Negative	Depends on cause of positive result

**Hepatitis B Virus Structure**

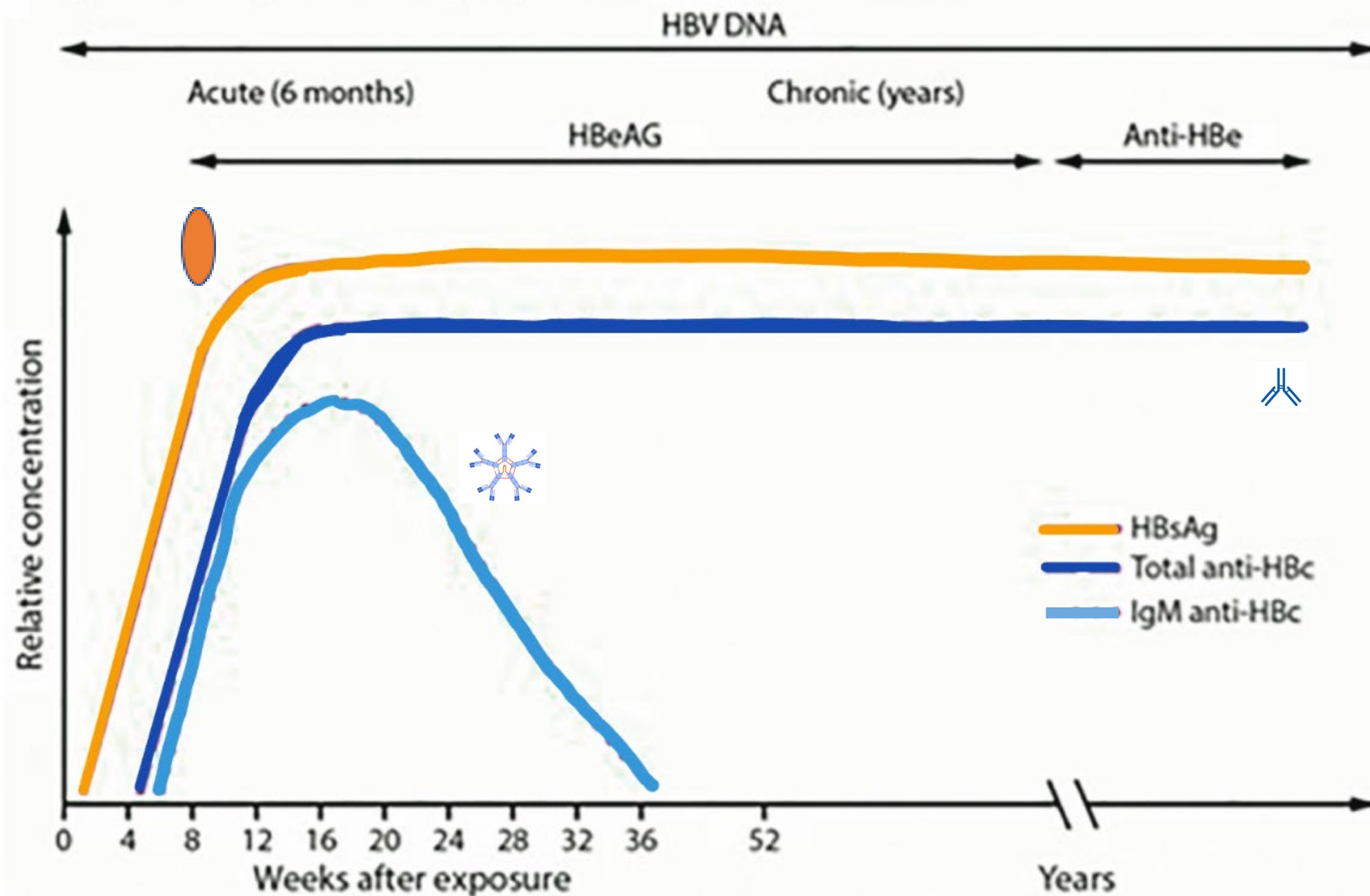




# A. Typical serologic course of acute HBV infection to recovery



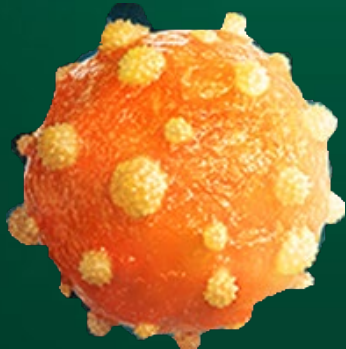
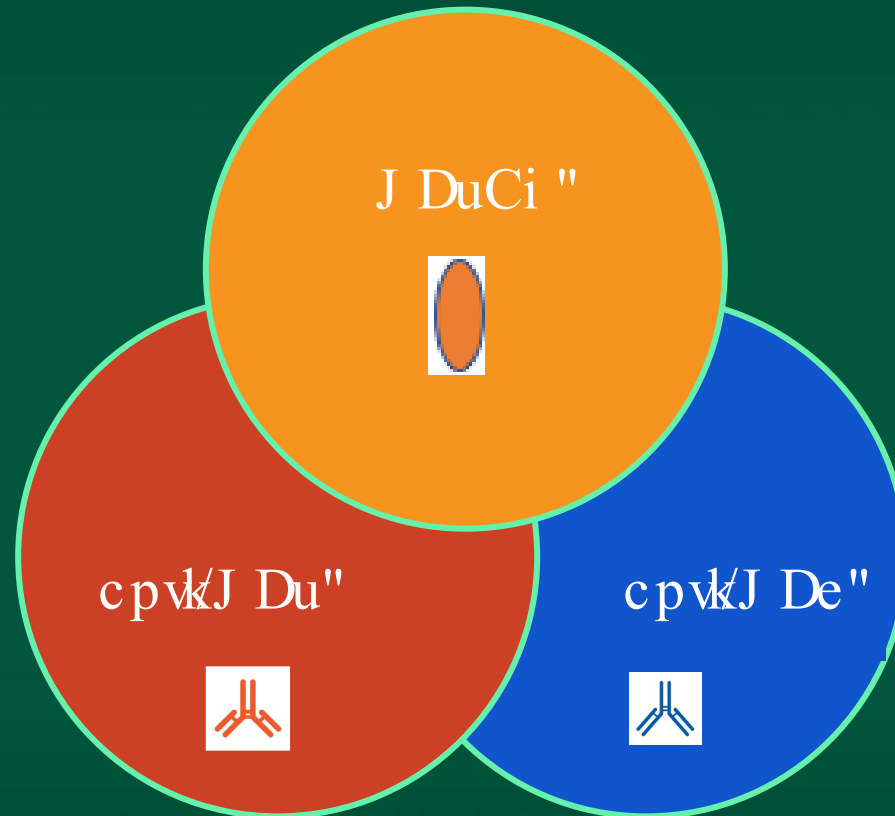
## B. Typical serologic course of progression to chronic HBV infection



