Project ECHO®
Chronic Liver Disease Foundation
New Jersey

HBV Alliance:

Expert Recommendations on Managing Patients with Chronic Hepatitis B

Accredited by

Rehoboth McKinley Christian Health Care Services

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Provided by

CLDF
Chronic Liver Disease Foundation

Chemotherapy/Reactivation

Learning Objectives
HBV ECHO Series

Upon completion of this activity, participants should be able to:

- Review data on the prevalence and transmission of HBV
- Define the risk of HBV among different patient populations, highlighting high-risk settings
- Describe the detrimental effects of untreated, chronic HBV to emphasize the need for diagnosis and treatment
- Demonstrate strategies to incorporate various diagnostic and treatment guidelines into clinical practice
- Analyze approved and emerging treatment options for HBV
- Identify patients that are likely to benefit from emerging treatment options versus currently available therapies

Understanding the Problem

Global Impact of HBV – Unmet Need

~ **292** million (3.9% prevalence)- > 67% from Africa, Asia, and the Pacific Islands

2.2 M in US

- Acute HBV rising in US since 2014

2 of every 3 persons with HBV are unaware

25% die prematurely of HCC, cirrhosis, ESLD

Only 10-15% of candidates are on Rx

Only about 1 in 4 adults are fully immunized

Prevalence of Chronic Hepatitis B Infection in the U.S.

Estimated prevalence of 1.59 million persons (range 1.25-2.49 million)

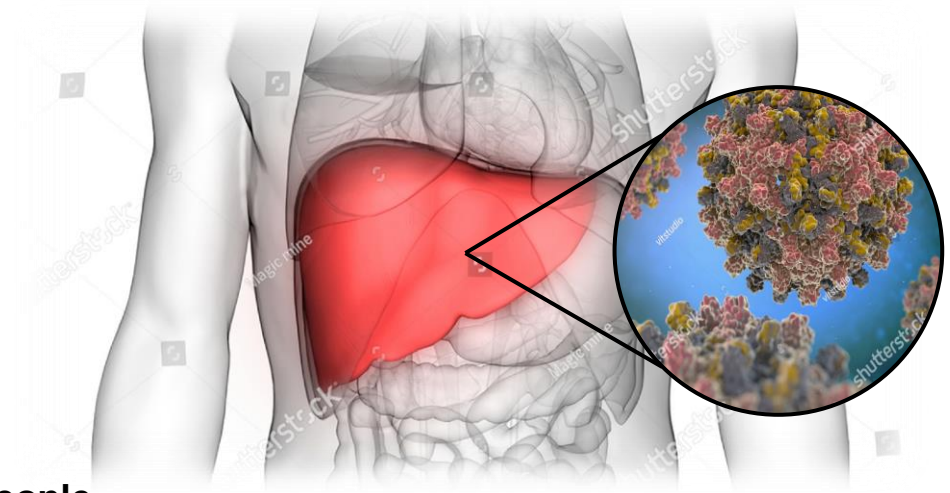
Individuals at-risk for HBV are those who are unvaccinated, fall into high-risk groups or are foreign-born and immigrating from HBV endemic regions (e.g. Asia, Africa)

Veterans
0.3 – 0.84%

Healthcare Professionals
0.1-8.1%

Prisoners
0.9-11.4%

Homeless People
0.4-1.17%



Men Who Have Sex with Men
Prevalence unknown

People Who Inject Drugs
11.8%

Patients with HIV Coinfection
0.7-5.8%

Patients HCV Coinfection
3.0-8.4%

Newborns Born to HBV-Infected Mothers
3.84%

Lim J et al. *Am J Gastroenterol.* 2020, in press.

Understanding Hepatitis B Serology

- HBsAg (hepatitis B surface antigen)
  - A protein on the surface of HBV
  - Can be detected during acute or chronic HBV infection
  - Presence indicates an individual is INFECTED
- Anti-HBs (hepatitis B surface antibody)
  - Presence indicates recovery and IMMUNITY from HBV infection
  - Also develops following vaccination against hepatitis B
- Anti-HBc (total hepatitis B core antibody)
  - Appears at the onset of symptoms in acute hepatitis and persists for life
  - Presence indicates EXPOSURE (previous or ongoing infection with HBV)

