AETC AIDS Education & Training Center Program Southeast

Monthy 1st and 3rd Wednesday and
12:00pm-1:00pm EST
11:00am-12:00pm CST
09:00am-10:00am PST

4th Wednesday
12:00pm-1:00pm CST
01:00pmpm-2:00pm EST
10:00am-11:00am PST

South East Viral Hepatitis Interactive Case Conference

Disclosures

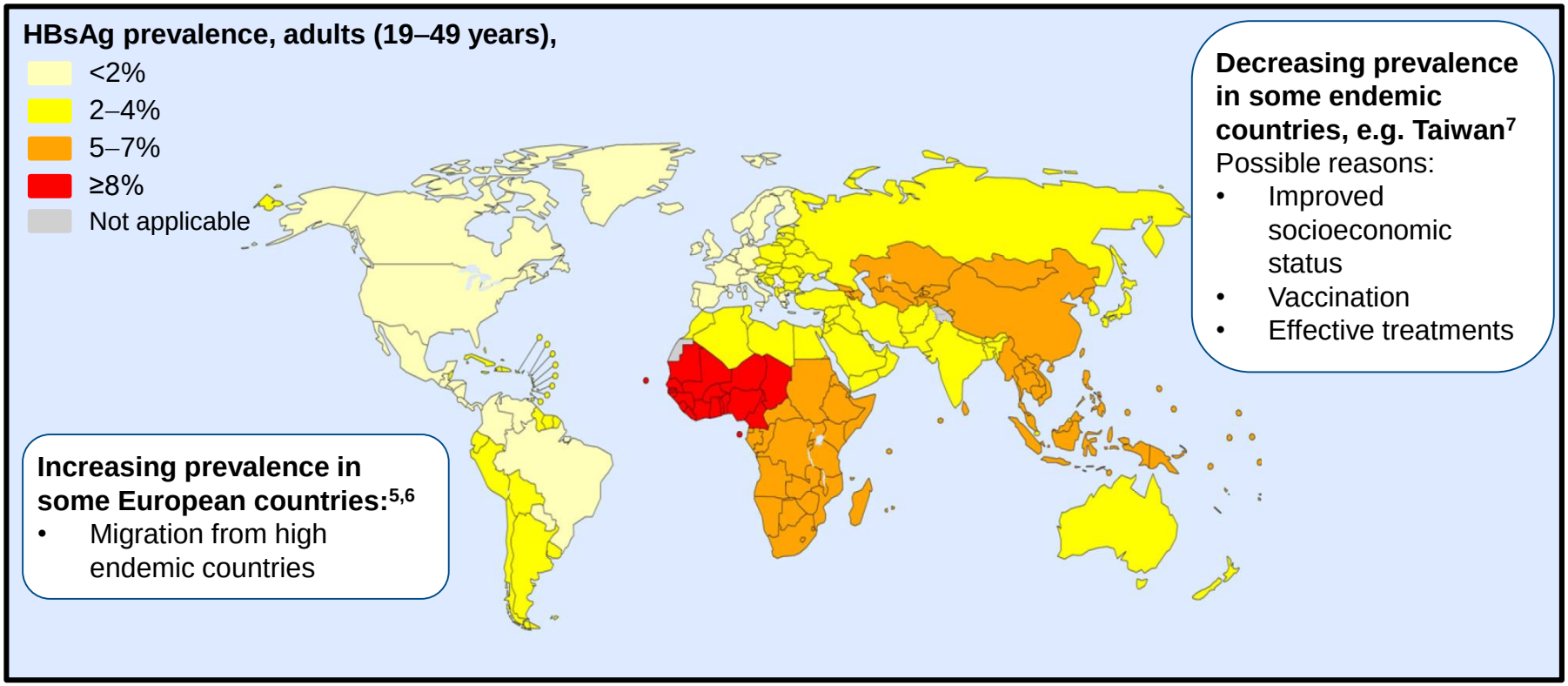
- None

Topic for today

- HIV/HBV co-infection

Epidemiology and public health burden[1]

- Worldwide ≈250 million chronic HBsAg carriers[2,3]
- 686,000 deaths from HBV-related liver disease and HCC in 2013[4]



1. EASL CPG HBV. J Hepatol 2017;67:370–98; 2. Schweitzer A, et al. Lancet 2015;386:1546–55;
3. Ott JJ, et al. Vaccine 2012;30:2212–9; 4. GBD 2013 Mortality and Causes of Death Collaborators. Lancet 2015;385:117–71;
5. Coppola N, et al. Euro Surveill 2015;20:30009; 6. Hampel A, et al. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2016;59:578–83; 7. Chen C-L, et al. J Hepatol 2015;63:354–63.