# Hepatitis C: New Screening Recs

CDC: screen  
all adults once

CDC:  
vaccinate if  
susceptible



# Hepatitis B Screening

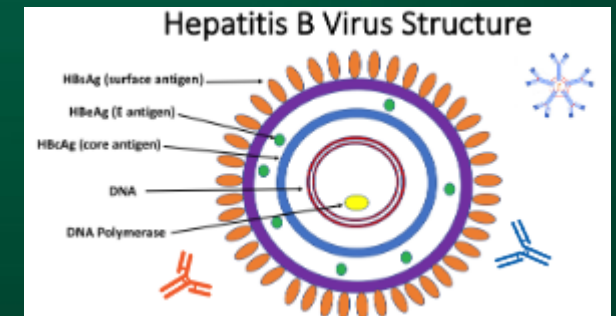
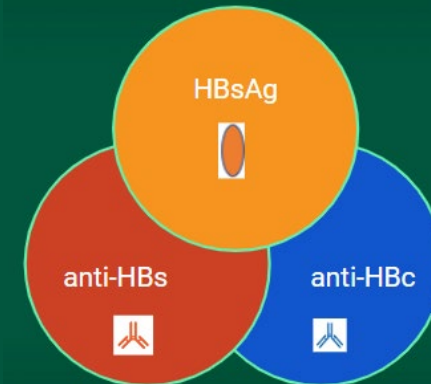
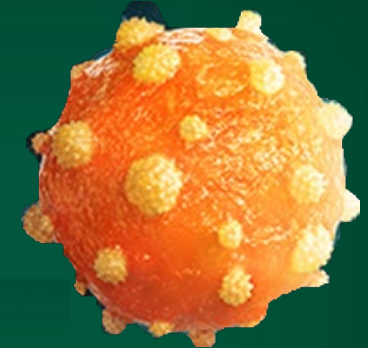
Two goals: screening for INFECTION and IMMUNITY

## 1. INFECTION

- Hepatitis B surface antigen (**HBsAg**)
- Test each pregnancy
- If positive, further evaluation is indicated

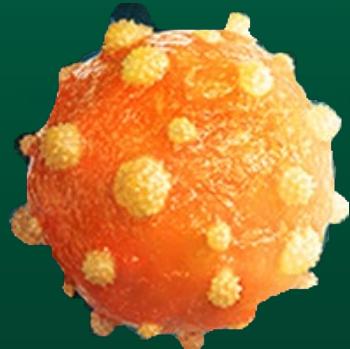
## 2. IMMUNITY

- **Anti-HBs** + **anti-HBc**
- Test once per adult lifetime
- Part of “triple panel screening”



# Why Triple Panel Screening?

- 10,000 new Hep B cases annually adults age 30-49
- 20 mil patients with chronic Hep B (70% born outside of the US)
- 2/3 with chronic Hep B are unaware of their infection
- The previous risk-based screening insufficient



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# Theoretical 3.6 million pregnant patients Universal screening + vaccination prevents:

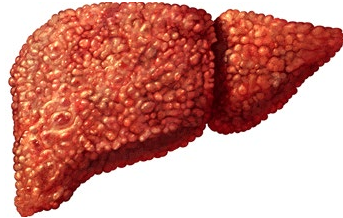
3924

Ecugu"qh"J gr "D



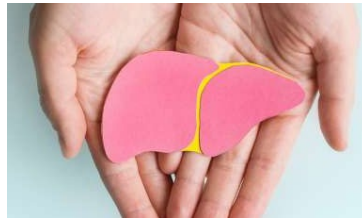
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Ektj quku



6

Vtcpu r pvu



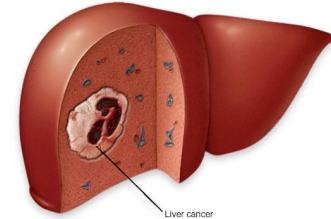
33

Fgc vj u



3

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J gr c v q e g m w r t "  
Ectekpqo c



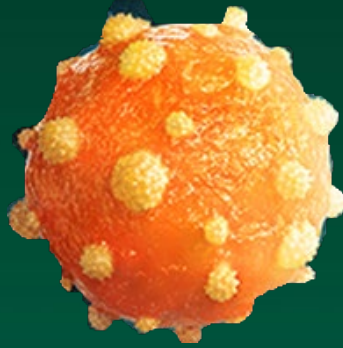
## Universal Hepatitis B Antibody Screening and Vaccination in Pregnancy

*A Cost-Effectiveness Analysis*

*Malavika Prabhu, MD, Marguerite K. Susich, BA, MSN, Claire H. Packer, MPH, Alyssa R. Hersch, MD, MPH,  
Laura E. Riley, MD, and Aaron B. Caughey, MD, PhD*

*Obstet Gynecol 2022;139: 357*





## CPG 6: Viral Hepatitis

Recommends triple panel screening for:

- All pregnant patients without documented triple neg screen after 18 yo
- Or who haven't completed a HepB vaccine series
- Patients with ongoing risk of hepatitis B infection, regardless of vax status or prior testing