Evaluation of the HBsAg-Positive Patient

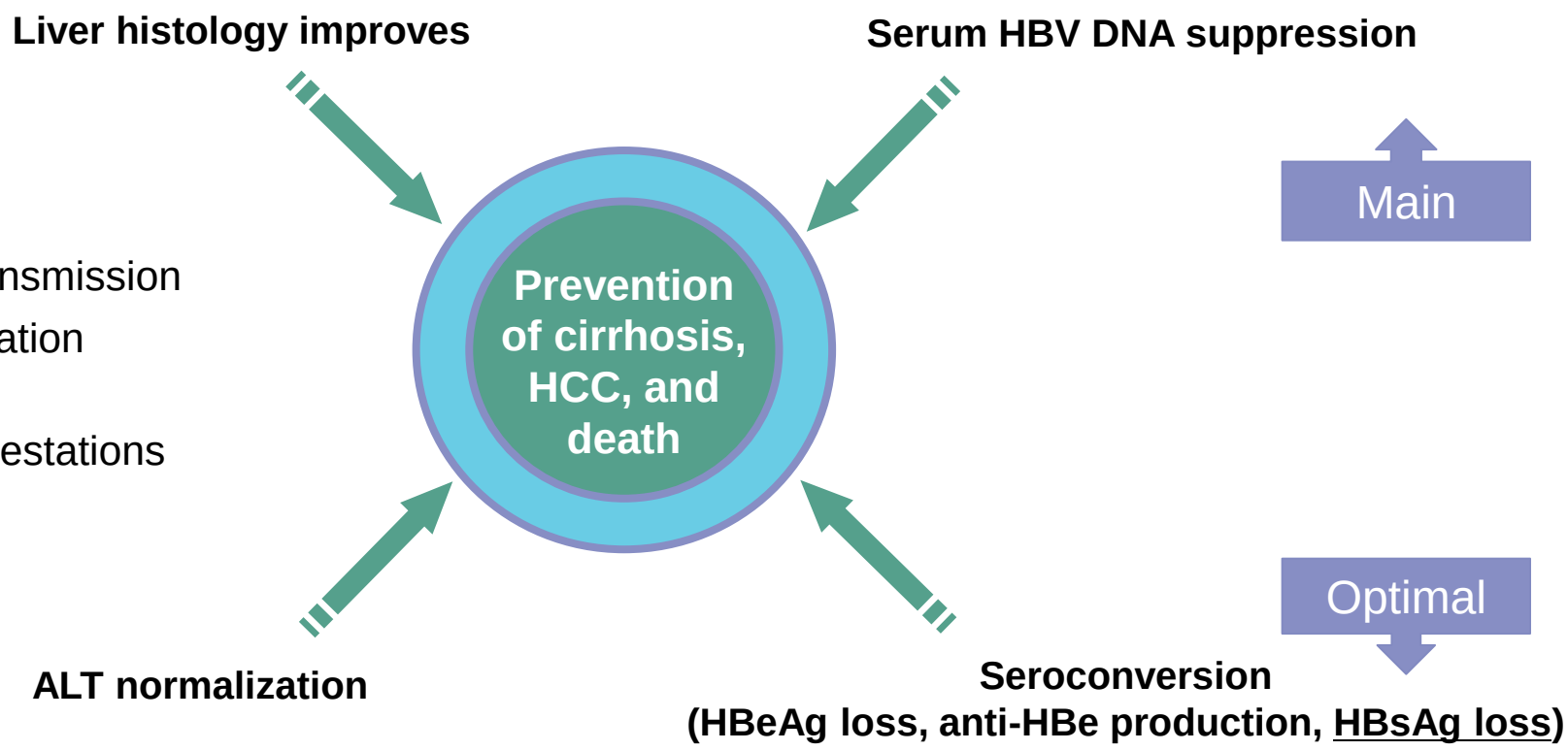
- History of risk factors, including family history
- Alcohol use, medications, general medical assessment
- Assessment of need for vaccination of family members, household contacts, partners, etc
- CBC, hepatic panel, AFP, HBV DNA, HBeAg, anti-HBe, HCV antibody, hepatitis D (delta) antibody, HIV antibody
- Exclusion of non-viral liver diseases as appropriate
- Baseline imaging (generally ultrasound) and initiation of regular HCC screening as indicated
- Noninvasive fibrosis assessment:
  - APRI
  - FIB-4
  - Other serum markers
  - Ultrasound based elastography

HBV Treatment: Who, When, Why?

