



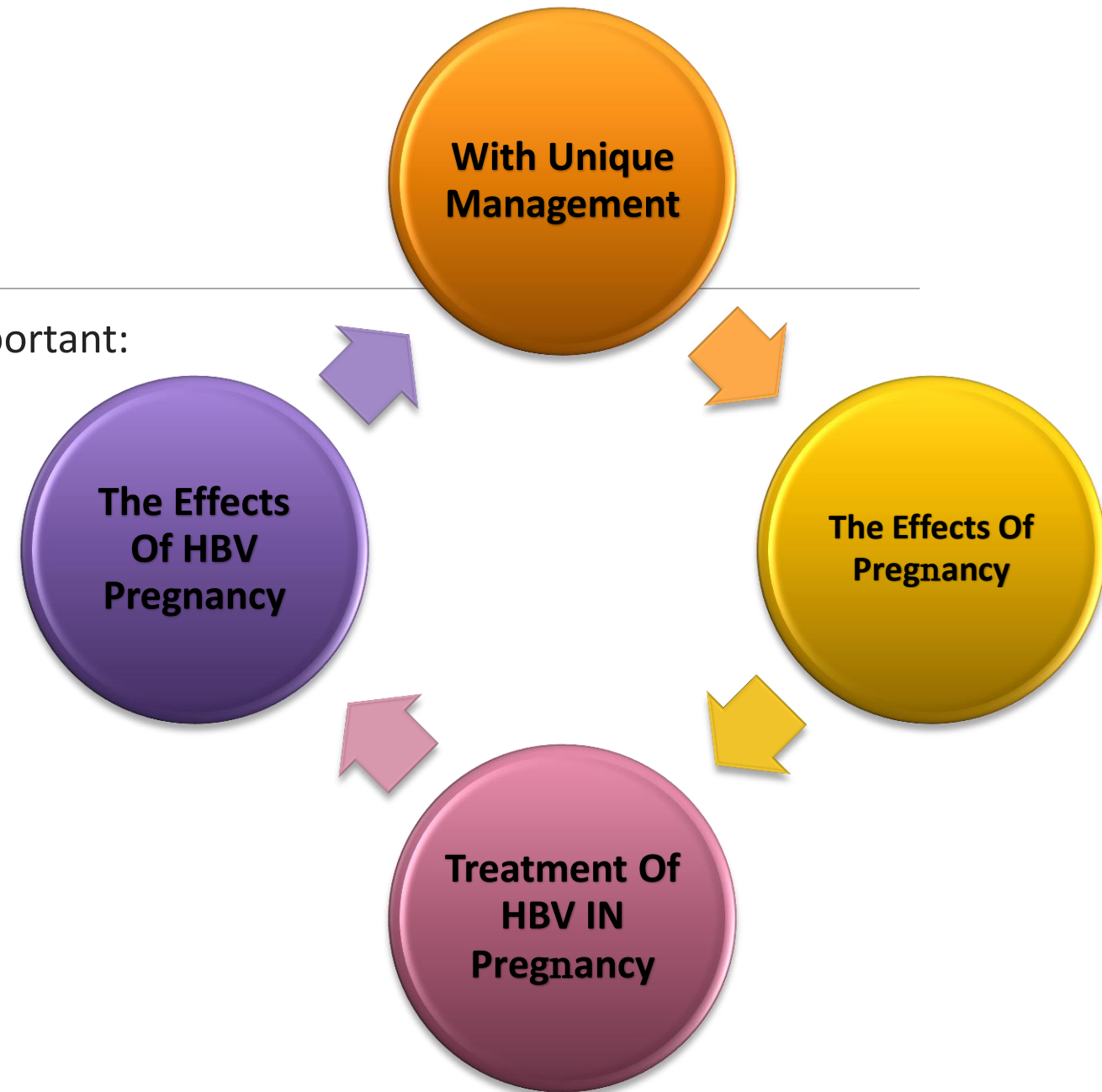
Preventive therapy during pregnancy in chronic HBV

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پائیز 1403

Introduction

Hepatitis B virus (HBV) during pregnancy is important:



Why Prevention Of Mother-to-child Transmission(MTCT) Is Important?

vertical transmission is responsible for approximately one-half of chronic infections worldwide.