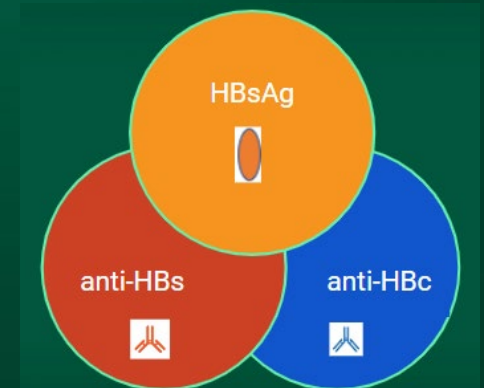
Check HBsAg in every pregnancy

## Consult Series 69: Hepatitis B in Pregnancy

Recommends triple panel screening:

- At the initial prenatal visit if not previously documented or known to have been performed

Check HBsAg in every pregnancy



# Implementing Triple Panel Screening

3

Consider at preconception visit

4

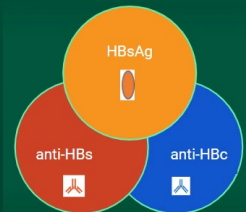
First prenatal visit: determine if previously sent by PCP

5

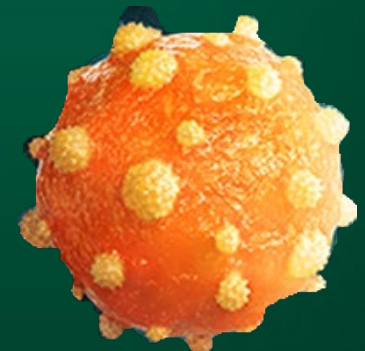
If uncertain, send as part of initial prenatal labs

6

If already complete, only send HBsAg

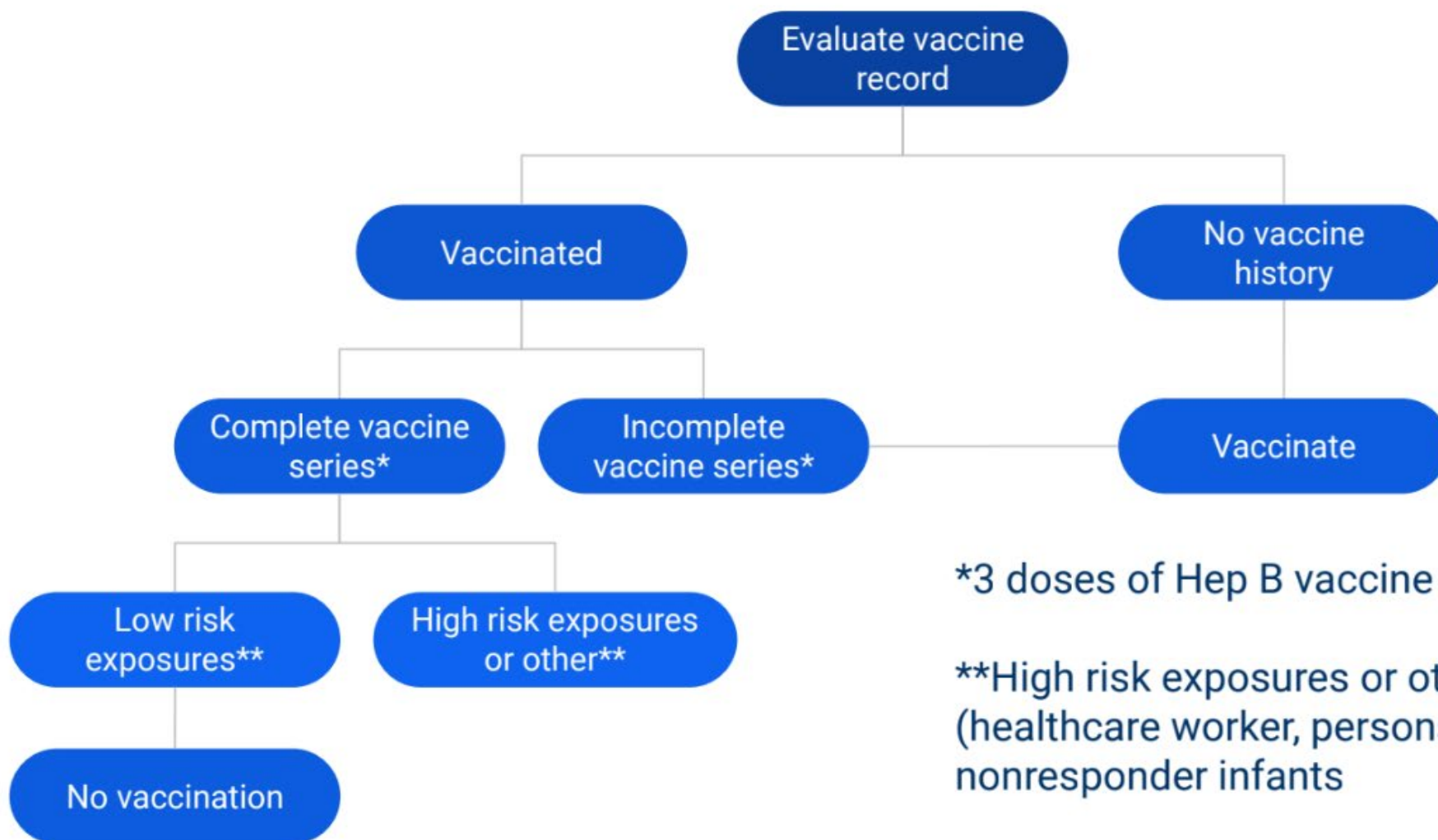


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# What if my patient is susceptible?

## Triple-neg Panel



\*3 doses of Hep B vaccine (unless HEPLISAV-B)

\*\*High risk exposures or other: exposure to blood (healthcare worker, persons on hemodialysis), or nonresponder infants

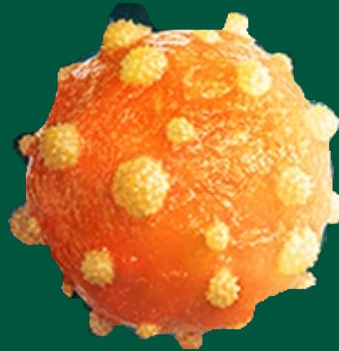
# Does Hep B Vax work in pregnancy?

