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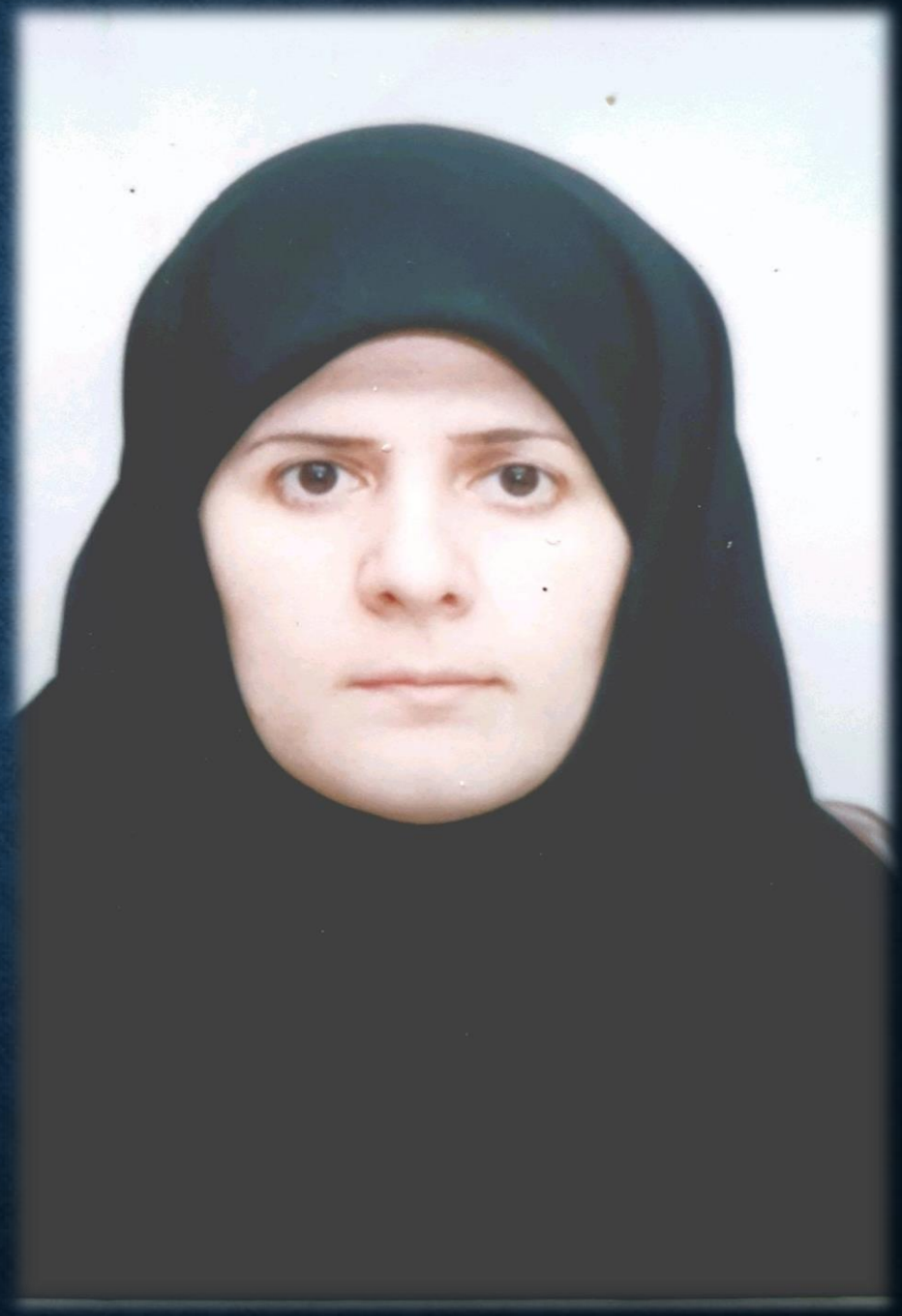
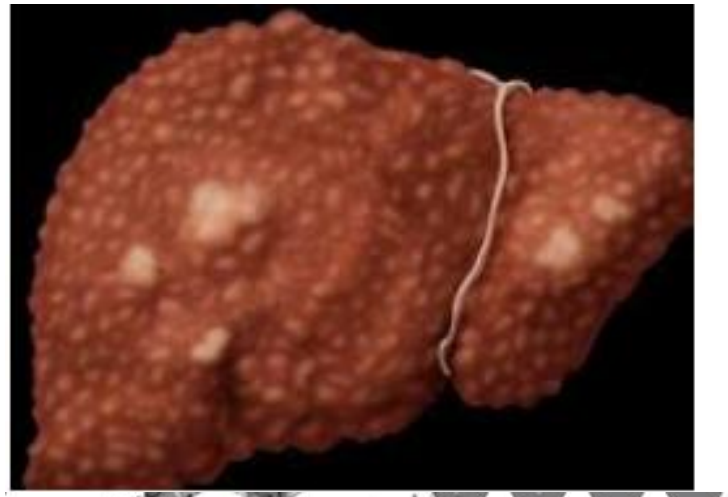
- **Assistant prof. at TUMS**
- **Infertility fellowship**