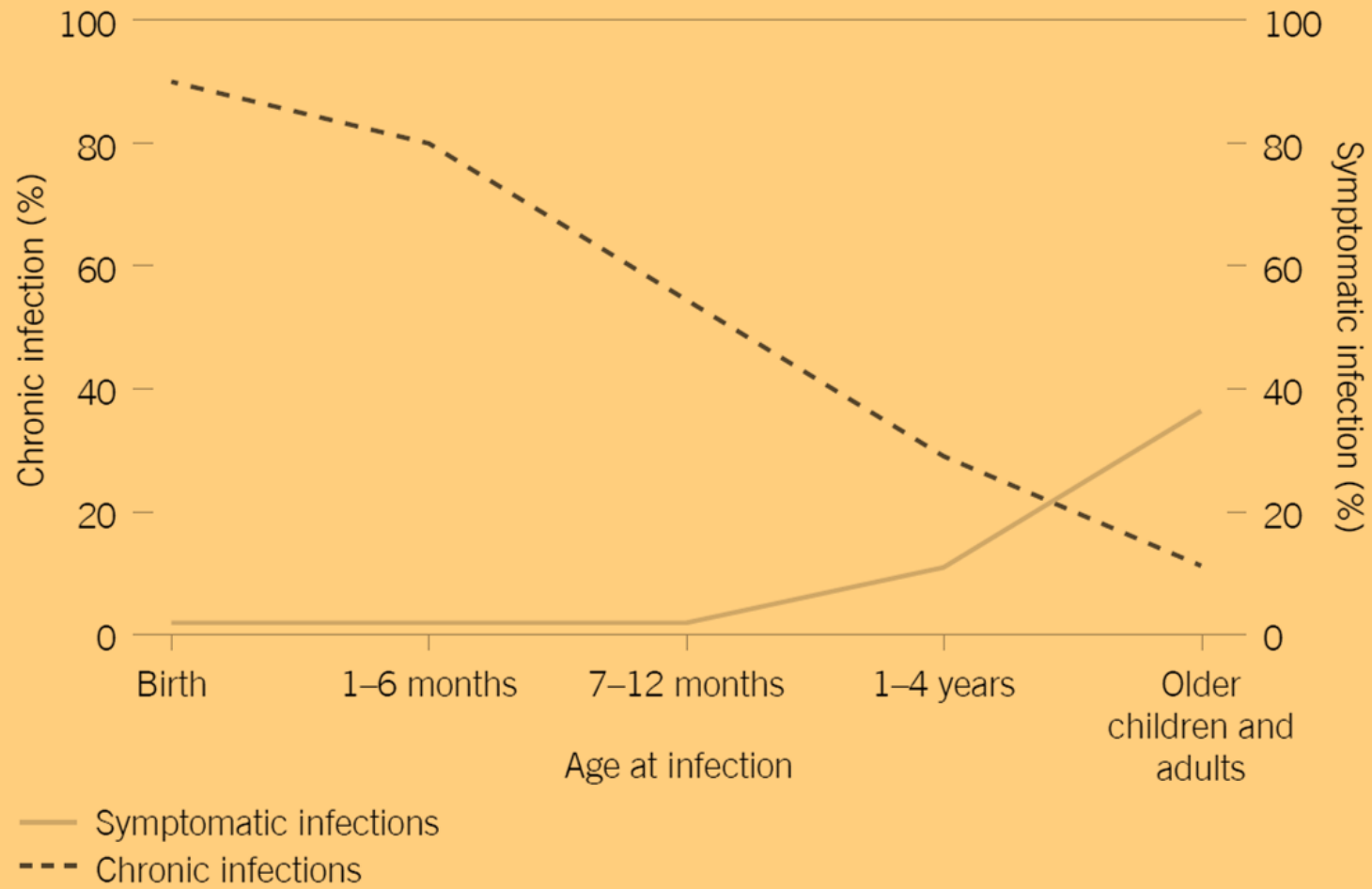
Transmission can occur in utero, at birth, or after birth.

