Preventive therapy during pregnancy in chronic HBV

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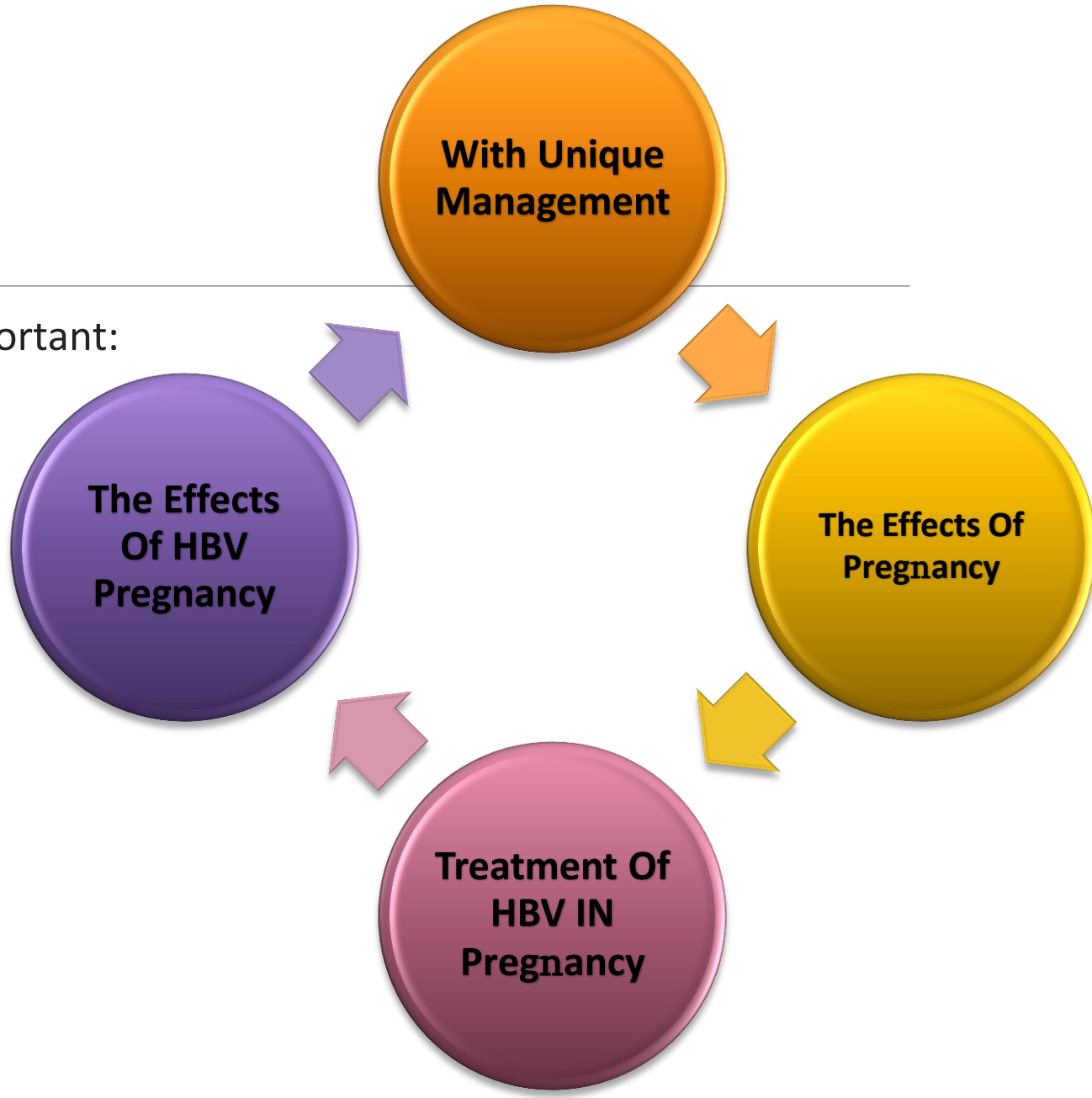
پائیز 1403

Introduction

Hepatitis B virus (HBV) during pregnancy is important:



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

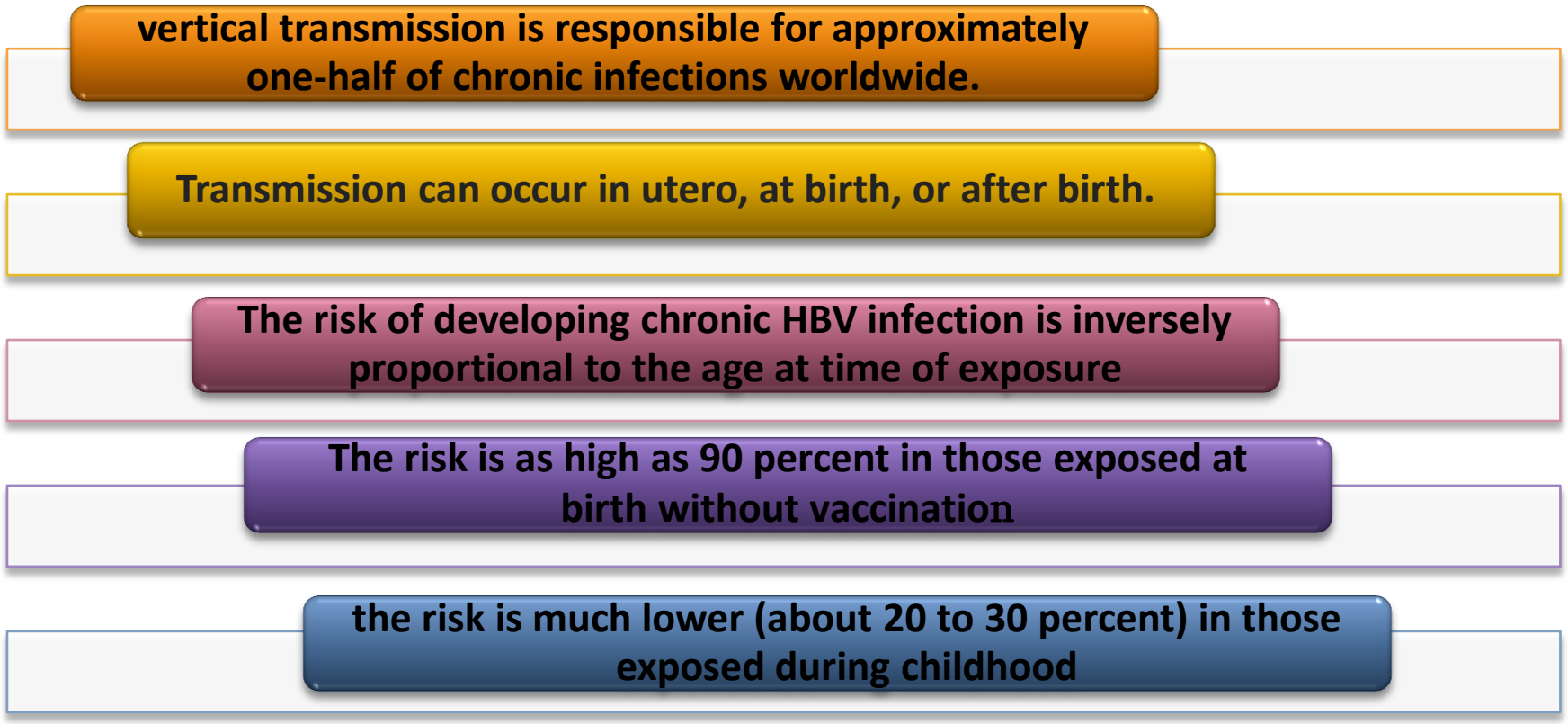