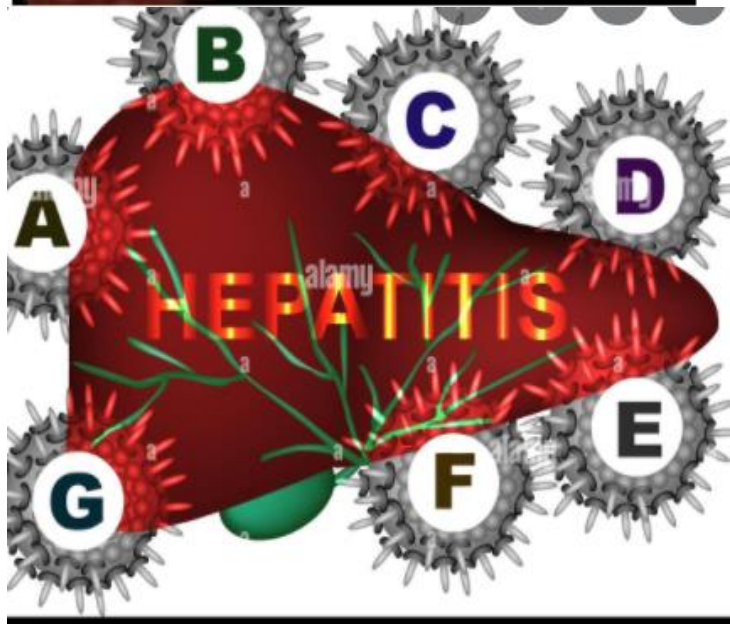


Viral hepatitis in pregnancy

There are at least five distinct types of viral hepatitis:

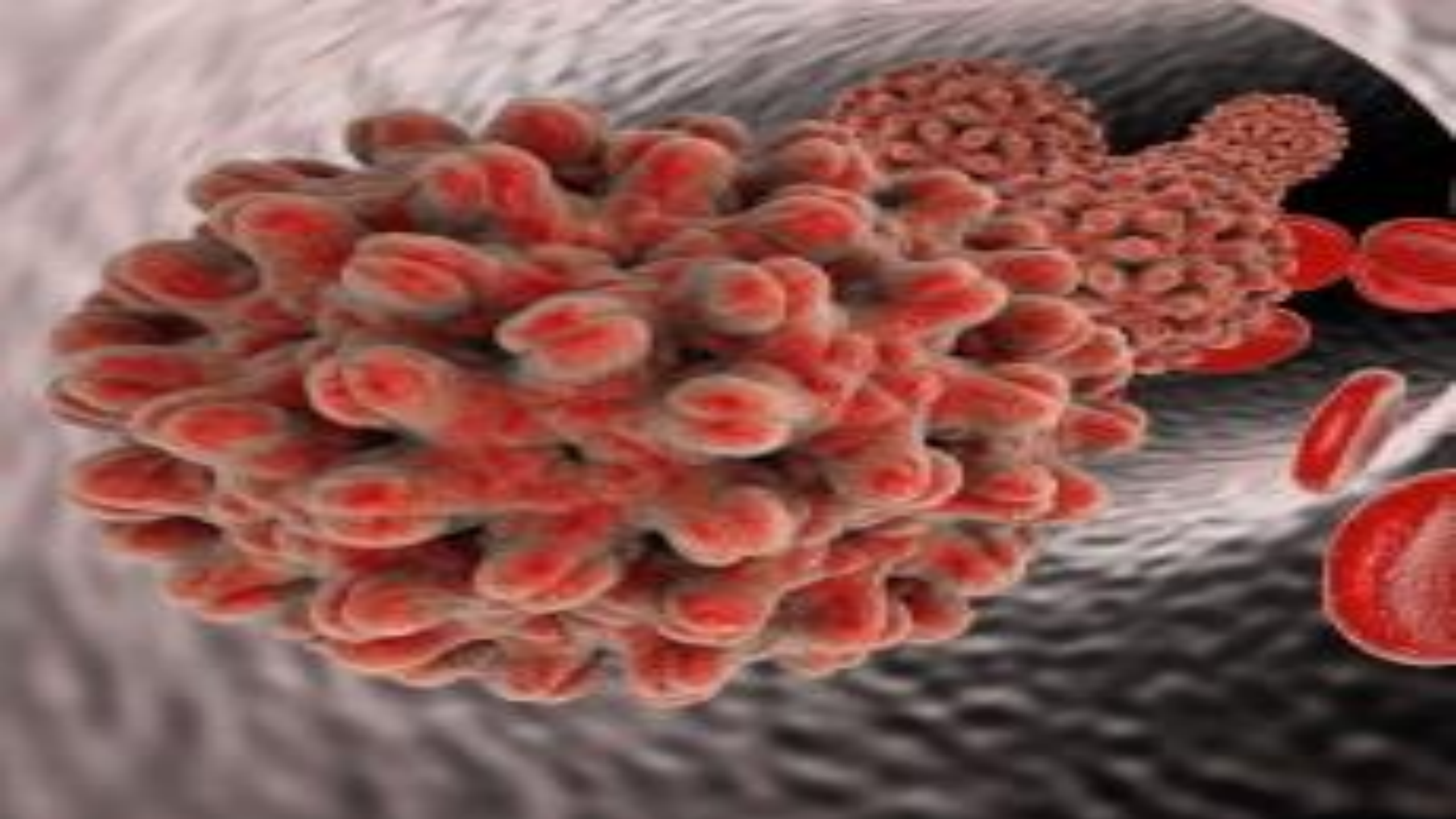
1. A (HAV),
2. B (HBV),
3. C (HCV),
4. D (HDV)caused by the hepatitis B-associated delta agent,
5. E (HEV).