Goals and Endpoints of Therapy for HBV

Prevent:

- Mother-to-child transmission
- Hepatitis B reactivation
- HBV-associated extrahepatic manifestations



EASL CPG HBV. *J Hepatol.* 2017;67:370–98.

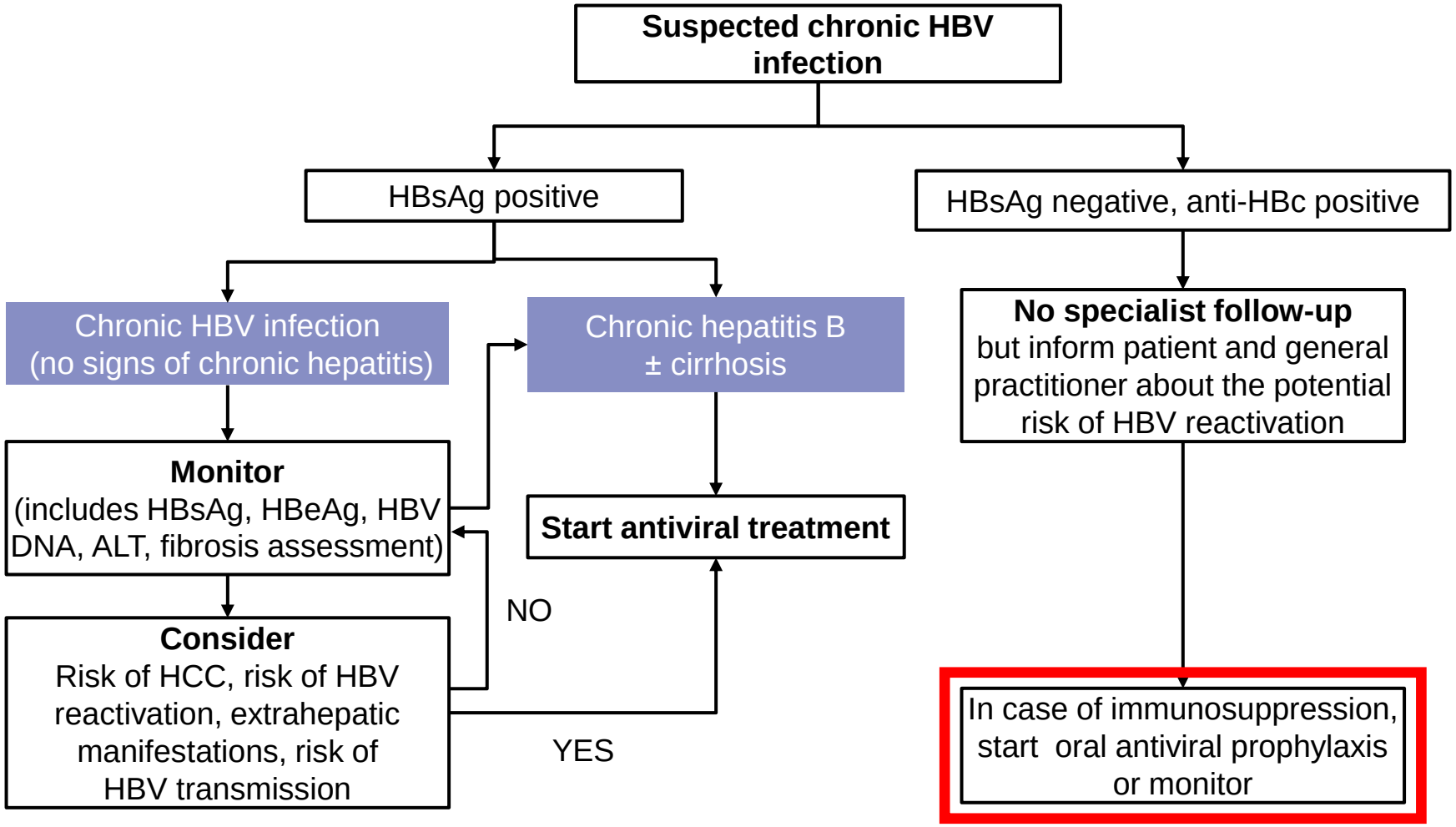
Chronic HBV: Goals of Therapy

- Achieve sustained suppression of HBV replication and remission of hepatic disease
- Prevent the development of cirrhosis, hepatic failure, and hepatocellular carcinoma
- HBV probably is never cured, but rather controlled by limiting viral replication
  - Markers of treatment response
    - Decreased serum HBV DNA to low or undetectable levels
    - Improved liver histology
    - Decreased or normalized serum ALT
    - HBeAg loss or seroconversion (in HBeAg-negative patients)
    - HBsAg loss or seroconversion

*HBV ccc DNA persists, making HBV incurable with current treatments.