**Yes!**

- Protein subunit vaccine, 3 doses needed
- No reported adverse maternal, fetal or neonatal outcomes with prenatal vaccination
- 90% seroconversion rate (same as outside of pregnancy)

OK in Pregnancy  
in Pregnancy

Enderix B  
Heplisav  
Recombivax HB

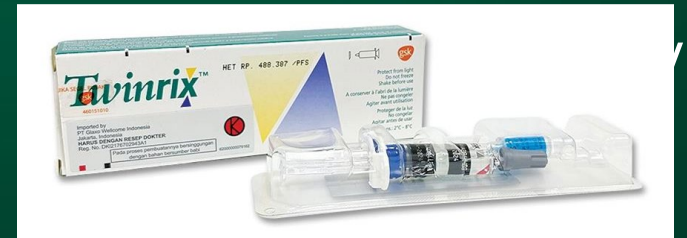


Avoid



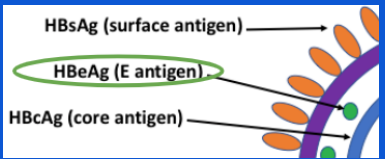
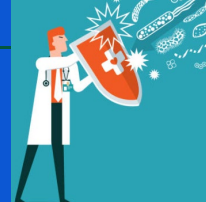


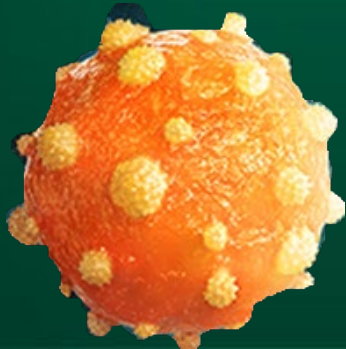
B)

**UT** THE UNIVERSITY OF  
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# What if I diagnose Hepatitis B?

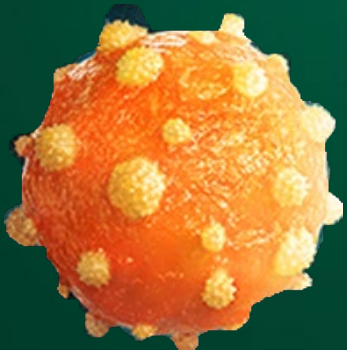
3	Diagnosing HIV	×	✓	
4	Diagnosing HIV	×	✓	
5	Hepatitis B e antigen	×	✓	
6	Diagnosing HIV	×	✓	





# Counseling Your Patient: Pregnancy

- Risk of vertical transmission
  - viral load
  - antiviral treatment
- Antivirals recommended for fetal benefit if:
  - VL >200k at the beginning of the third trimester
- Antivirals recommended for maternal benefit if:
  - eAg Neg, VL >2k and ALT >2x ULN
  - eAg pos, VL >20k and ALT >2x ULN

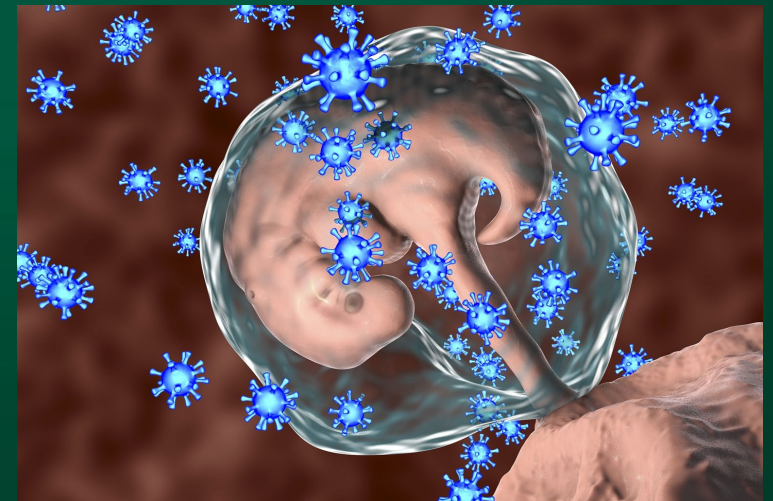




# Counseling Your Patient: Pregnancy

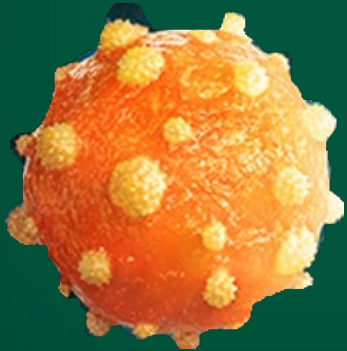
- Antivirals
  - **Tenofovir** is the antiviral of choice
  - TDF is safer than TAF for maternal kidneys and bone, but both are reduce rates of perinatal transmission
  - Continue if using pre-pregnancy
  - Discontinuation is associated with PP flare

[\*\*TAF at 25 mg daily or  
TDF at 300 mg daily]



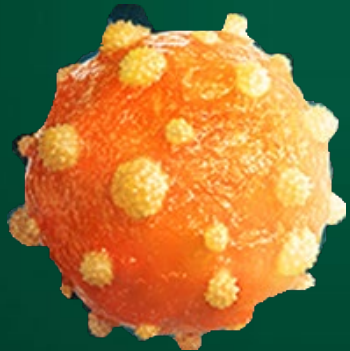
# Counseling Your Patient: Pregnancy

- Recommend Hepatitis A vaccine for the patient and her family
- Recommend Hepatitis B vaccine for members of her household



# Counseling Your Patient: Delivery & PP

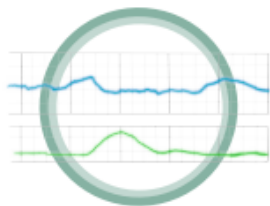
- Baby needs **HBIG** and **Hepatitis B vaccine** within 12 hours of birth
- Routine intrapartum management is fine if neonatal tx planned
  - AROM, FSE, IUPC, operative VD all OK
  - Regardless of VL
- Breastfeeding is fine if HBIG and HBV vaccine are planned
  - Avoid BF if bleeding from nipples



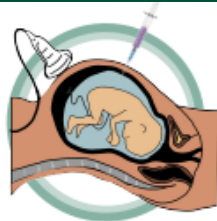
Chronic HBV infection will develop  
in up to **90%** of perinatally  
exposed neonates who do not  
receive immunoprophylaxis