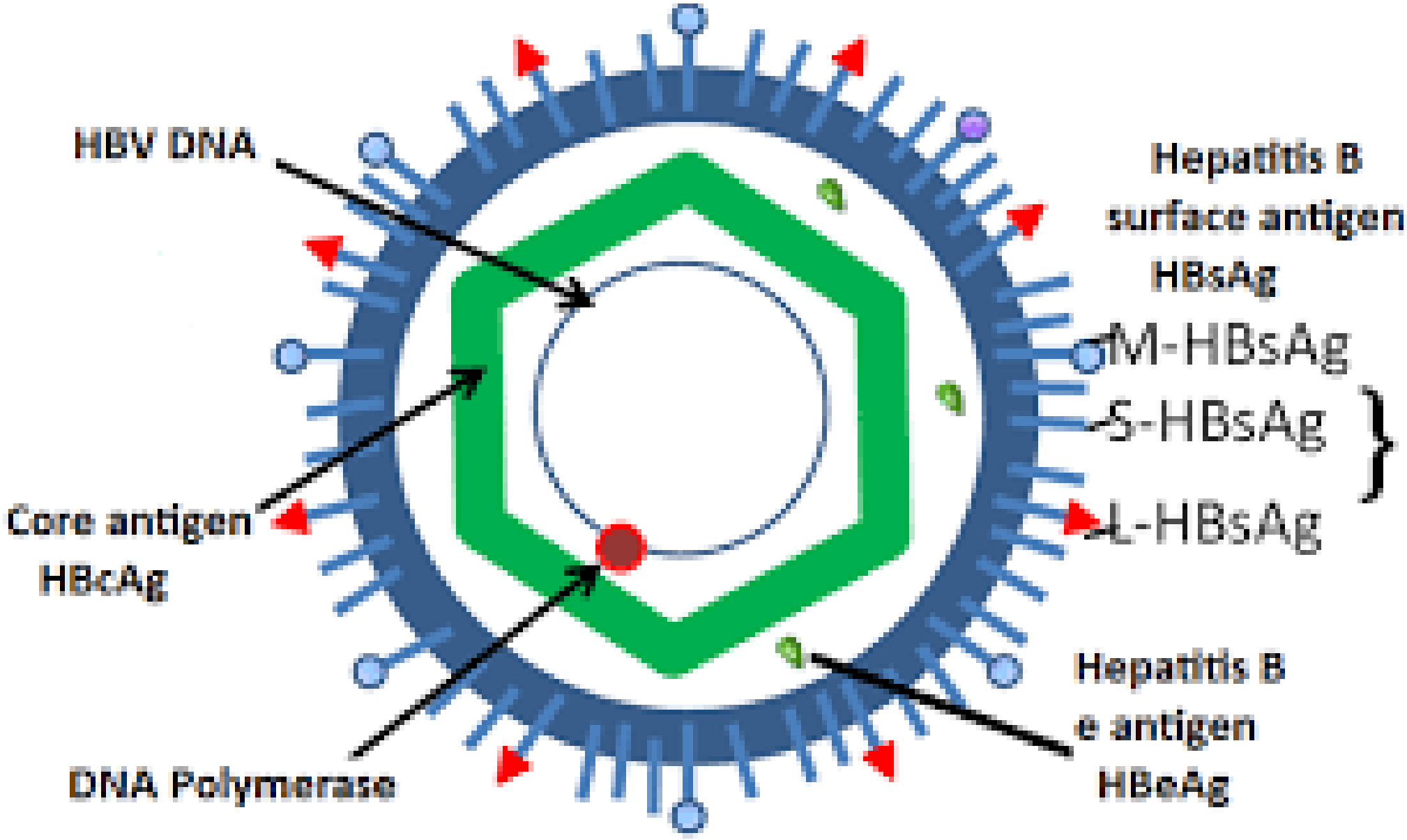


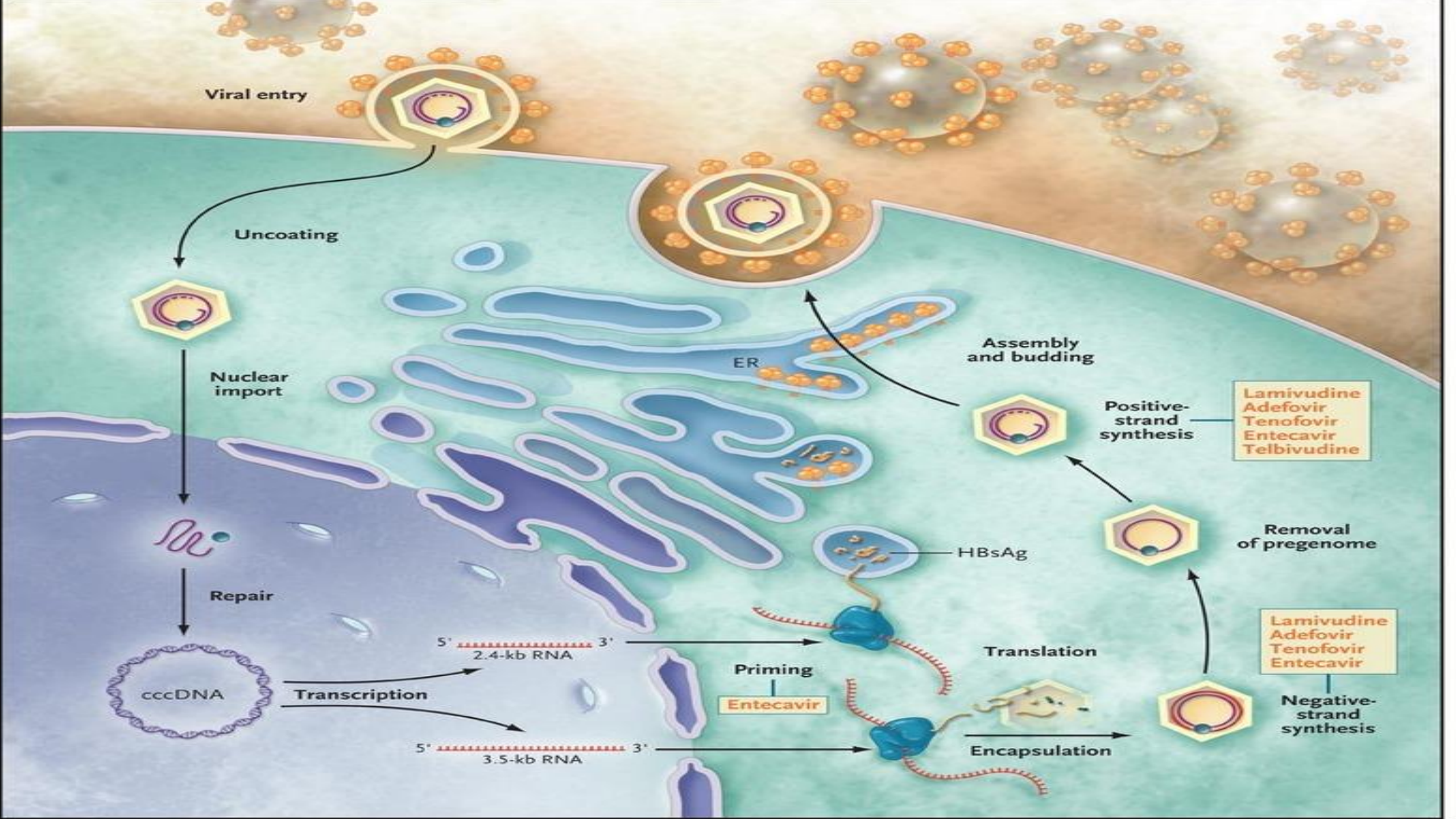


the viruses themselves probably **are not hepatotoxic,**

the immunological response to them causes hepatocellular necrosis




HBV DNA
Core antigen
HBcAg
DNA Polymerase
Hepatitis B
surface antigen
HBsAg
M-HBsAg
S-HBsAg
L-HBsAg
Hepatitis B
e antigen
HBeAg