The risk of developing chronic HBV infection is inversely proportional to the age at time of exposure

The risk is as high as 90 percent in those exposed at birth without vaccination

the risk is much lower (about 20 to 30 percent) in those exposed during childhood

FIGURE 2.1 Outcome of hepatitis B infection by age at infection



Chronic HBV & Pregnancy Outcomes

**Some Study: No
Differences Were
Seen.**

**Gestational Diabetes
Mellitus
Prematurity
Lower Birth Weight
Antepartum Hemorrhage**

Cirrhosis Outcomes

fetal outcome

intrauterine fetal demise.

intrauterine infection

premature delivery

intrauterine growth restriction

Maternal complication

gestational hypertension

placental abruption

Higher mortality rate

15 percent of mothers developed hepatic decompensation.

peripartum hemorrhage



Risk Factors For Transmission

The most important risk factors for mother-to-child transmission, despite proper administration of prophylaxis is



a positive HBeAg and/or a high HBV DNA level in the mother.

Transplacental transmission infrequent causes

Transmission due to obstetrical procedures are infrequent causes,
and Breastfeeding does not appear to pose a substantial risk.

the benefit of cesarean delivery in protecting against transmission has not been
clearly established.



The Clinical Manifestations In Chronic HBV:

Pregnancy is generally well tolerated in HBV who do not have advanced liver disease.

pregnancy is an immune-tolerant state and is associated with high levels of adrenal corticosteroids that may modulate immune sys.



Hepatic flares

A flare of HBV infection is typically defined as a **greater than two- to three** fold rise in the alanine aminotransferase (**ALT**) that is at least three to five times above the reference range. The immunological changes happen:

during pregnancy

the postpartum period



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.

progression to cirrhosis **is not expected** within such a short time for most patients, decompensation can occur in the setting of a severe flare.

the progression of liver in pregnancy is difficult .



HBV DNA

The immunologic changes associated with pregnancy



can increase HBV viremia

Management Considerations



Screening

HBsAg testing among pregnant women and adolescent girls (2)

All pregnant women should be tested for HIV, syphilis and hepatitis B surface antigen (HBsAg) at least once and as early as possible during their pregnancy.

(strong recommendation, low-certainty evidence)



Repeated HbsAg Late In Pregnancy (28 weeks)

high risk for HBV infection

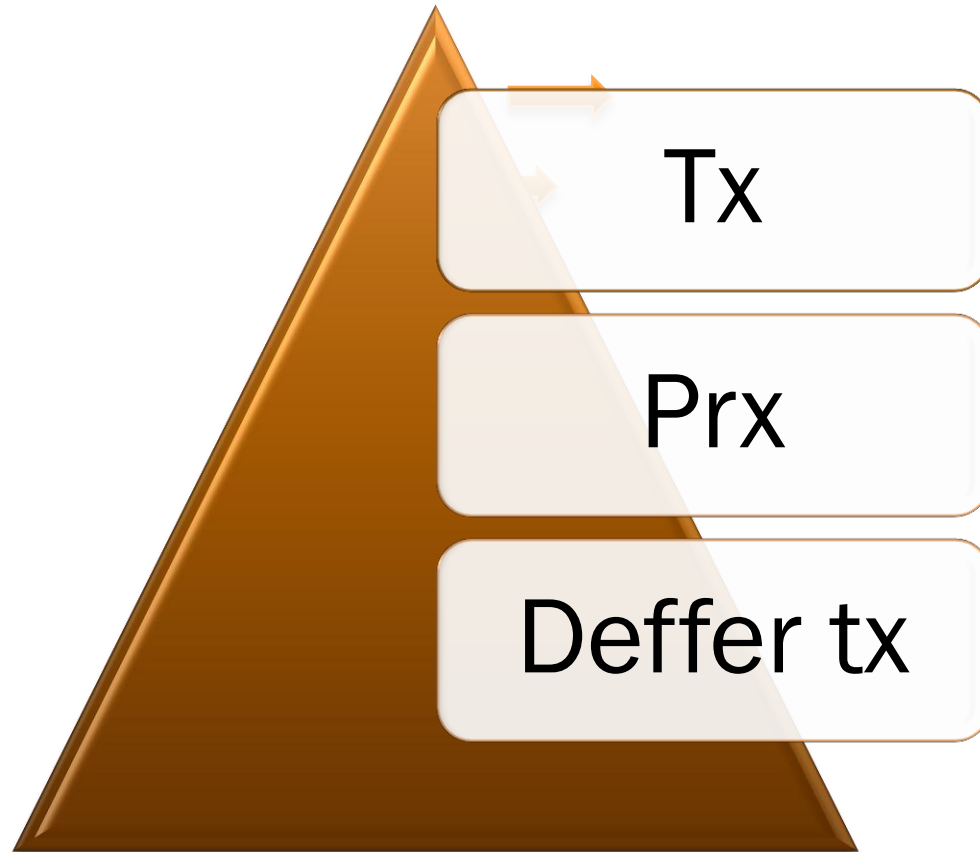
injection drug use

having a sexual partner or household contact with chronic HBV

having had more than one sex partner in the previous six months

having been evaluated or treated for a STI

Mothers with CHBV:



ALGORITHM FOR ASSESSMENT, TREATMENT AND MONITORING OF PEOPLE WITH CHRONIC HEPATITIS B INFECTION*

HBsAg positive

ASSESSMENT FOR TREATMENT ELIGIBILITY

1. Severity of liver disease using non-invasive tests (APRI or transient elastography)
2. ALT and HBV DNA level
3. Medical history: Screening for presence of coinfections (eg. HIV, HDV or HCV), comorbidities (eg. diabetes, steatotic liver disease) immune suppression (eg. long term steroids, transplant), extrahepatic manifestations (eg. glomerulonephritis, vasculitis), or family history of liver cancer or cirrhosis

GENERAL CARE MEASURES

1. Counselling on lifestyle eg. alcohol consumption, diet and physical activity
2. Preparation for starting treatment eg. adherence support, risk factors for renal dysfunction^h and baseline renal function (as indicated)
3. Preventive measures eg. HBsAg screening of family and household members and sexual contacts, with HBV vaccination of those negative

TREAT ALL ADULTS and ADOLESCENTS (aged ≥12 years^h) (including pregnant and non-pregnant women and girls of reproductive age) WITH:

1. SIGNIFICANT FIBROSIS (≥F2) or CIRRHOSIS (F4) (regardless of HBV DNA or ALT levels)
 - Clinical criteria for cirrhosis^h
 - Non-invasive tests: APRI >0.5 or transient elastography >7 kPa (adults)^h
2. HBV DNA >2000 IU/mL AND ALT level > ULN^h
3. PRESENCE OF any of following (regardless of APRI score, HBV DNA or ALT level)
 - Coinfection (eg. HIV, HDV, HCV)
 - Family history of liver cancer or cirrhosis
 - Immune suppression
 - Comorbidities (eg. diabetes, metabolic dysfunction-associated steatotic liver disease)
 - Extrahepatic manifestations (eg. glomerulonephritis or vasculitis)
4. PERSISTENTLY ABNORMAL ALT LEVELS ALONE^h

- ALT Persistently normal^h
- AND
- HBV DNA <2000 IU/mL
- AND
- Absence of coinfections, comorbidities, immune suppression, extrahepatic manifestations family history of liver cancer or cirrhosis

INITIATE ANTIVIRAL THERAPY AND MONITOR^h

- TDF or ETV
- TDF + 3TC or TDF + FTC (if no access to TDF monotherapy)
- ETV or TAF in persons with osteoporosis or impaired kidney function or in children and adolescents

DEFER TREATMENT AND MONITOR

- Every 6 months
- SURVEILLANCE FOR (AFP and ultrasound) (persons with cirrhosis or family history of liver cancer or cirrhosis)
- Every 12 months
- TREATMENT RESPONSE AND/OR DISEASE PROGRESSION^h
- Adherence at each visit, if on treatment
 - Non-invasive tests (APRI or transient elastography)
 - ALT and HBV DNA level
 - Monitoring of renal function (creatinine), as indicated



ALT
Persistently normal^{f,g}

AND

HBV DNA
<2000 IU/mL

AND

Absence of coinfections, comorbidities, immune suppression, extrahepatic manifestations family history of liver cancer or cirrhosis

DEFER TREATMENT AND MONITOR

*ALT: alanine aminotransferase, APRI: aspartate aminotransferase-to-platelet ratio index.