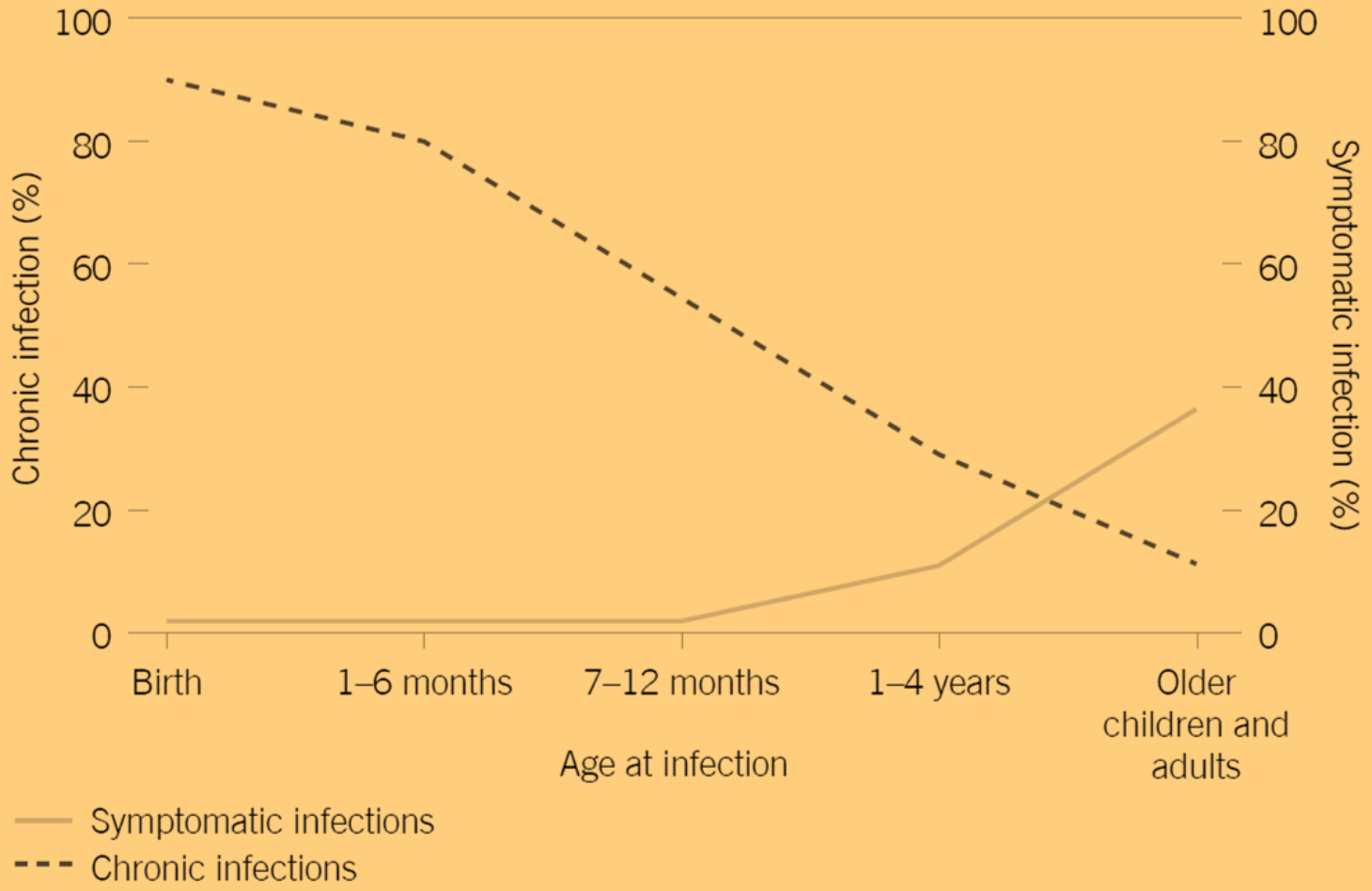
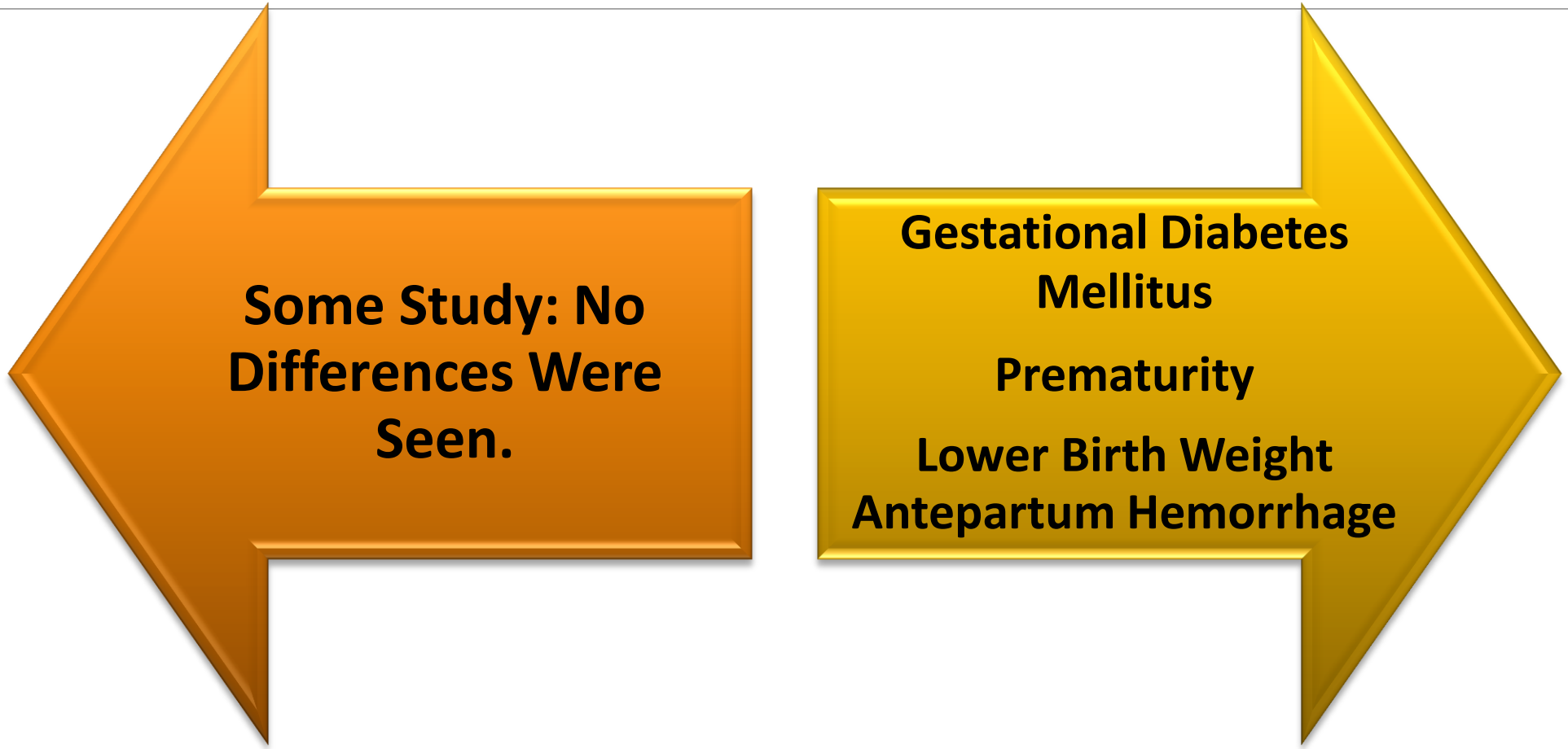