Viral entry
Uncoating
Nuclear import
ER
Assembly and budding
Positive-strand synthesis
Lamivudine
Adefovir
Tenofovir
Entecavir
Telbivudine
Removal of pregenome
HBsAg
Repair
cccDNA
Transcription
5' 2.4-kb RNA 3'
5' 3.5-kb RNA 3'
Priming
Entecavir
Translation
Encapsulation
Lamivudine
Adefovir
Tenofovir
Entecavir
Negative-strand synthesis

- hepatitis B to be second only to tobacco among human carcinogens.

- HBV can be transmitted by any body fluid, but exposure to virus-laden serum is the most efficient.

Acute hepatitis B develops after an incubation period of **30 to 180** days with a mean of **8 to 12 weeks**

At least **half of acute infections** are **asymptomatic**.

If symptoms are present, they are usually mild and include

- Anorexia
- nausea
- vomiting,
- Fever
- abdominal pain
- Jaundice

Acute HBV accounts for half of cases of fulminant hepatitis.

Complete resolution of symptoms occurs **within 3 to 4 months in more than 90 percent** of patients.

Any evidence for severe disease should prompt hospitalization.

- incessant nausea and vomiting
- Prolonged pt
- low serum albumin
- hypoglycemia
- high serum bilirubin
- central nervous system symptoms

Chronic HBV infection

is often asymptomatic but may be clinically suggested by persistent **anorexia, weight loss, fatigue, and hepatosplenomegaly.**

Extrahepatic manifestations may include **arthritis, generalized vasculitis, glomerulonephritis,**

pericarditis, myocarditis, transverse myelitis, and peripheral neuropathy.

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1. One risk factor for chronic disease is age at acquisition

- 90 percent in newborns,
- 50 percent in young children
- less than 10 percent in immunocompetent adults.