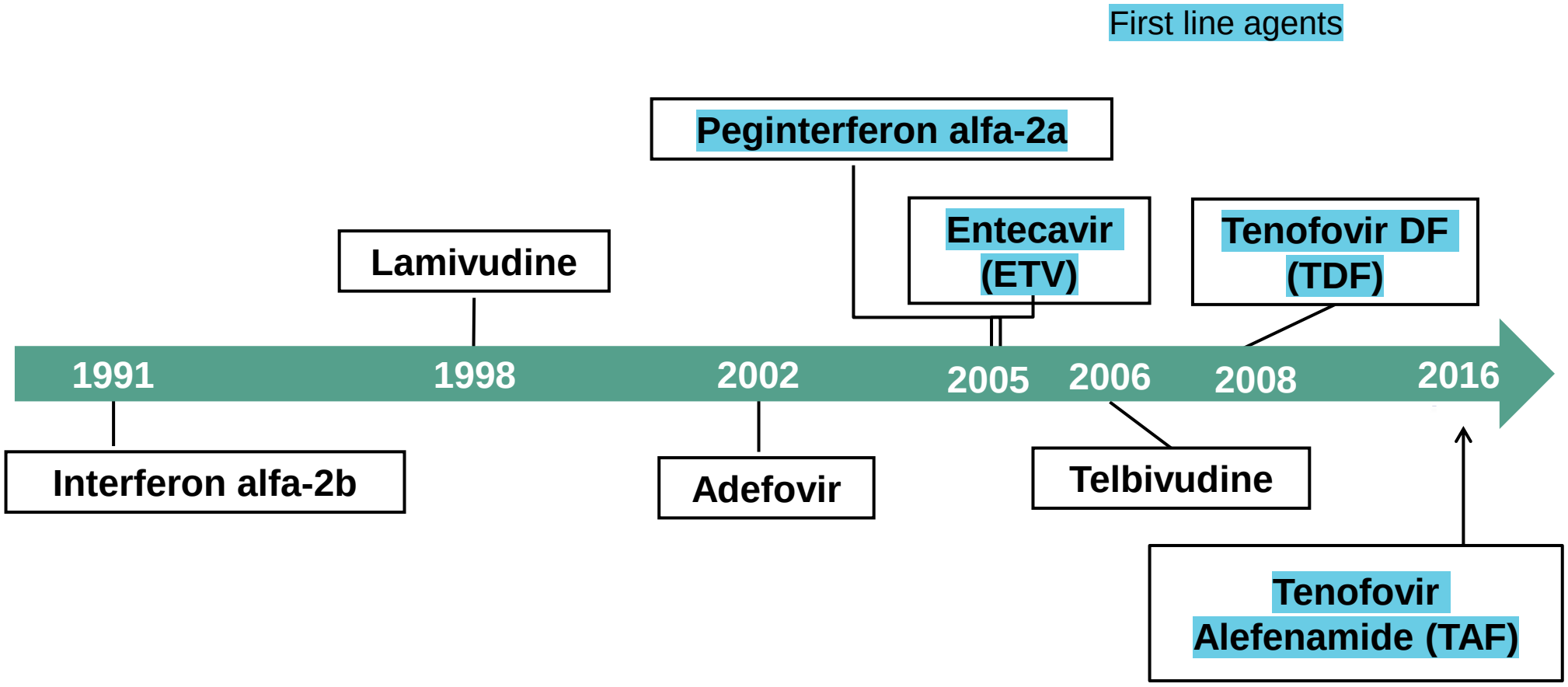
Terrault NA, et al. *Hepatology*. 2016; 63:261-283; Martin P, et al. *Clin Gastroenterol Hepatol.* 2015; 13:2071-2087.

Algorithm for the Management of Chronic HBV Infection



EASL CPG HBV. *J Hepatol.* 2017; 67:370–98.