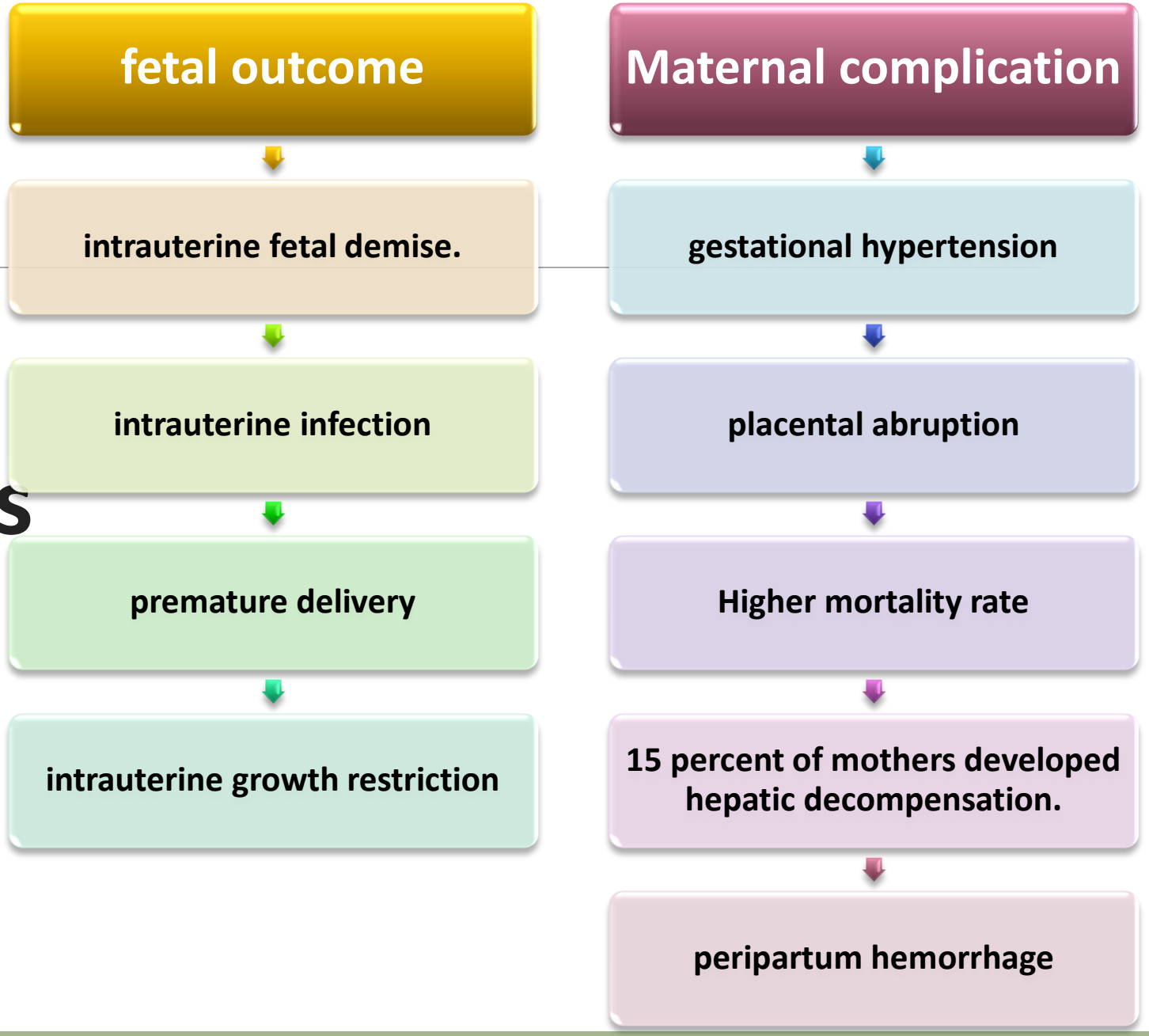
FIGURE 2.1 **Outcome of hepatitis B infection by age at infection**



Chronic HBV & Pregnancy Outcomes



Cirrhosis Outcomes



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

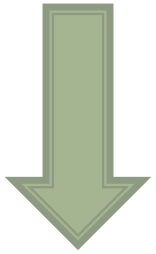
The immunologic, metabolic, and hemodynamic changes that occur during pregnancy have the potential to worsen or unmask underlying liver disease.