2.Another risk is an immunocompromised state such as those with

- HIVinfection,
- transplant recipients
- persons receiving chemotherapy

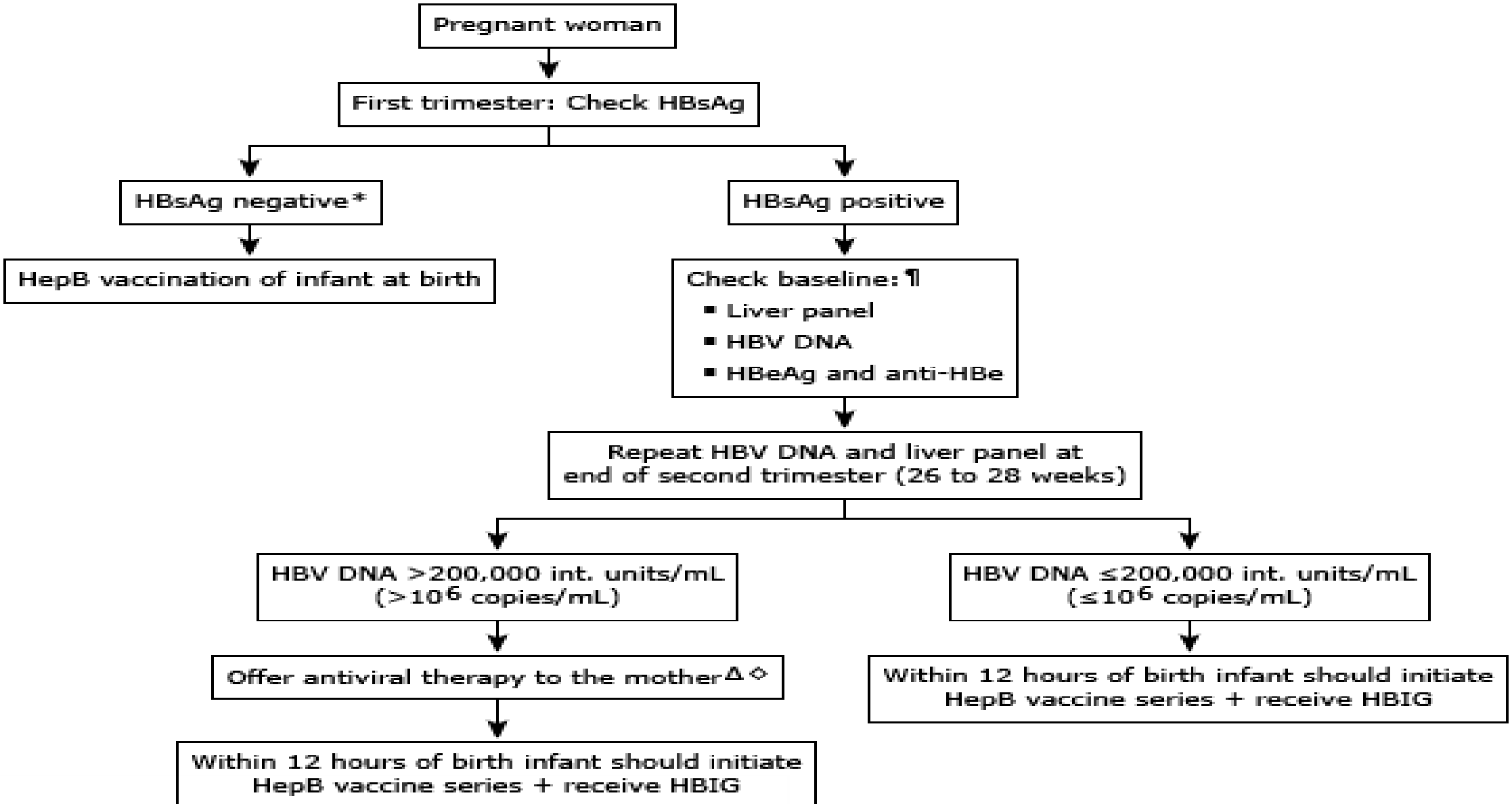
Chronically infected persons

- may be asymptomatic carriers with or without cirrhosis.

- The patients with evidence of high viral replication—HBV DNA
- with or without HBeAg, have the highest likelihood of developing
- cirrhosis and hepatocellular carcinoma.

Hepatitis B and pregnancy

Algorithm for hepatitis B virus during pregnancy



Maternal HBsAg status	Single-antigen vaccine*	
	Dose	Age
Positive ¶	1	Birth (≤12 hours)*
	HBIG Δ	Birth (≤12 hours)
	2	1 to 2 months*
	3	6 months ◇§
Unknown ¥	1	Birth (≤12 hours)*
	2	1 to 2 months*
	3	6 months ◇
Negative	1	Birth (≤24 hours)*
	2	1 to 2 months*
	3	6 to 18 months ◇

Acute hepatitis B virus (HBV) infection during pregnancy

- is usually mild and not associated with increased mortality or teratogenicity
- increased incidence of low birth weight and
- Transmission rates significantly increase if acute infection occurs at or near the time of delivery, with rates as high as 60 percent reported

- **serial monitoring** should be performed throughout pregnancy,

- and if the mother remains HBsAg positive or has detectable serum HBV DNA, the infant should receive hepatitis B immune globulin in addition to the first dose of the hepatitis B vaccine at birth.

- Antiviral therapy to reduce maternal viral load should also be considered if the mother has high serum HBV DNA levels near the time of delivery.

Treatment.

- Liver biochemical tests and prothrombin time should be monitored

- Antiviral therapy is usually unnecessary,

  except in women who have acute liver failure and protracted severe hepatitis

- Tenofovir disoproxil fumarate (TDF) (300 mg daily)
- lamivudine (100 mg daily) are both suitable options

- in this setting because both have been safely used during pregnancy, and the risk of developing resistance is low since the duration of treatment is expected to be short
- we prefer TDF as there is less risk of resistance

CHRONIC HEPATITIS B VIRUS INFECTION

- **Impact of pregnancy on the natural history of chronic HBV** — Pregnancy is generally well tolerated in women with chronic hepatitis B virus infection who do not have advanced liver disease.

- However, pregnancy is considered to be an immune tolerant state and is associated with high levels of adrenal corticosteroids that may modulate immune response.
- Thus, the following clinical manifestations may be seen in pregnant women with chronic HBV

Impact of pregnancy on the natural history of chronic HBV

- **Hepatic flares**
- **Progression of liver disease**
- **HBV DNA**

- **Hepatic flares** – including hepatic failure

- A flare of HBV infection is typically defined as a greater than two- to threefold rise in the ALT
- In a prospective study that followed 126 women during pregnancy and the postpartum period, 2 patients developed a flare during pregnancy whereas 27 (25 percent) developed a flare in the postpartum period
- During the postpartum period, flares may be related to immune reconstitution, a situation immunologically analogous to flares that have been described following the withdrawal of corticosteroids in nonpregnant patients with chronic HBV

- flares appear to be more common in women who are HBeAg positive

- **Progression of liver disease** – The immunologic, metabolic, and hemodynamic changes that occur during pregnancy have the potential to worsen or unmask underlying liver disease.
- In particular, serum albumin and hematocrit often decrease, while alkaline phosphatase and alpha fetoprotein increase.
- palmar erythema, lower extremity edema, and spider angiomata.