Monitoring of Mother who deferred tx

annually

- disease progression

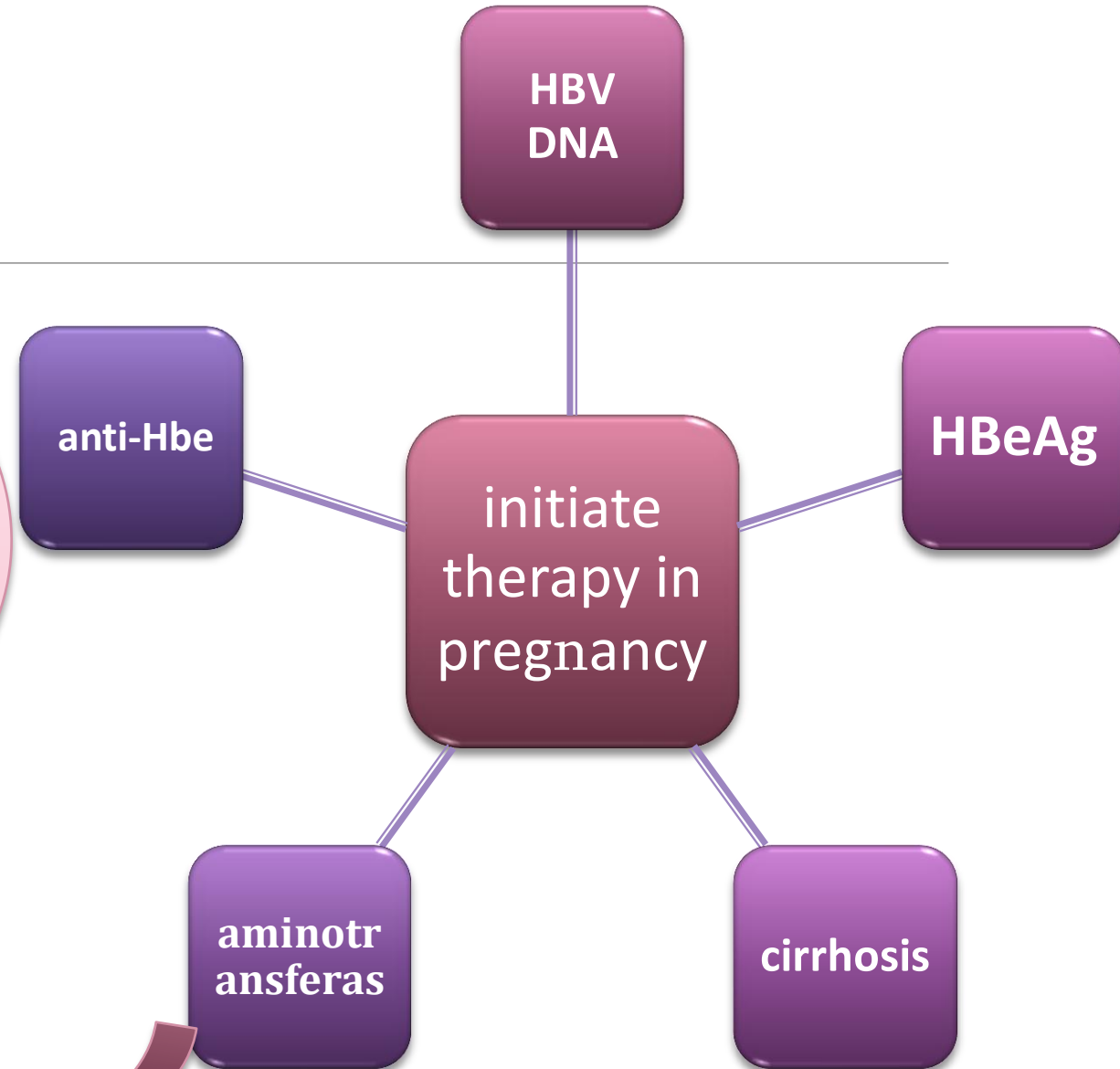
annually

- ALT

