Overview of Hepatitis B

Southeast AIDS Education and Training Center
National Wednesday webcast

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Objectives

- Describe the natural history of HBV infection
- Define the populations in the U.S. who should be tested for chronic HBV infection
- Be familiar with treatment and monitoring for HIV-HBV coinfection
- Understand when to initiate therapy in HBV monoinfection

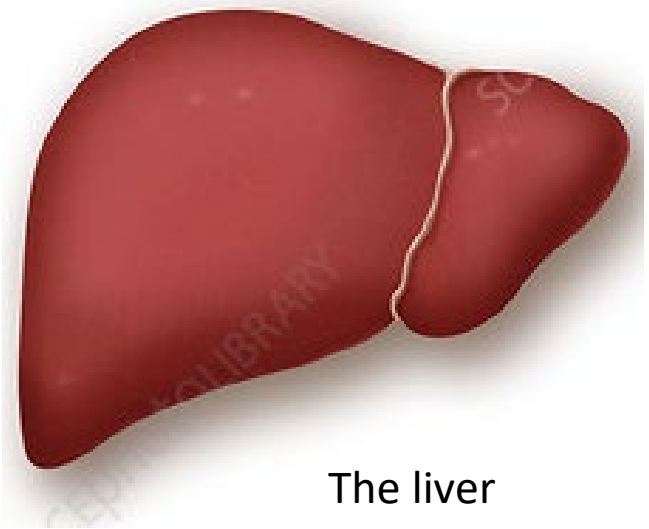
Hepatitis B virus can be transmitted in several ways

Percutaneous
(IV drugs, unsterile injections, needle stick injury, blood transfusions)

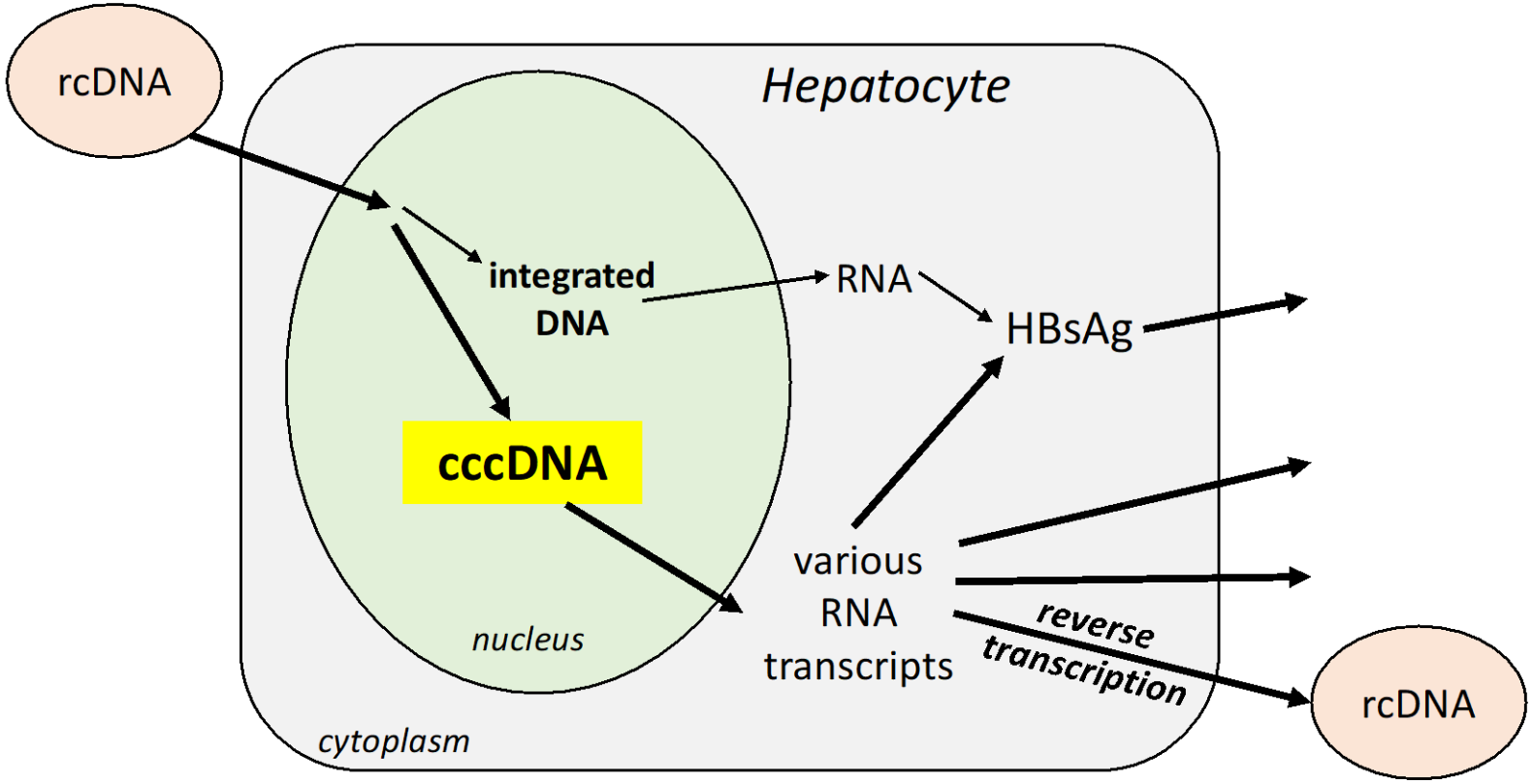
Mother-to-child
(via perinatal transmission – at the time of birth)