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

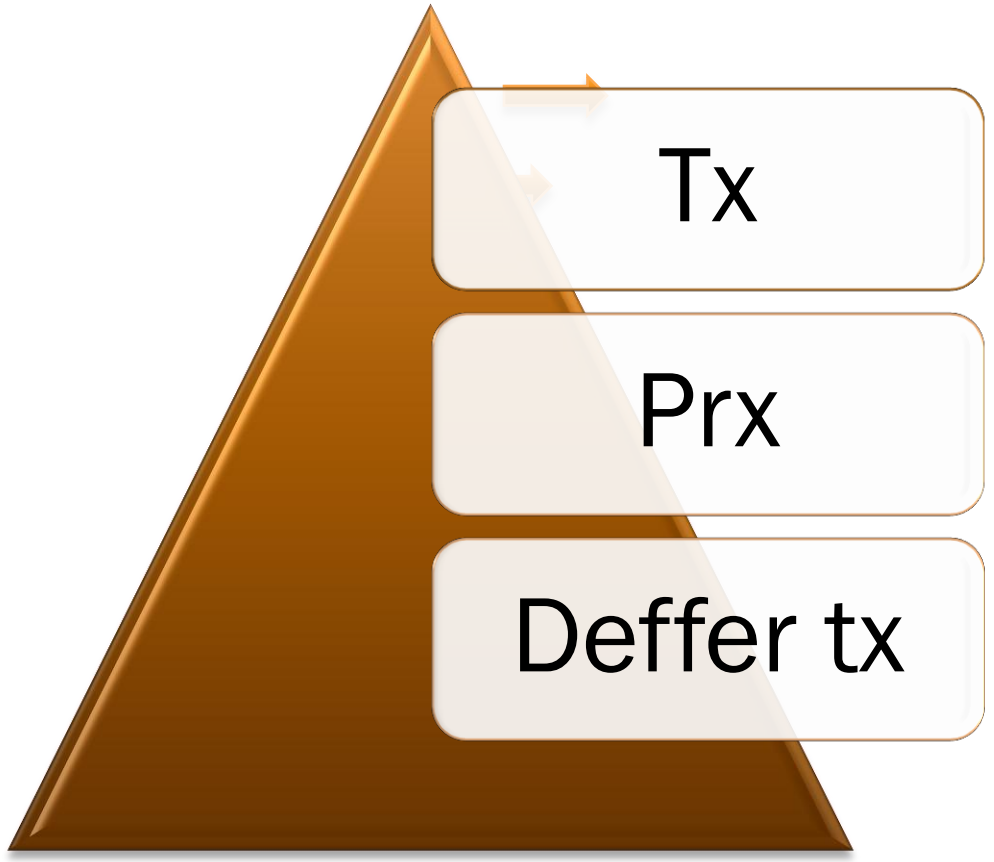
injection drug use

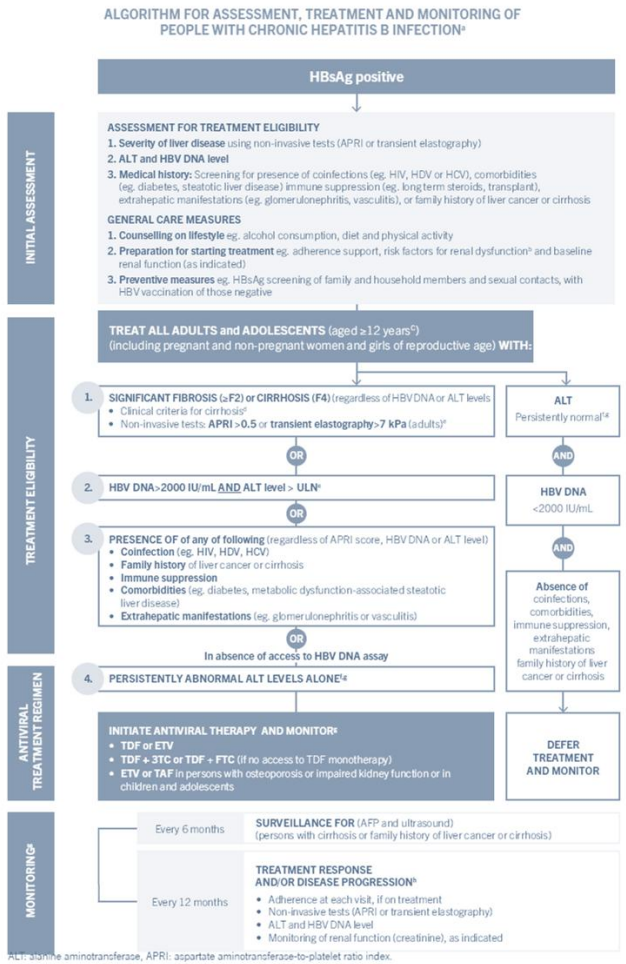
having a sexual partner or household contact with chronic HBV