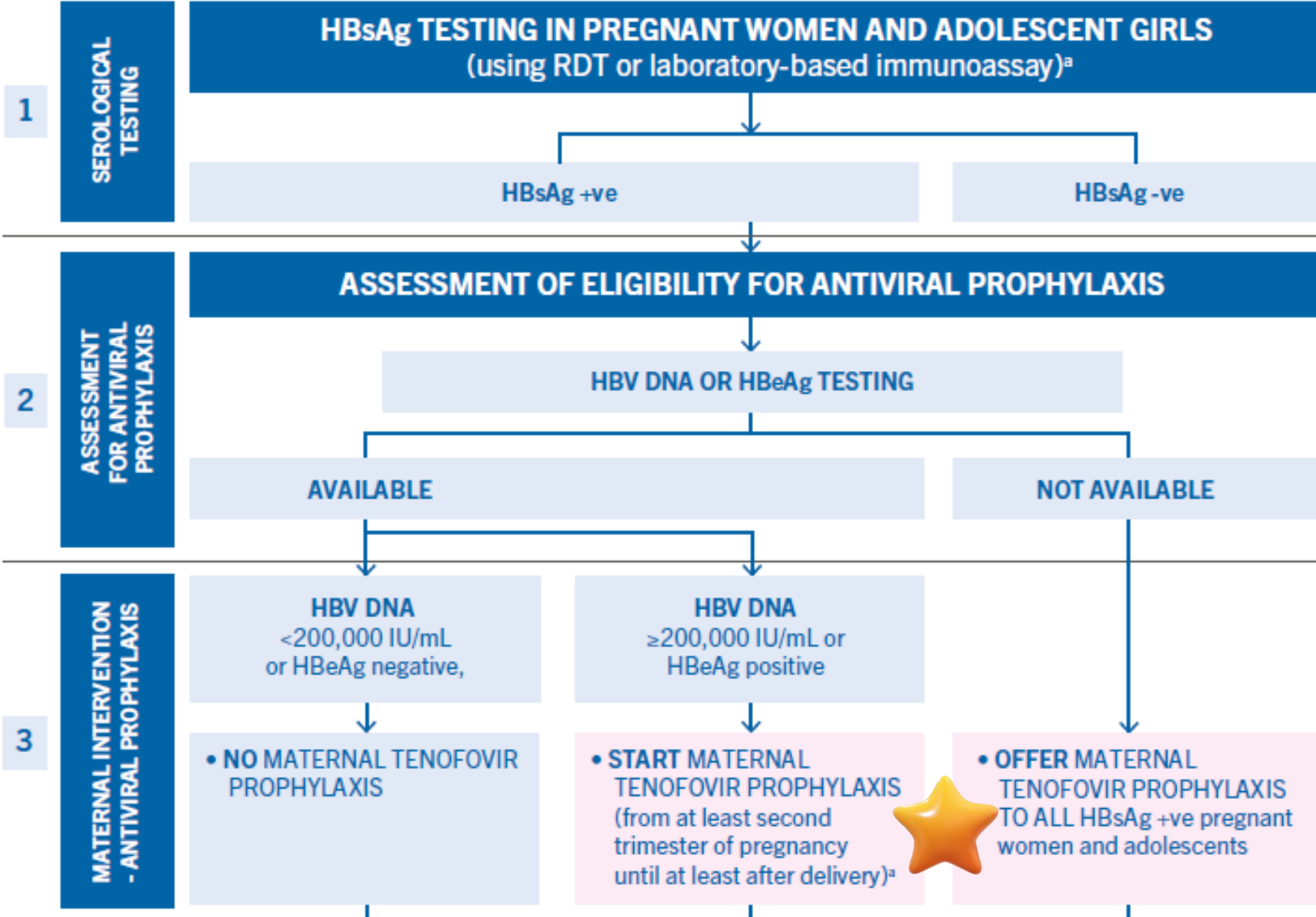
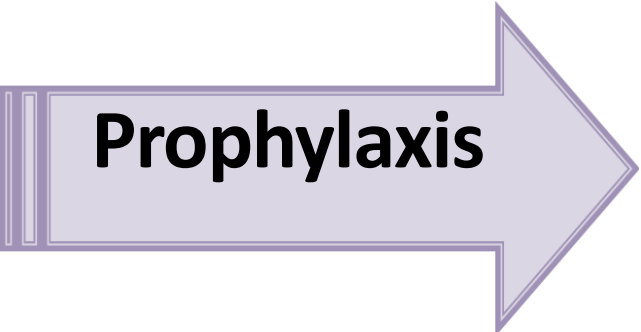
annually

- HBV DNA levels (when HBV DNA testing is available).