Sexual transmission

Early childhood horizontal transmission
(children <5y exposed to trace particles of blood)

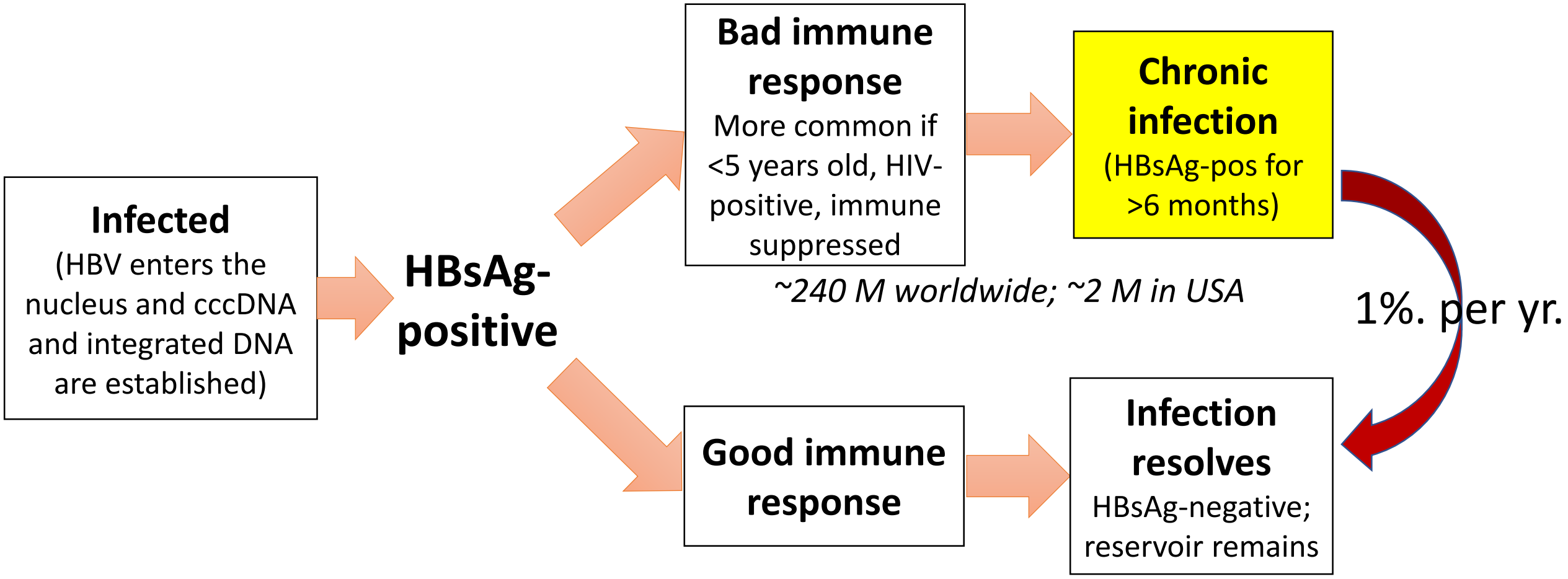


The liver



- Several different things can be measured in the blood related to Hepatitis B
- The most important test is **hepatitis B surface antigen (HBsAg),** which when detected in blood indicates '**current infection'.**

What happens after infection?