HBV Treatment Landscape in 2020



Reactivation of HBV

HBV Reactivation

Well-Characterized Syndrome

- Abrupt reappearance or rise of HBV DNA in previously inactive or resolved HBV infection
  - *≥ 2 log rise in HBV DNA from baseline or reversion of HBsAg from neg to pos*
- Often, but not always, accompanied by reappearance of disease activity
- May occur spontaneously or as a result of immunosuppression

Potential Consequences

- May lead to clinically apparent acute hepatitis
  - *ALT increase to >3x ULN or >100*
  - Can be severe
  - Can result in acute liver failure and death
- Many cases are subclinical and resolve spontaneously, or result in persistent infection
- May go undetected until
  - Advanced liver disease is present
  - Disease has been transmitted to sexual or family contacts

Who Should Be Screened for HBV

- Persons born in high and intermediate endemic areas (≥2% prevalence)
- US born children of immigrants from high-risk areas
- Household and sexual contacts of HBsAg-positive persons
- Persons who have ever injected drugs
- Persons with multiple sexual partners, or history of STDs
- Men who have sex with men
- Inmates of correctional facilities
- Individuals with chronically elevated ALT/AST
- Individuals infected with HIV or HCV
- Patients undergoing dialysis
- All pregnant women
- Patients undergoing immunosuppression, chemotherapy, transplantation

Screening tests:
HBsAg and anti-HBc

Weinbaum CM, et al. *MMWR Recomm Rep.* 2008; 57(RR-8):1-20;
LeFevre ML on behalf of the U.S. Preventive Services Task Force. *Ann Intern Med.* 2014; 161:58-66.

Who Should Be Screened for HBV

Heme-Oncology:
Chemotherapy, Biologics, BMT

Inflammation:
Biologics, TNF inhibitors

Transplantation:
Immunosuppression

Viral Coinfection:
HIV, HCV

Risk of HBV Reactivation

HBV Status	Reactivation Risk
• HBsAg+	• **High risk (≥10%)**
• Isolated anti-HBc+	• **Moderate risk (1% to <10%)**
– HBsAg neg, HBV DNA neg	• **Low risk (<1%)**

AASLD Guidance

- HBsAg+ patients should initiate anti-HBV prophylaxis UNLESS **very low risk**
- Anti-HBc+ patients should initiate anti-HBV prophylaxis ONLY IF **high risk**
  - Rituximab
  - Stem cell transplantation
  - Option to consider prophylaxis in **moderate risk**
- Entecavir, Tenofovir (either as TDF or TAF) preferred
  - Antiviral therapy should be continued for at least 6 months after completion of immunosuppressive therapy or for at least 12-24 months for patients receiving anti-CD20 therapies
  - Long-term if transplant recipient

Terrault N et al. *AASLD Guidance*. 2018;67:1560-99; EASL Hepatitis Guidelines. *J Hepatol.* 2017.

HBsAg+Risk

Reactivation risk	Immunosuppressive therapies
High (≥10%) ⬇ **Treat**	**B-cell depleting biologics** (rituximab, ofatumumab, ustekinumab, natalizumab, alemtuzumab, ibritumomab) **Stem cell transplant recipients** **Moderate (10-20 mg/day) or high-dose corticosteroids (>20 mg/day) for >4 weeks** **Anthracyclines** (eg, doxorubicin, epirubicin) **More potent TNF-α inhibitors** (eg, infliximab, adalimumab, certolizumab, golimumab)
Moderate (1-10%) ⬇ **Treat**	**Systemic chemotherapy** **Less potent TNF-α inhibitors** including etanercept **Cytokine-based therapies** including abatacept, ustekinumab, mogamulizumab, vedolizumab **Immunophilin inhibitors** including cyclosporine **Tyrosine-kinase inhibitors** including imantnib, nilotinib **Proteasome inhibitors** such as bortezomib **Histone deacetylase inhibitors** (HDIs) **Moderate-dose corticosteroids (10-20 mg/day)**
Low (<1%) Monitor	**Antimetabolites**, azathioprine, 6-MP, MTX **Short-term low dose** corticosteroids **Intra-articular steroid injections**

Loomba. *Gastro*. 2017.