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

having been evaluated or treated for a STI

Mothers with CHBV:





Defer TX

ALT
Persistently normal[f,g]

AND

HBV DNA
<2000 IU/mL

AND

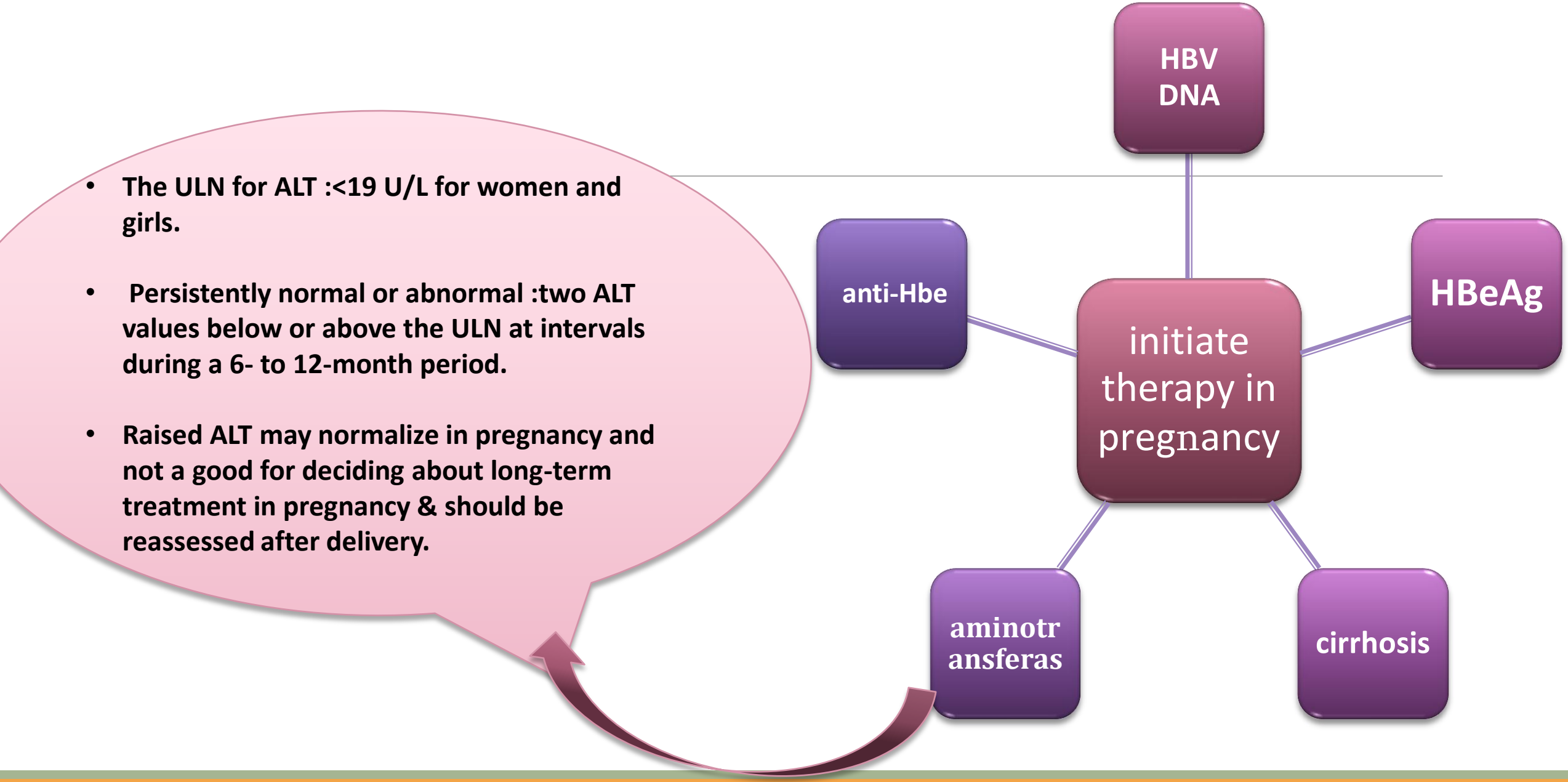
Absence of
coinfections,
comorbidities,
immune suppression,
extrahepatic
manifestations
family history of liver
cancer or cirrhosis