- **The ULN for ALT :<19 U/L for women and girls.**
- **Persistently normal or abnormal :two ALT values below or above the ULN at intervals during a 6- to 12-month period.**
- **Raised ALT may normalize in pregnancy and not a good for deciding about long-term treatment in pregnancy & should be reassessed after delivery.**



ALGORITHM ON USE OF ANTIVIRAL PROPHYLAXIS FOR PREVENTION OF MOTHER-TO-CHILD TRANSMISSION IN PREGNANT WOMEN AND ADOLESCENT GIRLS WITH CHB AND ASSESSMENT OF TREATMENT ELIGIBILITY FOR THEIR OWN HEALTH

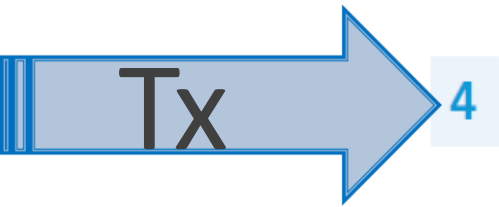


Prophylaxis

ELIGIBILITY FOR ANTIVIRAL PROPHYLAXIS among pregnant women and adolescent girls who do not meet treatment eligibility criteria

Note: For women of childbearing age planning additional pregnancies, TDF prophylaxis can also be maintained after delivery and during subsequent pregnancies or reproductive years, or for lifelong treatment.





MATERNAL INTERVENTION
LONG TERM ANTIVIRAL TREATMENT

ASSESSMENT OF ELIGIBILITY FOR LONG-TERM TREATMENT IN PREGNANT WOMEN AND ADOLESCENT GIRLS FOR THEIR OWN HEALTH

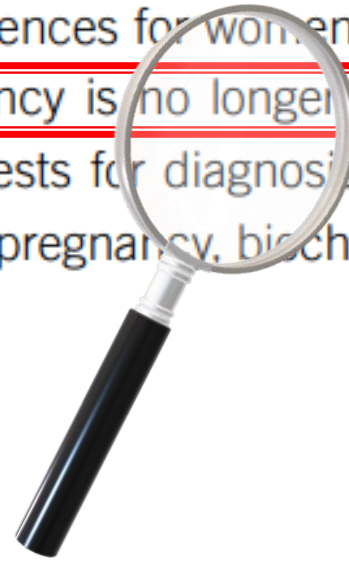
1. **SIGNIFICANT FIBROSIS (\geq F2) or CIRRHOSIS (F4)** (regardless of HBV DNA or ALT levels)
 - Clinical criteria for cirrhosis
 - Non-invasive tests: **APRI >0.5** or **transient elastography >7 kPa** (adults)
- OR

2. **HBV DNA > 2000 IU/mL AND ALT level > ULN**
- OR

3. **PRESENCE OF any of following**
Coinfection (eg. HIV, HDV, HCV); **Family history** of liver cancer or cirrhosis; **Immune suppression**;
Comorbidities (eg. diabetes, metabolic dysfunction-associated steatotic liver disease);
Extrahepatic manifestations (eg. glomerulonephritis or vasculitis);
- OR

4. **PERSISTENTLY ABNORMAL ALT LEVELS ALONE** (in absence of access to HBV DNA assay)

-
- **Accurate diagnostic strategies to identify pregnant women with advanced fibrosis, cirrhosis or HCC:** Although cirrhosis and HCC are uncommon during pregnancy, hepatitis B is a major cause, and both can have dramatic consequences for women and their babies (37). Since 2017, the use of FibroScan® during pregnancy is no longer contraindicated, but there is a lack of validated cut-offs of non-invasive tests for diagnosis of liver fibrosis for pregnant women. Because of haemodilution related to pregnancy, biochemical markers such as APRI may not be accurate.



INFANT
INTERVENTIONS



HEPATITIS B BIRTH DOSE VACCINATION OF THE
INFANT FOLLOWED BY 2 OR 3 DOSES OF VACCINE^b

HBIG (if available) is also offered mainly in high income settings for infants born to HBsAg positive mothers, especially with high HBV DNA.

Choice of agent

we prefer [tenofovir disoproxil fumarate](#) (TDF) rather than other antiviral agents since resistance to TDF is rare.

The FDA classified TDF as a Pregnancy Category B drug (while ETV is classified as Category C), meaning there is no adequate evidence of risk in humans.

A newer formulation of tenofovir, [tenofovir alafenamide](#) (TAF), is available.



Side effect

Bone abnormalities – TDF is associated with decreased bone mineral density, which usually stabilizes with continued use.