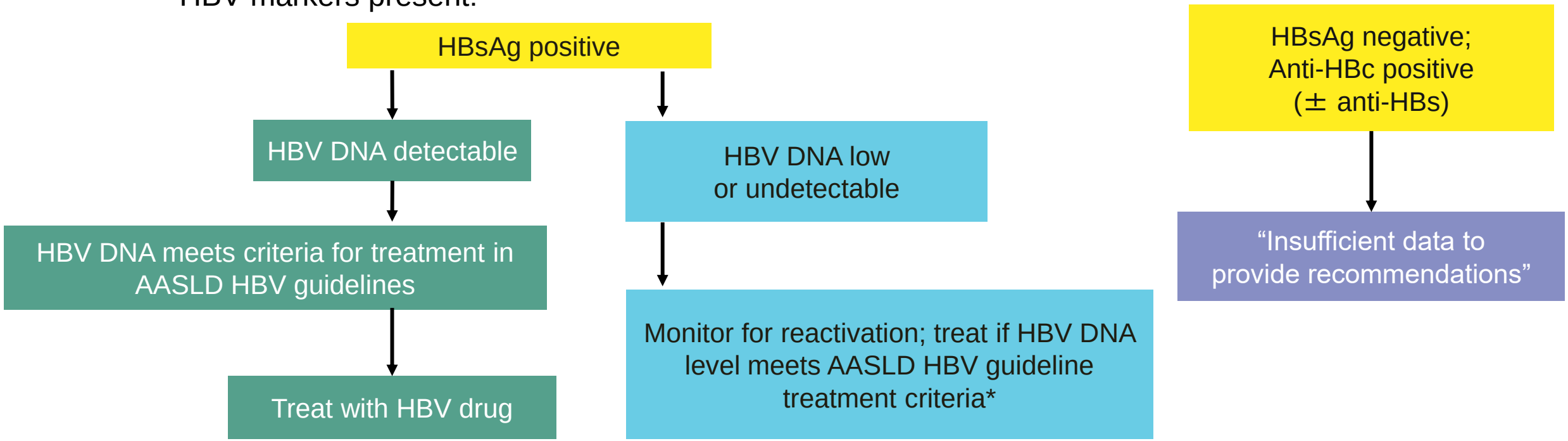
Anti-HBc+Risk

Reactivation risk	Immunosuppressive therapies
High (≥10%) ⬇ **Treat**	**B-cell depleting biologics** (rituximab, ofatumumab, ustekinumab, natalizumab, alemtuzumab, ibritumomab) **Stem cell transplant recipients**
Moderate (1-10%) ⬇ **Treat** *or* monitor	**High-dose corticosteroids (>20 mg/day) for >4 weeks** **Anthracyclines** (eg, doxorubicin, epirubicin) **More potent TNF-α inhibitors** (eg, infliximab, adalimumab, certolizumab, golimumab) **Systemic chemotherapy** **Cytokine-based therapies** including abatacept, ustekinumab, mogamulizumab, vedolizumab **Immunophilin inhibitors** including cyclosporine **Tyrosine-kinase inhibitors** including imantnib, nilotinib **Proteasome inhibitors** such as bortezomib **Histone deacetylase inhibitors** (HDIs)
Low (<1%)	**Moderate and low dose prednisone** **Antimetabolites,** azathioprine, 6-mercaptopurine, methotrexate

Loomba and Liang. *Gastro.* 2017

HBV Testing and Monitoring During HCV DAA Therapy: AASLD/IDSA Guidance

- Test all patients initiating HCV therapy for HBsAg, anti-HBc, and anti-HBs
  - No HBV markers: VACCINATE
  - HBV markers present:



*Some clinicians would treat all HBsAg+ persons until after HCV therapy completed (e.g. 12 weeks after completed).
hcvguidelines.org September 2017.

Case 1

- 54 yo WF with lymphoma
  - LFTs nl
  - HBsAg-, Anti-HBc+
- Plan for rituximab
- Next best steps?
  a. Monitor LFTs
  b. Initiate entecavir or tenofovir
  c. Monitor HBV DNA

Case 2

- 37 yo AM with chronic HCV
  - LFTs- ALT 76, AST 60, TB 0.9
  - HCV RNA 1,200,000
  - HBsAg+, Anti-HBc+, HBV DNA 1800 IU/ml
- Plan for HCV Rx initiation
- Next best steps?
  a. Monitor LFTs, HBV DNA
  b. Initiate entecavir or tenofovir
  c. Liver biopsy
  d. Fibroscan

Case 3

- 66 yo HM with IBD
  - ALT 30, TB 1.1
  - Anti-HBc+
  - Neg HBsAg, HBV DNA
  - US- normal
  - Plan for TNF inhibitor
- Next best step?
  a. Monitor labs
  b. Fibroscan
  c. Liver biopsy
  d. Entecavir or tenofovir initiation

- Any changes if:
  - HBsAg+
  - ALT 1900, TB 11, INR 3.5

Thank You!