DEFER TREATMENT AND MONITOR

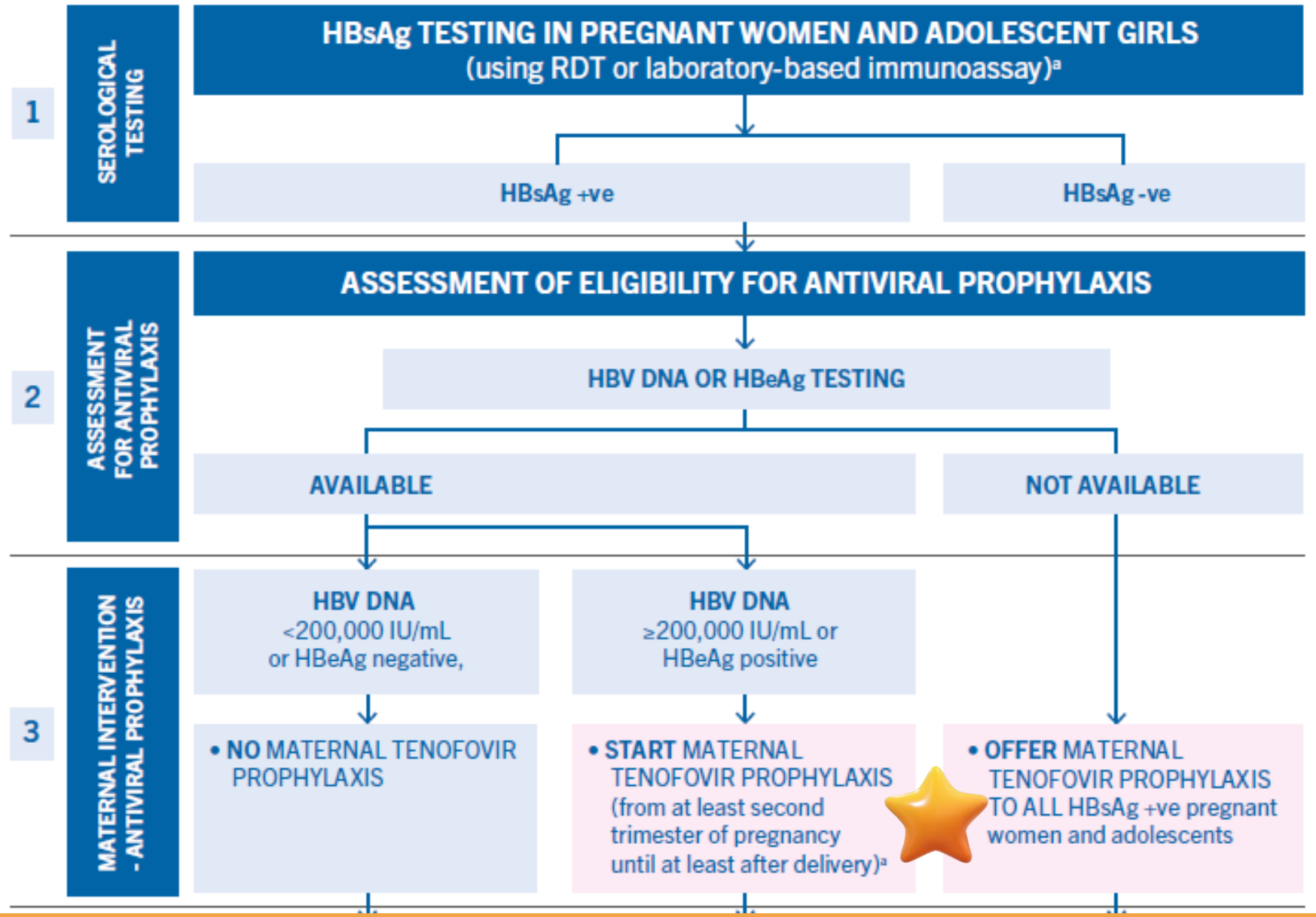
Monitoring of Mother who deferred tx

- 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.**



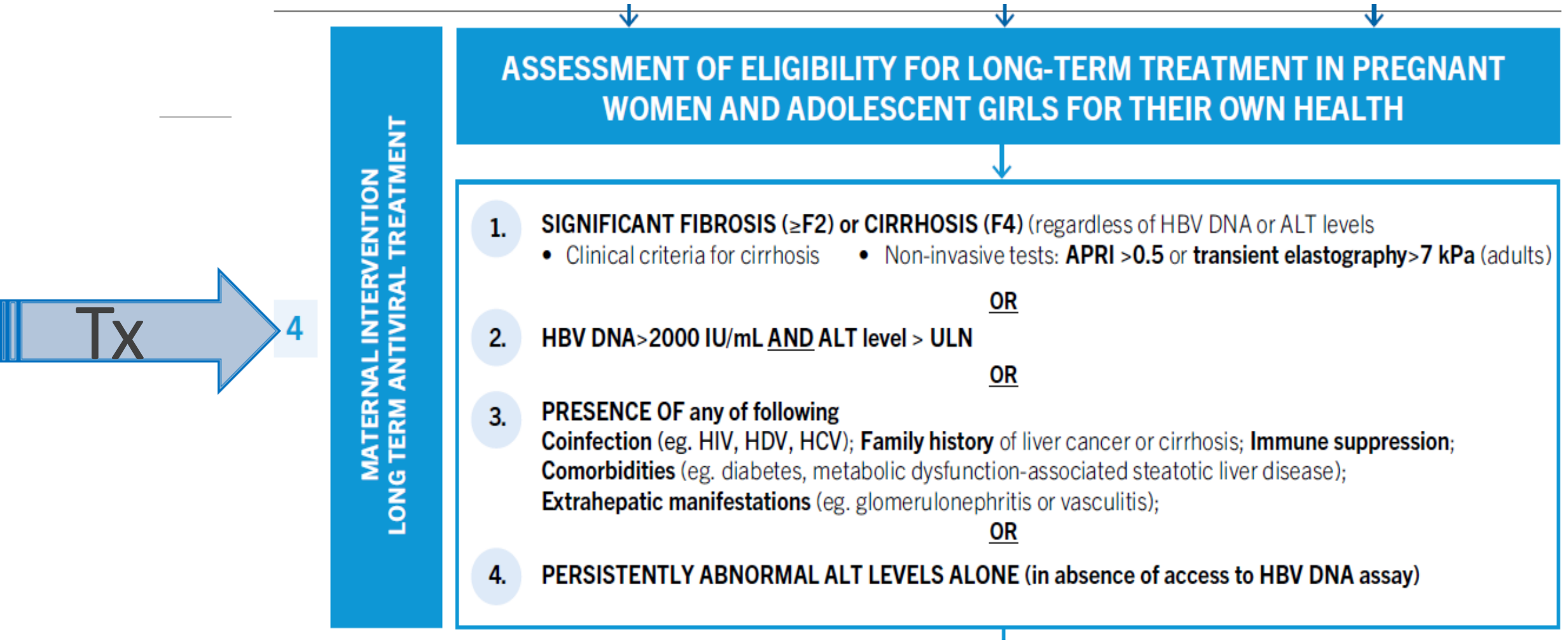
Prophylaxis



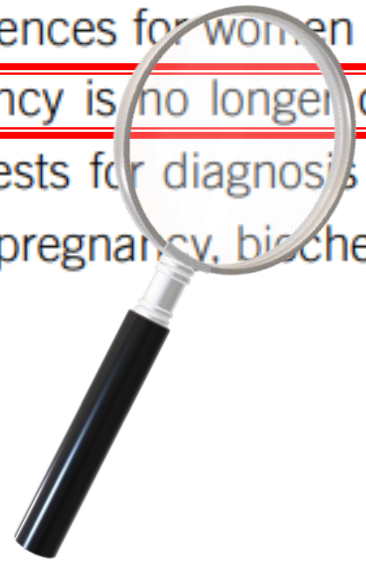
Prophylaxis

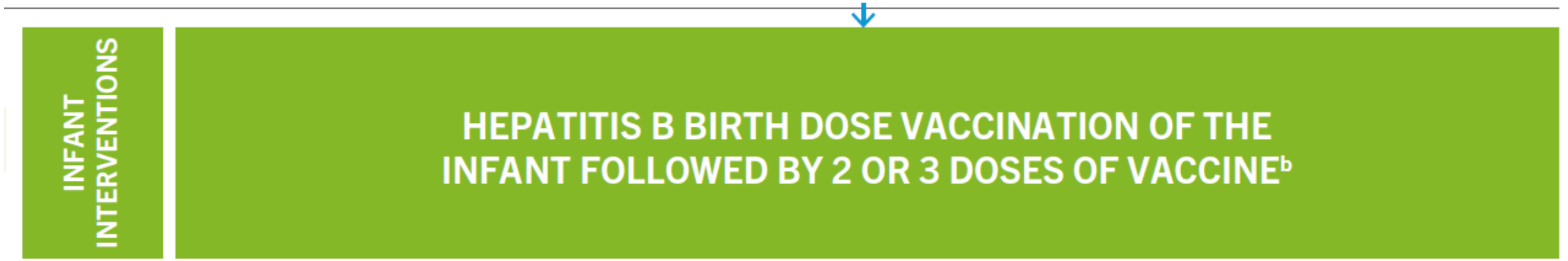
ELIGIBILITY FOR ANTIVIRAL PROPHYLAXIS among pregnant women and adolescent girls who do not meet treatment eligibility criteria

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.


Tx
4
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 (≥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.





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