Neonatal immunoprophylaxis is standard of care



No alteration of routine intrapartum care



Invasive testing may be performed after informed discussion



Hepatitis A vaccination if susceptible



Household contacts should be evaluated



Can breastfeed as long as the infant has received immunoprophylaxis

\*if bleeding nipples, discard milk from affected breast until healed to prevent direct exposure

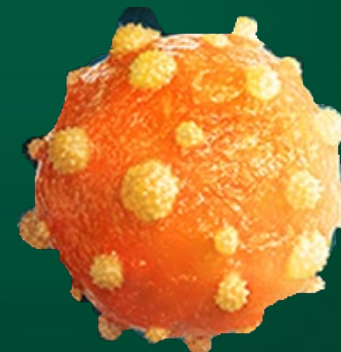


Society for Maternal-Fetal Medicine

Consult Series #69

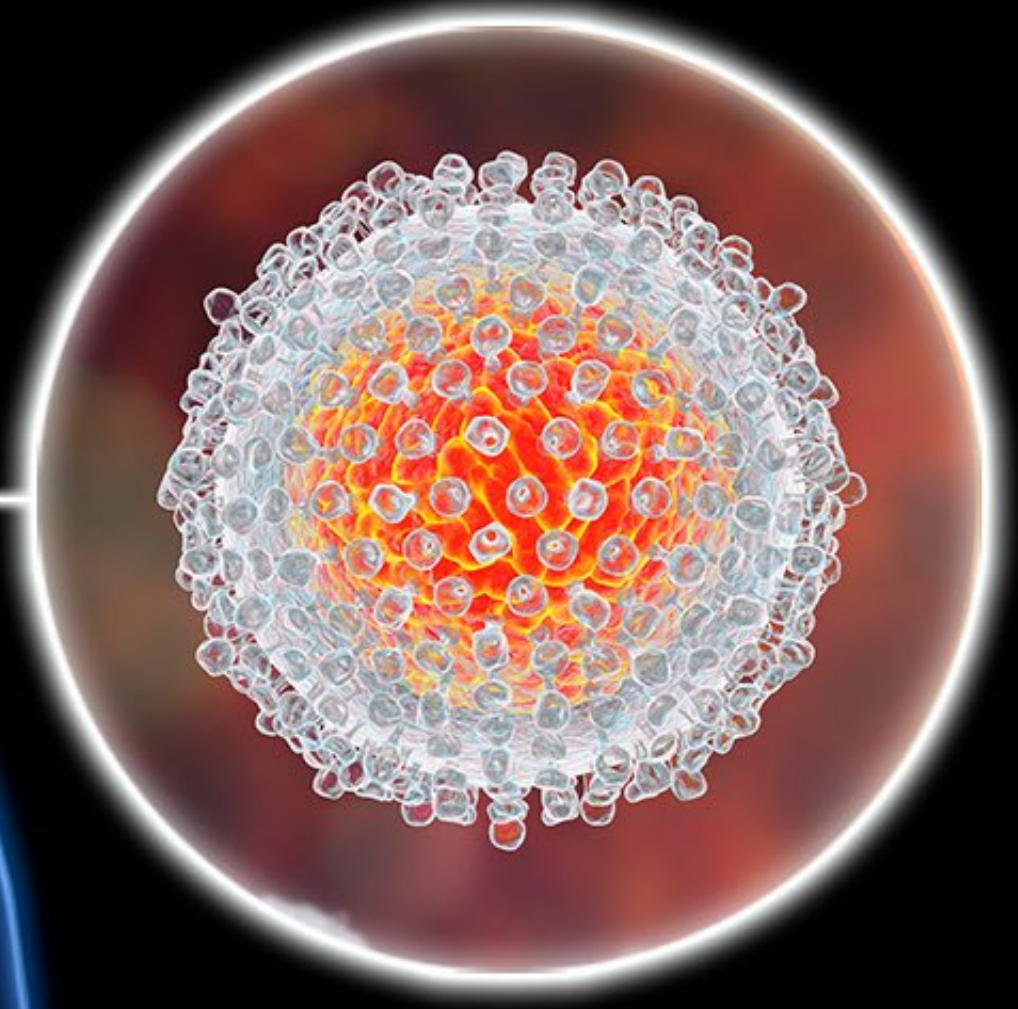
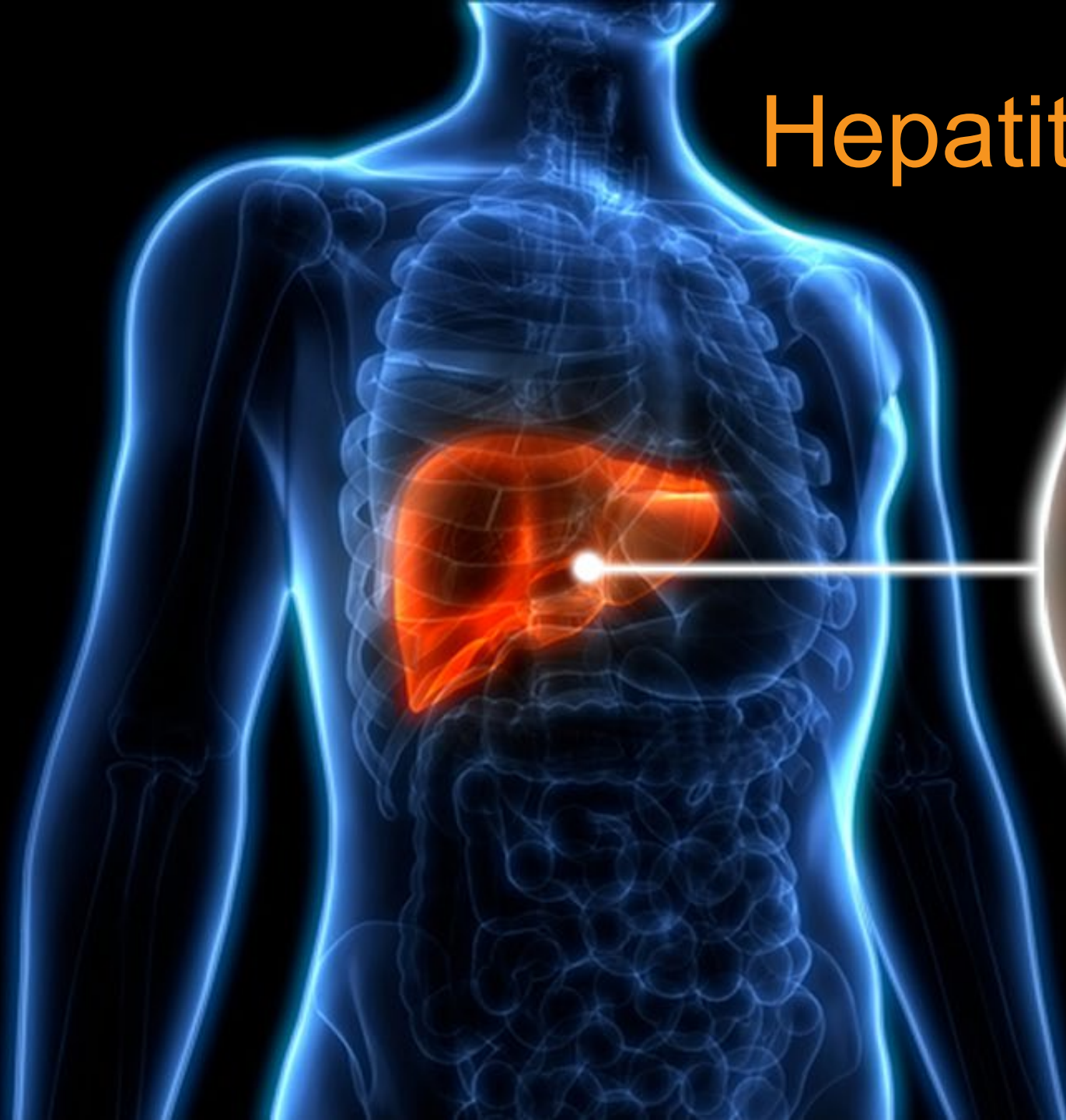