- **HBV DNA** – The immunologic changes associated with pregnancy also have the potential to increase HBV viremia; however, most studies have found that HBV DNA levels remain stable during pregnancy].

- **Effect of chronic HBV on pregnancy outcomes**

modest increase in **preterm birth rates**

- women **with cirrhosis are at significant risk for perinatal complications** and poor maternal and fetal outcomes,
  - including intrauterine growth restriction,
  - intrauterine infection, premature delivery, and
  - intrauterine fetal demise

- **Management considerations** Pregnant women with chronic HBV should be managed in conjunction with a hepatologist.

- **Women who are pregnant** — Some women with chronic HBV require antiviral therapy to prevent progression of liver disease

  eg, those with **immune-active hepatitis** while others can be observed.

Monitoring women without indications for antiviral therapy – Women who are

- obtain liver biochemical tests every three months during pregnancy and for up to six months postpartum.

- HBV DNA should be tested concurrently or when there is ALT elevation. In addition, the HBV DNA should be measured at 26 to 28 weeks to determine if antiviral therapy should be offered to reduce the risk of mother-to-child transmission.

Breast feeding

- Infants who received HBIG and the first dose of hepatitis B vaccine at birth can be breastfed.
- It is important that such infants complete the course of vaccination.

- The infection rate among infants born to HBsAg-positive mothers who do not receive any form of neonatal prophylaxis is as high as 90 percent.

However, administering HBIG and hepatitis B vaccine to infants at delivery can reduce transmission by at least 95 percent.

Hepatitis D

Also called *delta hepatitis*, this is a **defective RNA** virus that is a hybrid particle with an HBsAg coat and a **delta core**.

The virus must co-infect with hepatitis B either **simultaneously or secondarily**.

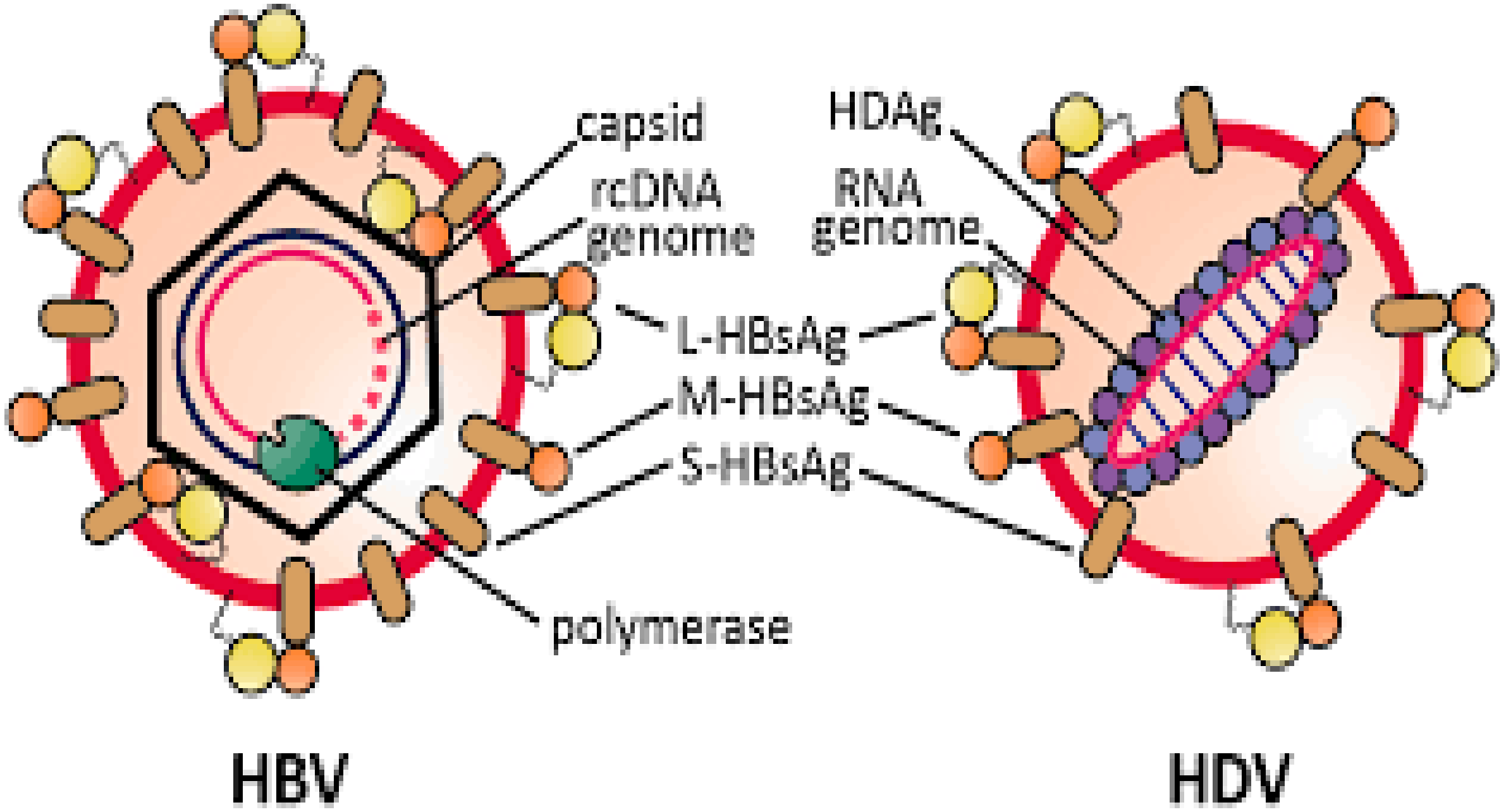
It **cannot persist in serum longer than hepatitis B virus**.