Worldwide 2 billion people have been infected

The infection resolves naturally ~90% of the time

The Hepatitis B cure agenda

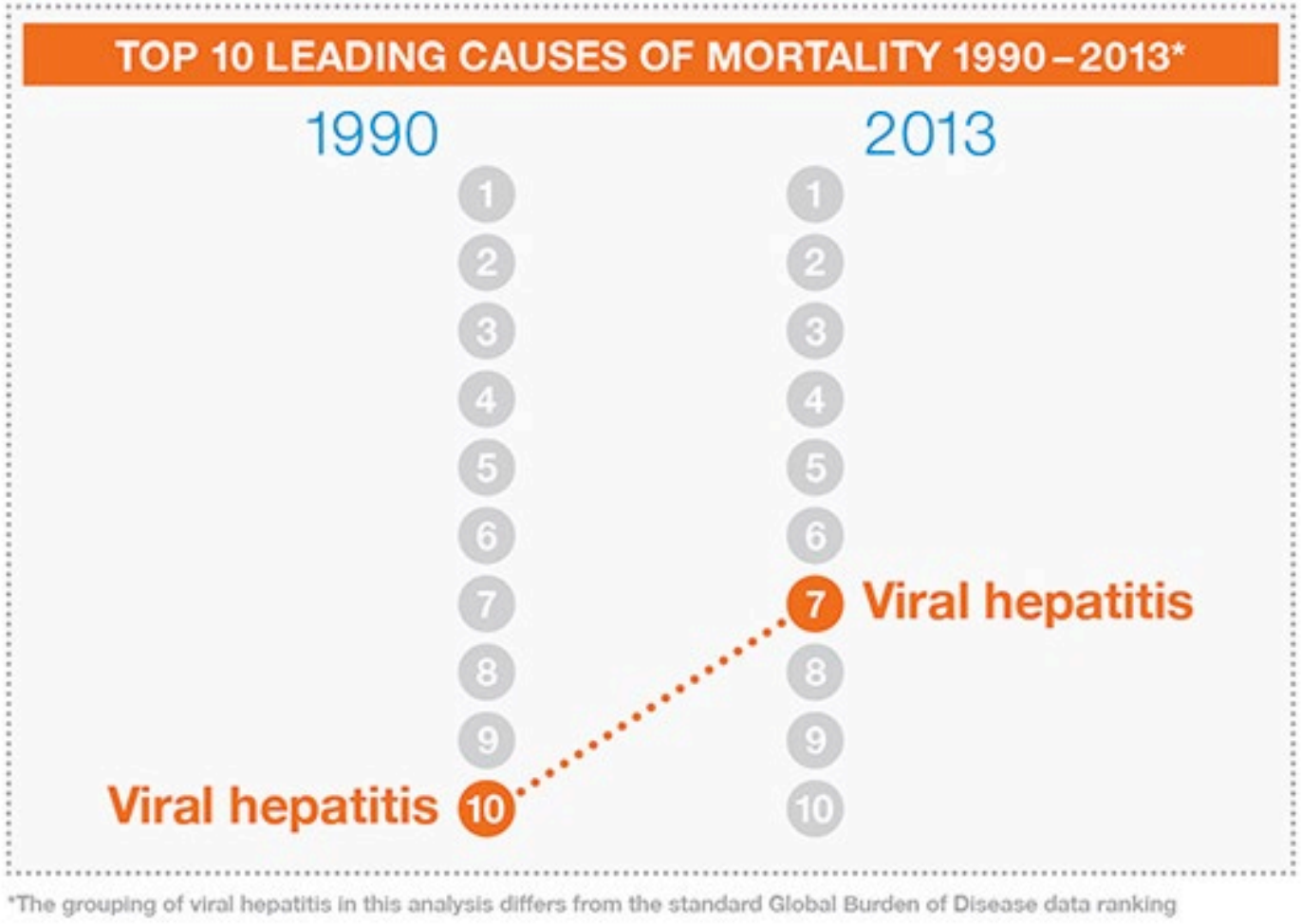
- In the past 10-15 years, understanding of the hepatitis C virus and host immune responses led to the development of drugs that are now able to cure >95% of hepatitis C infections
- Currently there is a growing movement to better understand why and how the 10% fail to resolve the infection and to develop drugs that lead to hepatitis B ‘functional cure’
- Two types of drugs are in development:
  - **Direct acting antiviral drugs** to clear the HBV reservoir in the liver
  - **Immune modulators** to boost the patients immune system to resolve the infection