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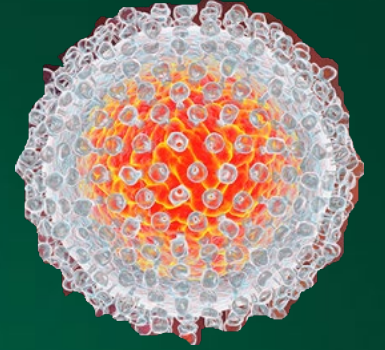


# Hepatitis C





# Hepatitis C: the basics



- Affects 1-4% of pregnant women in the US
- 75% with acute infection are asymptomatic
- 15-45% will clear HCV within 6 mos, remainder develop chronic HCV

*Research* Our cross-sectional study of U.S. births from 2009 to 2019 revealed that:

Between 2009 and 2019,  
**the overall rate of HCV** per 1000  
pregnant people *increased* from

**1.8 to 5.1**



HCV rates were  
*highest* among  
**American Indian/  
Alaska Native & White**  
pregnant people



Pregnant people  
**without a 4-year  
degree** were *at higher  
risk* for HCV than those  
with one

# SYMPTOMS



jaundice

nausea



anorexia

abdominal pain

malaise

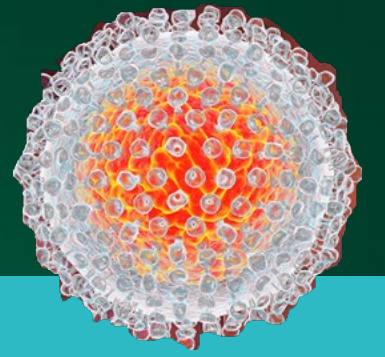


# TRANSMISSION

#1 percutaneous exposure to blood  
(injection of illicit drugs)

Other  
sharing contaminated devices  
exposure to infected blood  
sex

# Hepatitis C: the basics



Of every 100 people infected with Hepatitis C,  
**75-85 people will develop Chronic Hepatitis C.**

If left untreated:



**60-70 PEOPLE**  
will develop  
**CHRONIC LIVER  
DISEASE**



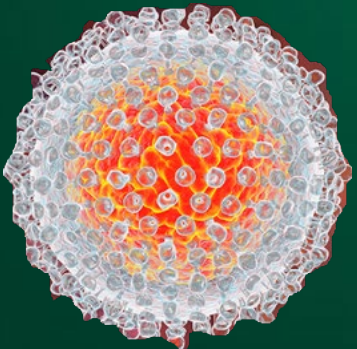
**5-20 PEOPLE**  
will develop  
**CIRRHOSIS**  
over a period of  
20-30 years



**1-5 PEOPLE**  
will die from  
**CIRRHOSIS** or  
**LIVER CANCER**

# Hepatitis C: the basics

- No vaccine at present... but curable (postpartum)
- Associated with PTB, SGA, LBW, and assisted ventilation
- Higher risk of infant feeding difficulties, cephalohematoma, brachial plexus injury, fetal distress, IVH, seizures
- 20 times odds of ICP





# Hepatitis C Screening

- Screen in each pregnancy (CDC, ACOG, SMFM)
  - no risk-based screening
- Think about it in patients with cholestasis <24w or BA >100

## How to Screen:

- Hepatitis C antibody
- If positive, send HCV RNA level





**Positive HCV Antibody**



**HCV RNA present**

**HCV RNA absent**



**Positive HCV Antibody**

**HCV RNA present**

**HCV RNA absent**

**Current HCV infection:**

- Get labs
- Vaccinate for HAV + HBV
- Refer to hepatologist



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## Positive HCV Antibody

HCV RNA present

### Current HCV infection:

- Get labs
- Vaccinate for HAV + HBV
- Refer to hepatologist

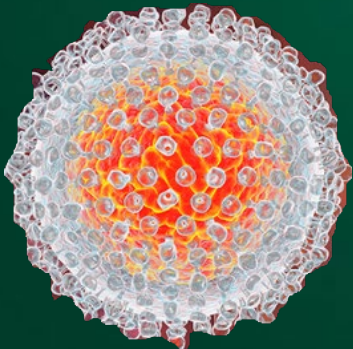
### BOX

#### Recommended laboratory tests for confirmed active HCV infection in pregnancy

- Liver function tests (AST, ALT, bilirubin)
- Albumin
- Platelet count
- Prothrombin time
- Quantitative HCV RNA
- HCV genotype (if not previously obtained)
- STI screening (HIV, syphilis, gonorrhea, chlamydia, and HBV)

*ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *HBV*, hepatitis B virus; *HCV*, hepatitis C virus; *HIV*, human immunodeficiency virus; *STI*, sexually transmitted infection.