Transmission is similar to hepatitis B.

Chronic co-infection with B and D hepatitis is more severe and accelerated than with HBV alone, and up to **75 percent of affected patients develop cirrhosis.**

HDV infection is detected by the presence of **anti-HDV and HDV DNA**.

Neonatal transmission is unusual as **neonatal HBV vaccination** usually prevents **delta hepatitis**


capsid
rcDNA
genome
L-HBsAg
M-HBsAg
S-HBsAg
polymerase
HDAg
RNA
genome
HBV
HDV

Hepatitis C

This is a **single-stranded RNA virus.**

ThTransmission occurs **via blood and body fluids, although sexual transmission is inefficient.**

- As many as **80 to 90 percent of patients with acute HCV** will be **chronically infected**.

- Although **most remain asymptomatic**,

- **approximately 20 to 30 percent progress to cirrhosis** within 20 to 30 years.

increased fetal risks for

- low birthweight,
- NICU admission,
- preterm delivery
- mechanical ventilation
- **vertical transmission**

breast feeding, and delivery mode are not associated with mother-to-child transmission

There is currently **no licensed** **vaccine for HCV prevention**.

The **chronic HCV infection treatment** has traditionally included **alpha interferon alone or in combination** with **ribavirin.**

This regimen is **contraindicated in pregnancy** because of the **teratogenic potential of ribavirin in animals**

Hepatitis A

vaccination programs -decreased 95 percent

This RNA virus is transmitted by the fecal–oral route

their blood is also infectious.

Symptoms usually last less than 2 months, although 10 to 15 percent of patients may remain symptomatic or relapse for up to 6 months

Management of hepatitis A in **pregnant women** consists

- balanced diet and
- diminished physical activity.

Women with **less severe illness may be managed as outpatients.**

- **Both perinatal and maternal mortality rates**, however, are substantively increased in **resource-poor countries.**

- There is **no evidence** that hepatitis **A virus is teratogenic**, and **transmission to the fetus is negligible**.

- **Preterm birth** may **be increased**, **and neonatal cholestasis has been reported**

- **no cases of neonatal hepatitis A have been reported** secondary to breast feeding Preventatively,

- **vaccination during childhood -90percent effective**.

Hepatitis E

This **water-borne RNA virus** usually is **enterically transmitted** by contaminated water supplies.

Hepatitis E is probably the most common cause of acute It causes **epidemic outbreaks in third-world countries with substantial morbidity and mortality** rates.

Pregnant women have a **higher case-fatality** rate than nonpregnant individuals.

Fulminant hepatitis, although rare overall, is more common in pregnant women and contributes to the increased mortality rates

- Higher hepatitis E viral loads and increased cytokine secretion in pregnant compared with nonpregnant women may be factors in the development of fulminant hepatitis

- **Recombinant HEV vaccine** efficacy is reported to be > 90 percent, and preliminary data from inadvertently vaccinated pregnant women have shown no adverse maternal or fetal events.

- Even so, there is no currently available Food and Drug Administration (FDA)-approved vaccine

Thank you for your attention!