Poll question #1

Which of the following does not put a person at higher risk to develop chronic infection after being infected with Hepatitis B virus?

a. Cancer chemotherapy
b. HIV infection
c. Alcohol use
d. Age <5 years old
e. Male sex

Why is HBV infection important?

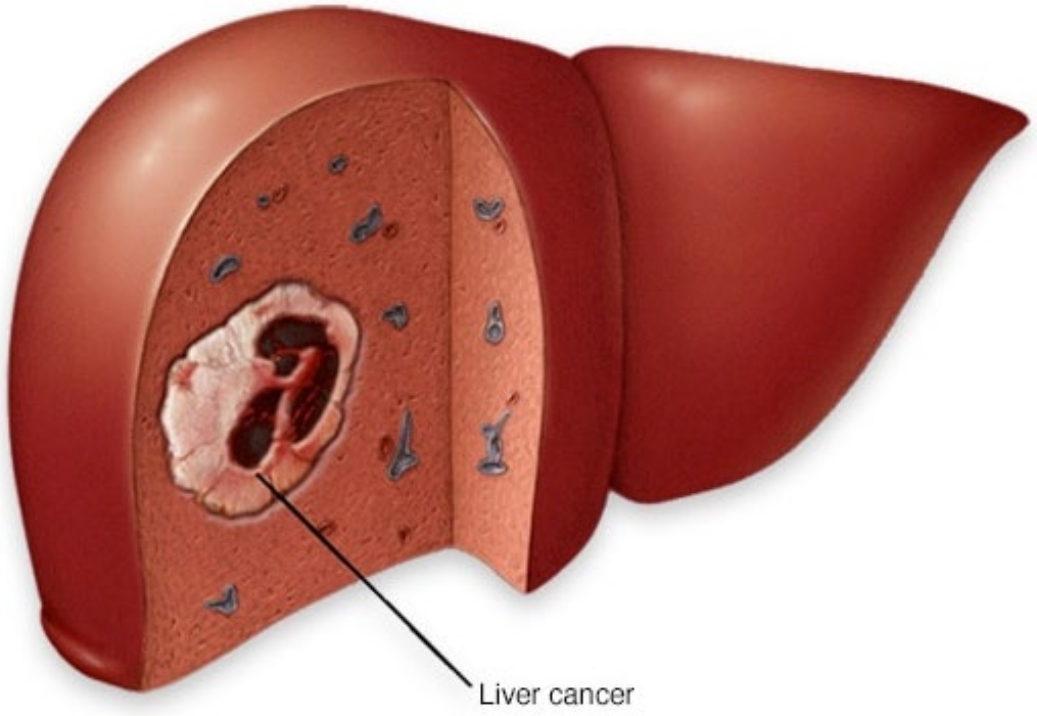


HBV-related mortality during chronic infection =

- Cirrhosis
- Hepatocellular carcinoma

19 million hepatitis-related deaths are anticipated worldwide between 2015-2020

Hepatocellular carcinoma (HCC; liver cancer)



- **42,030** cases will be diagnosed in the U.S. in 2019
- 5-year survival is only 26%
- 3 times as common in men (versus women)
- Incidence has tripled since 1980
- Causes: **hepatitis B**, hepatitis C, alcohol, fatty liver
- The hepatitis B vaccine was the 1st cancer preventing vaccine!