*Society for Maternal-Fetal Medicine. SMFM Consult Series #56: Hepatitis C in pregnancy. Am J Obstet Gynecol 2021.*



**Positive HCV Antibody**

**HCV RNA present**

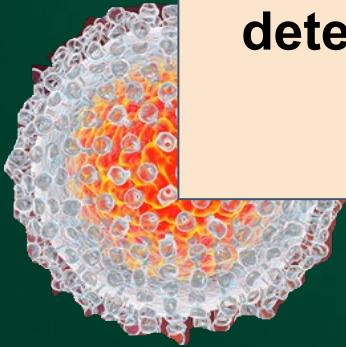
**HCV RNA absent**

**Current HCV infection:**

- Get labs
- Vaccinate for HAV + HBV
- Refer to hepatologist

**If new diagnosis...**

**Repeat HCV in 6 mos to determine if acute vs chronic dz**



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**Positive HCV Antibody**

**HCV RNA present**

**HCV RNA absent**

**Current HCV infection:**

- Get labs
- Vaccinate for HAV + HBV
- Refer to hepatologist

**False Positive  
or  
Resolved HCV Infection**



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**Positive HCV Antibody**

**HCV RNA present**

**HCV RNA absent**

**Current HCV infection:**

- Get labs
- Vaccinate for HAV + HBV
- Refer to hepatologist

**False Positive  
or  
Resolved HCV Infection**

*Retest **HCV Antibody** With  
a New  
Platform*



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**Positive HCV Antibody**

**HCV RNA present**

**HCV RNA absent**

**Current HCV infection:**

- Get labs
- Vaccinate for HAV + HBV
- Refer to hepatologist

**False Positive  
or  
Resolved HCV Infection**

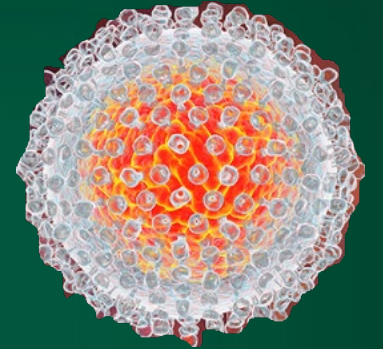
**Alternative assay negative  
=  
HCV Ab False Positive**

**Alternative assay positive  
=  
Cleared infection**



# Hepatitis C: Management

- Alcohol worsens progression
- Acetaminophen max daily dose 2g if cirrhosis present
- Transmission prevention
  
- Third trimester growth scan
- Intrapartum: avoid IUPC/FSE and early AROM; augment after ROM
- Breastfeeding OK, but avoid when nipples are bleeding/cracked