There were no statistically significant differences in lumbar spine bone mineral density measured at one year of age.

renal toxicity – There are **limited** data on the optimal assay to monitor TDF-related renal toxicity

Effects on growth – Studies mainly in the HIV population have not revealed an effect of TDF on birth **weight**, although there are conflicting results regarding the effect on **head circumference** and **growth (eg, length)**.

Breastfeeding

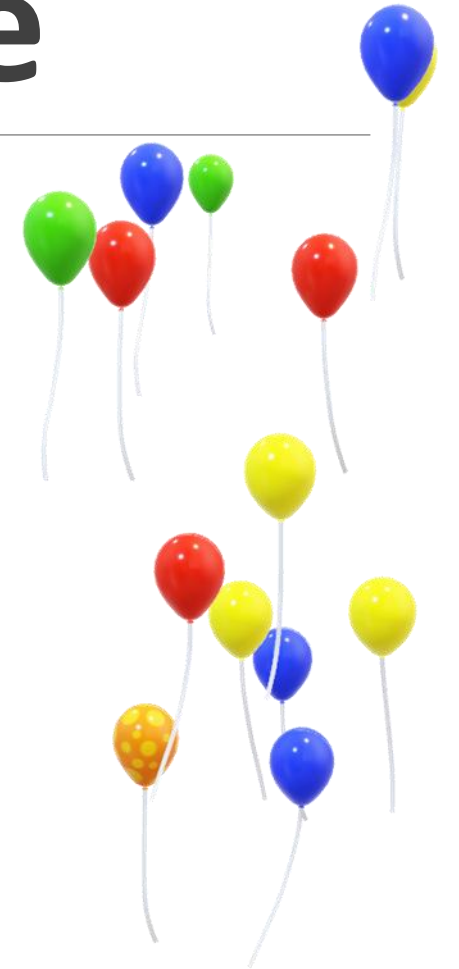
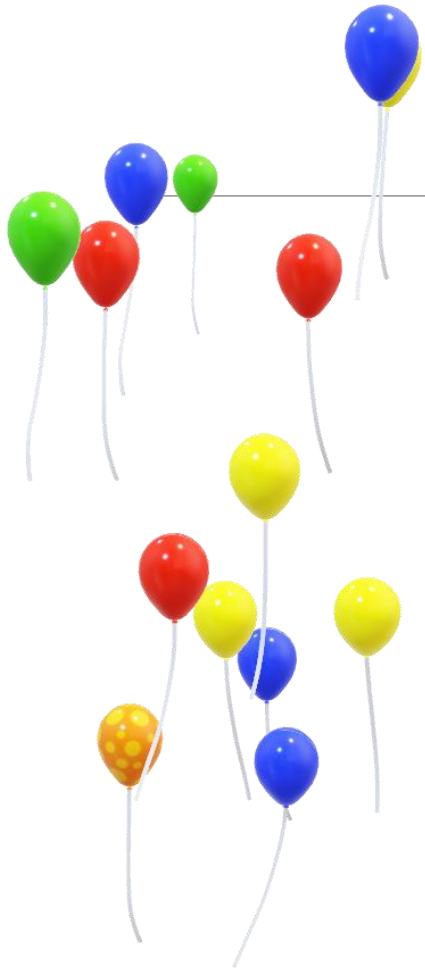
Infants who received HBIG and the first dose of hepatitis B vaccine at birth can be breastfed.

Mothers with chronic hepatitis B who are breastfeeding should also exercise **care to prevent bleeding from cracked nipples.**

HBsAg-positive mothers should **not participate in donating** breast milk

Breastfeeding is not contraindicated among women taking TDF, since TDF has very low concentrations in breast-milk and no evidence of toxicity among infants exposed to TDF through breastfeeding

Take Home Message



New recommendation

In settings where neither HBV DNA nor HBeAg testing^b is available, prophylaxis with tenofovir disoproxil fumarate (TDF)^c for all HBV-positive (HBsAg-positive) pregnant women may be considered (preferably from the second trimester of pregnancy until at least delivery or completion of the infant HBV vaccination series), to prevent MTCT of HBV.

(conditional recommendation, low-certainty evidence)

All interventions should be given in addition to at least three doses of hepatitis B vaccination for all infants, including a timely birth dose.



از توجه شما سپاسگزارم