American Cancer Society; www.cancer.gov; Mayo Foundation for Medical Education and Research

	Who to routinely test for hepatitis B surface antigen
1	Born in regions where population prevalence of HBsAg-positivity is intermediate (>2%)
2	US-born persons not vaccinated as infants whose parents were born in regions where HBsAg positivity is high (>8%)
3	Injection drug users
4	Men who have sex with men
5	Persons needing immunosuppressive therapy
6	**Patients initiating hepatitis C DAA therapy**

75% of chronic HBV infections in the US are 'imported' from other countries

Centers for Disease Control and Prevention; American Association for the Study of the Liver

	Who to routinely test for hepatitis B surface antigen
6	Persons with elevated ALT/AST of unknown etiology
7	Donors of blood, plasma, organs, tissues, or semen
8	Hemodialysis patients
9	All pregnant women
10	Infants born to HBsAg-positive mothers
11	Household, needle-sharing, or sex contacts of persons known to be HBsAg-positive
12	Persons who are the sources of blood or body fluids resulting in an exposure that might require post-exposure prophylaxis
13	HIV-positive persons

Centers for Disease Control and Prevention; American Association for the Study of the Liver

Who to test for hepatitis B core antibodies (anti-HBc)

- This test becomes positive with infection (not vaccine) and stays positive lifelong.
- The following groups who could experience reactivation should be tested for anti-HBc:
  - Persons living with HIV
  - Persons about to be treated for Hepatitis C infection
  - Persons about to be given immunosuppressive therapy (for autoimmune disease, cancer, etc.)

HIV-HBV coinfection: overview

- Affects 5-10% of persons living with HIV in the United States
- Compared to living with HBV alone, in HIV-HBV coinfection:
  - Higher HBV viral loads
  - Higher HBsAg levels
  - Higher risk of liver cancer and cirrhosis
- Patients with both HIV and HBV have higher risk of liver-related death compared to HIV alone or HBV alone.

HIV-HBV co-infection: testing

- Persons living with HIV should be tested for HBsAg, hepatitis B core antibody (anti-HBc total), and hepatitis B surface antibody (anti-HBs).
- **HBsAg** is used to guide the choice of ART
- **Anti-HBc** (‘core antibodies’) tells you whether the person has a prior infection that could reactivate
- **Anti-HBs** (‘surface antibodies’) tells you whether to vaccinate the person

U.S. Department of Health and Human Services; https://aidsinfo.nih.gov/guidelines

HBsAg-positive persons living with HIV should be on an ART regimen that covers HBV

- ART regimens should include combination **tenofovir DF (TDF) + emtricitabine** or **tenofovir alafenamide (TAF) + emtricitabine**.
- Both TDF and TAF are effective, but if moderate kidney impairment (eGFR 30-50), TAF is preferred over TDF
- At eGFR <30, renally-adjusted entecavir should be used together with ART regimen
- If CrCl is <30 ml/min and improvement in kidney function is not expected, renally-adjusted TDF is okay.

U.S. Department of Health and Human Services; https://aidsinfo.nih.gov/guidelines

HIV-HBV coinfection: monitoring ART

- HBV goals of ART: reduce HBV viral load, achieve or maintain normal liver function tests (ALT), minimize risk of liver cancer (HCC).
- Monitor ALT- every 3 months for first 6 months, then every 6-12 months
- HBV DNA (viral load)- every 6 months until HBV viral suppression is obtained, then yearly
- It usually takes longer to suppress HBV than HIV
- Recheck the HBsAg each year to see if infection has resolved

HBV IRIS (immune reconstitution inflammatory syndrome)

- “Hepatitis flares,” may occur shortly (1-6 months) after ART initiation in HIV-HBV coinfection, especially in patients with low nadir CD4 counts.
- Flare is defined as acute increase (2-5x) in ALT level
- Often asymptomatic; sometimes patients may have non-specific fatigue, anorexia. Rarely it can lead to liver failure.
- DDx includes liver injury from ART, other drugs, exposures (alcohol)
- Consult a liver specialist if jaundice or liver synthetic impairment (increased INR, low albumin)

Poll question #2

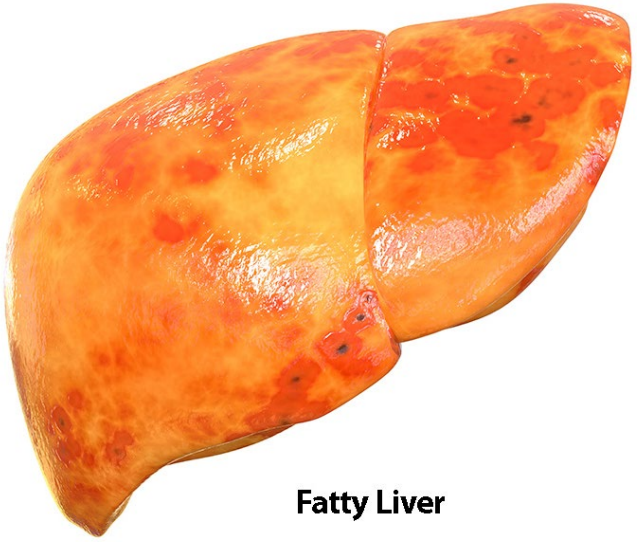
Which of the following ART regimens is **not appropriate** for a person living with HIV and chronic HBV coinfection (HBsAg-positive)?