## Risk factors

VL > 10<sup>6</sup>

Antepartum bleeding

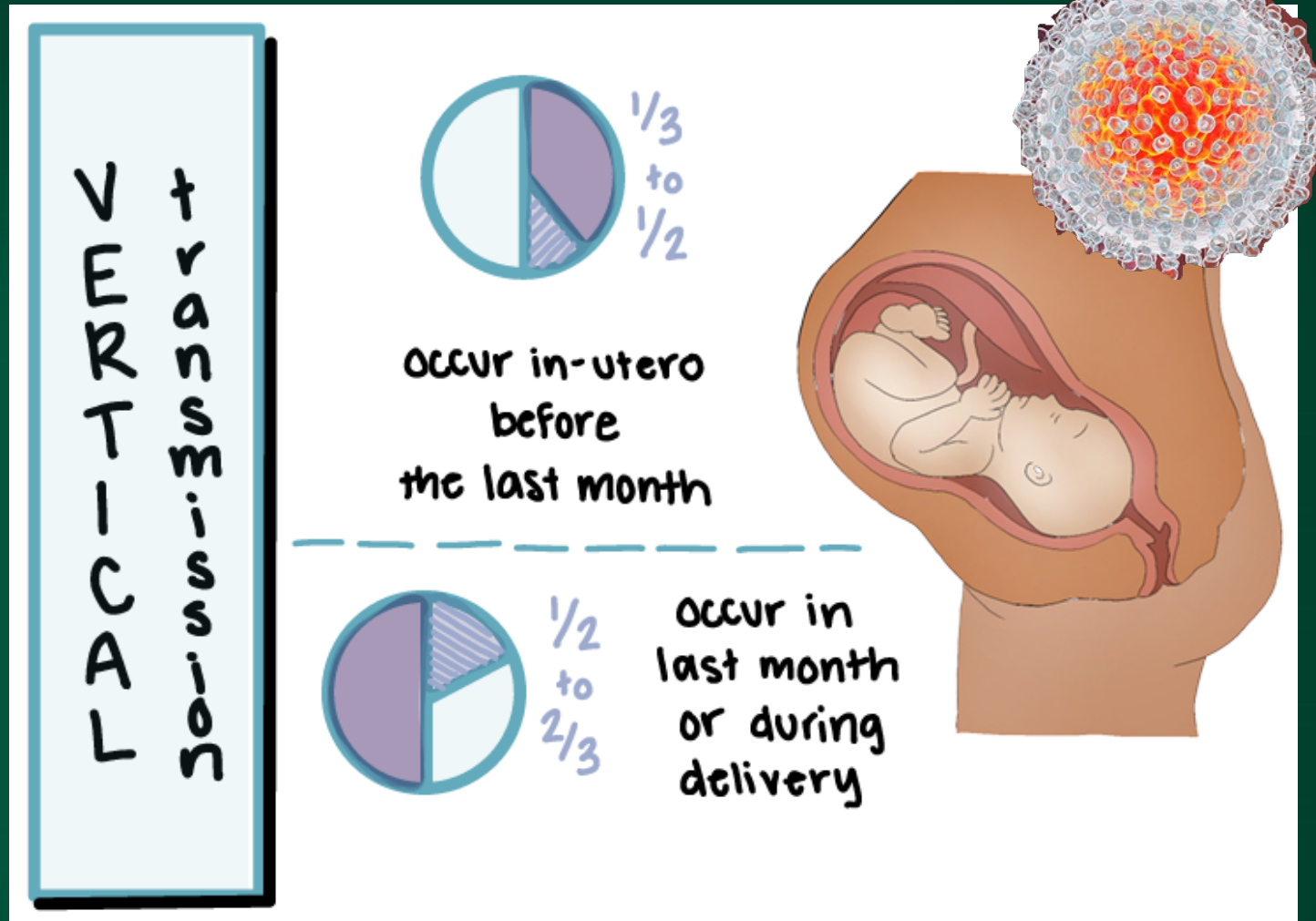
## Risk depends on viral load

Undetectable VL: approx 0%

HIV coinfection: 10%

Viremic: 8%

Overall: 6%





**Research** Our study of maternal-infant dyads on Medicaid in Tennessee from 2005-2014 revealed that:

HCV-exposure **varied widely by county.**

Number of exposed infants per 1,000 live births:



**23%** of HCV-exposed infants were **tested for HCV** in the *first 24 months of life.*



and **only 18%** of the *HCV-exposed infants tested* met our definition for **adequate testing.**



Only **1 in 10** HCV-exposed African American infants were *tested* compared to 1 in 4 overall infants.



HCV-exposed infants in **rural counties** were *less likely* to be tested. (aOR 0.73)

**Recommendations:**

1. **Universal** HCV screening for **pregnant women**
2. Increased **provider education** on national guidelines for HCV testing, esp for *at-risk groups*

**AAP/CDC Recommend:**

- HCV antibodies after 18 mos or
- HCV RNA on two occasions after 1 month



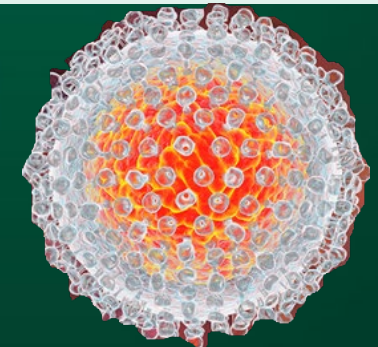
**VANDERBILT**  
Center for  
Child Health Policy

Lopata SM, McNeer E, Dudley JA, Wester C, Cooper WO, Carluccio JG, Espinosa C, Dupont W, Patrick SW. Hepatitis C Testing Among Perinatally Exposed Infants. *Pediatrics*.

Supported by NIDA K23DA038720 & R01DA045729



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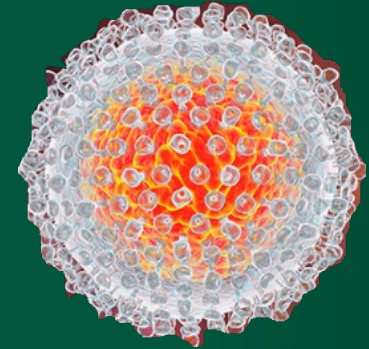




# Hepatitis C: Long-term Management

Referral to Hepatology for Direct Acting Antiviral (DAA)

- Goal of treatment: SVR
  - Undetectable HCV RNA 12-24w after treatment
  - Achieved in >9
- SVR is considered curative
- Liver disease resolves if no cirrhosis
- Even with cirrhosis, fibrosis may regress and complications are lower

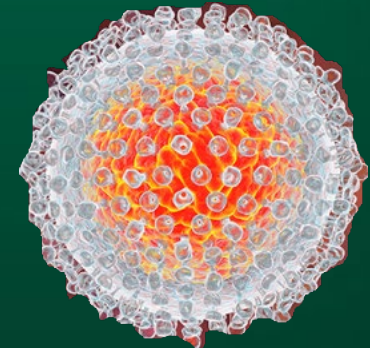


# DAA Treatment in Pregnancy



Phase 1 study (ledipasvir/sofosbuvir - Harvoni)

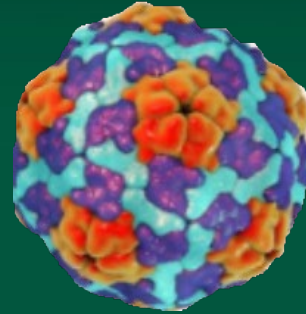
- n=9, 100% cure
- No adverse outcomes
- Pharmacokinetic study
- Genotype 1 HCV
- 12 week course of Harvoni, start at 23-24w
- AUC similar btw pregnant and non-pregnant subjects



# Recap – What's New?

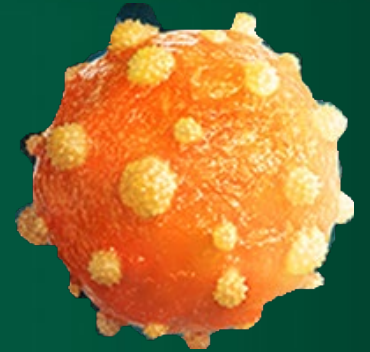
## Hepatitis A

OK to vaccinate in pregnancy  
Vaccinate patients with Hep B or C



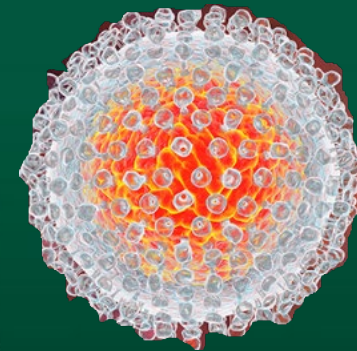
## Hepatitis B

Triple panel testing and vaccination  
Tenofovir therapy  
No changes to routine intrapartum management when neonatal immunoprophylaxis planned



## Hepatitis C

Perinatal transmission data  
Promising DAA treatment in pregnancy



**Questions?**

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