a. Triumeq (DTG/ABC/3TC or dolutegravir/abacavir/lamivudine)
b. Biktarvy (BIC/FTC/TAF or bictegravir/emtricitabine/tenofovir alafenamide)
c. Stribild (EVG/COBI/FTC/TDF or elvitegravir/cobicistat/emtricitabine/tenofovir DF)
d. Delstrigo (DOR/3TC/TDF or doravirine/lamivudine/tenofovir DF)
e. Atripla (EFV/FTC/TDF or efavirenz/emtricitabine/tenofovir DF)

Screening for HCC in chronic HBV

- In chronic HBV infection, HCC screening is recommended in certain groups, including:
  - Aged >40 years, cirrhosis, HIV-coinfection
- Screening = abdominal ultrasound every 6 months
- Alpha fetoprotein (AFP) is an alternative if low access to ultrasound
- The goal of screening is to identify HCC early to increase survival

Preventing other liver diseases



Fatty Liver

- Hepatitis A vaccination
- Avoid or reduce alcohol consumption
- Optimize body weight, treatment of diabetes and dyslipidemia to prevent metabolic syndrome and fatty liver

When to initiate therapy in HBV monoinfection

Therapies are initiated in specific circumstances when the patient is at **elevated risk of HCC or cirrhosis** and the data suggest the benefits outweigh the risks.

	Cirrhosis	HBeAg status	ALT level	HBV viral load (IU/ml)
Adults	No	HBeAg-positive	ALT >=2 ULN	>=20,000
	No	HBeAg-negative	ALT >=2 ULN	>=2,000
	Yes	Any	Any	>20
Pregnant woman	No	Any	Any	>=200,000

Longitudinal follow-up often required to decide when and whether to treat HBV monoinfection

- The disease is dynamic
- 30-50% are inactive carriers with low ALT, low HBV viral load, no cirrhosis, and a very very low risk of liver cancer -> they do not need antiviral therapy
- At the first visit, 40% of patients have ‘indeterminate’ phenotype, meaning viral load is high but ALT is low or vice versa.
- Unlike HIV, where we start ART as soon as possible, in HBV monoinfection there is often a period of observation.

What to initiate in HBV monoinfection

- Preferred options are the nucleos(t)ide analogs:
  - Tenofovir DF
  - Tenofovir alafenamide
  - Entecavir
- **Only a single drug is required**
- Interferon alpha is recommended but rarely used because of side effects

AASLD 2018 guidelines

Duration of therapy in HBV monoinfection

- In HIV-HBV coinfection, even if the infection resolves (i.e., HBsAg negative), ART is continued
- In HBV monoinfection there are several circumstances when you can stop therapy:
  - HBsAg negative (i.e., resolved infection)
  - After an HBeAg-positive patient becomes HBeAg-negative
- For the most part, therapy is lifelong as these endpoints are uncommonly achieved.

AASLD 2018 guidelines

Prevention: Who should be vaccinated against Hepatitis B?

Universal	All infants
	All children and adolescents not previously vaccinated
On the basis of risk	Inmates of long-term correctional facilities
	Injection drug users
	Sexually-active men who have sex with men
	Anyone with high risk sexual activity
	Household and sexual contacts to known HBsAg-positives
	Persons with occupational exposure to blood or body fluids
	Hemodialysis patients
	Recipients of clotting factor concentrates
	Long-term international travelers
	Clients and staff of institutions for the developmentally disabled

Centers for Disease Control and Prevention

Poll question #3

Which of the following persons is **not** on the high priority list for hepatitis B vaccination?

a. Laboratory technician at the local hospital
b. Guard at the correctional center
c. Supervisor of an HBsAg-positive employee at fast food restaurant
d. A commercial sex worker
e. A child born via home birth