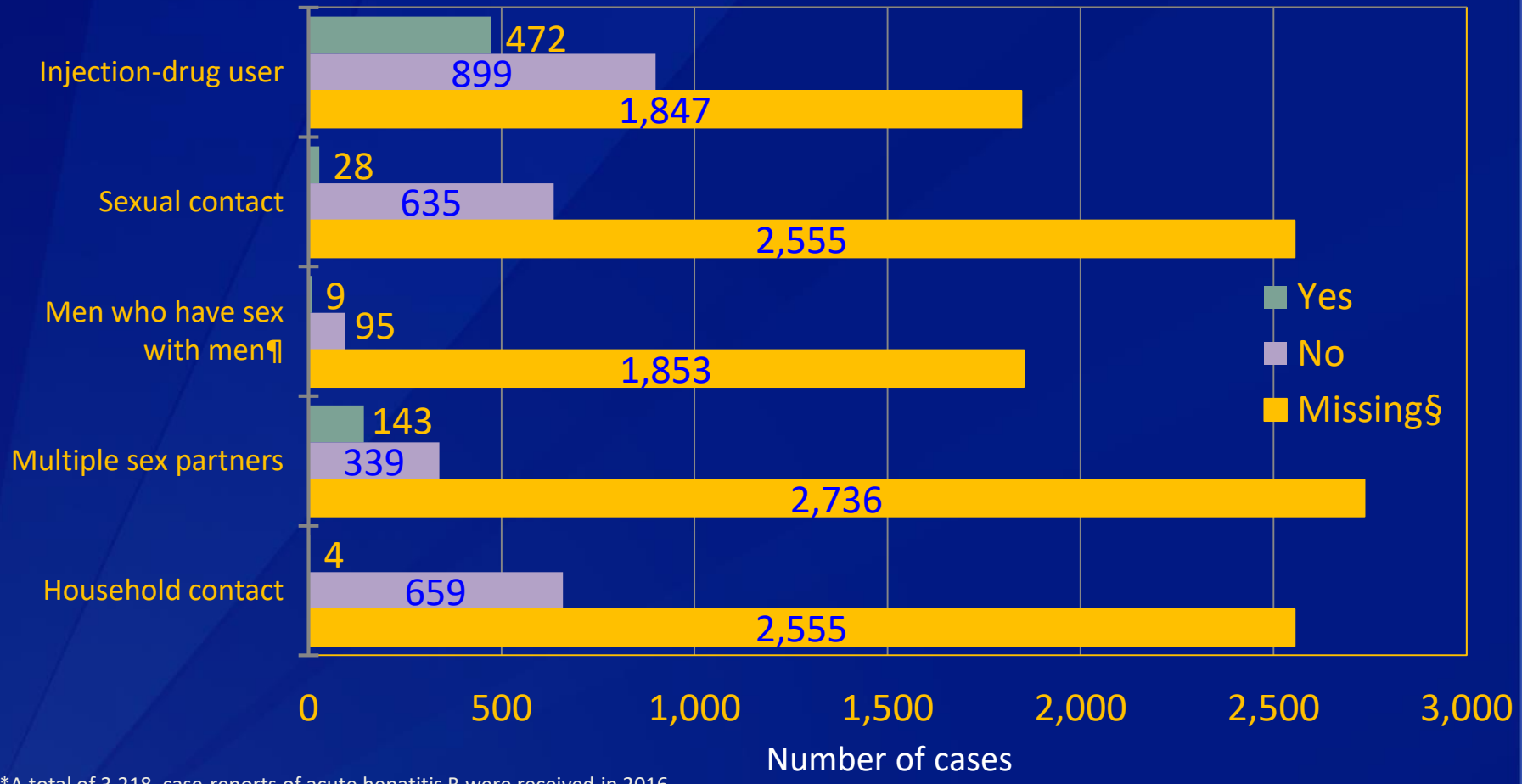
EASL™ The Home of Hepatology

Candidates for HBV Screening

- Persons born in high and intermediate endemic areas (≥ 2% prevalence)
- US-born children of immigrants from high endemic areas (≥ 8%)
- Household and sexual contacts of HBV carriers
- IVDUs
- 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 with HIV or HCV
- Patients undergoing dialysis
- Patients undergoing immunosuppressive therapy
- All pregnant women
- Infants born to HBV carrier mothers

Weinbaum CM, et al. MMWR Recomm Rep. 2008;57(RR-8):1-20.
Lok AS, et al. Hepatology. 2009;50:661-662.

Figure 3.6a. Acute hepatitis B reports*, by risk exposure/behavior† — United States, 2016



*A total of 3,218 case-reports of acute hepatitis B were received in 2016.

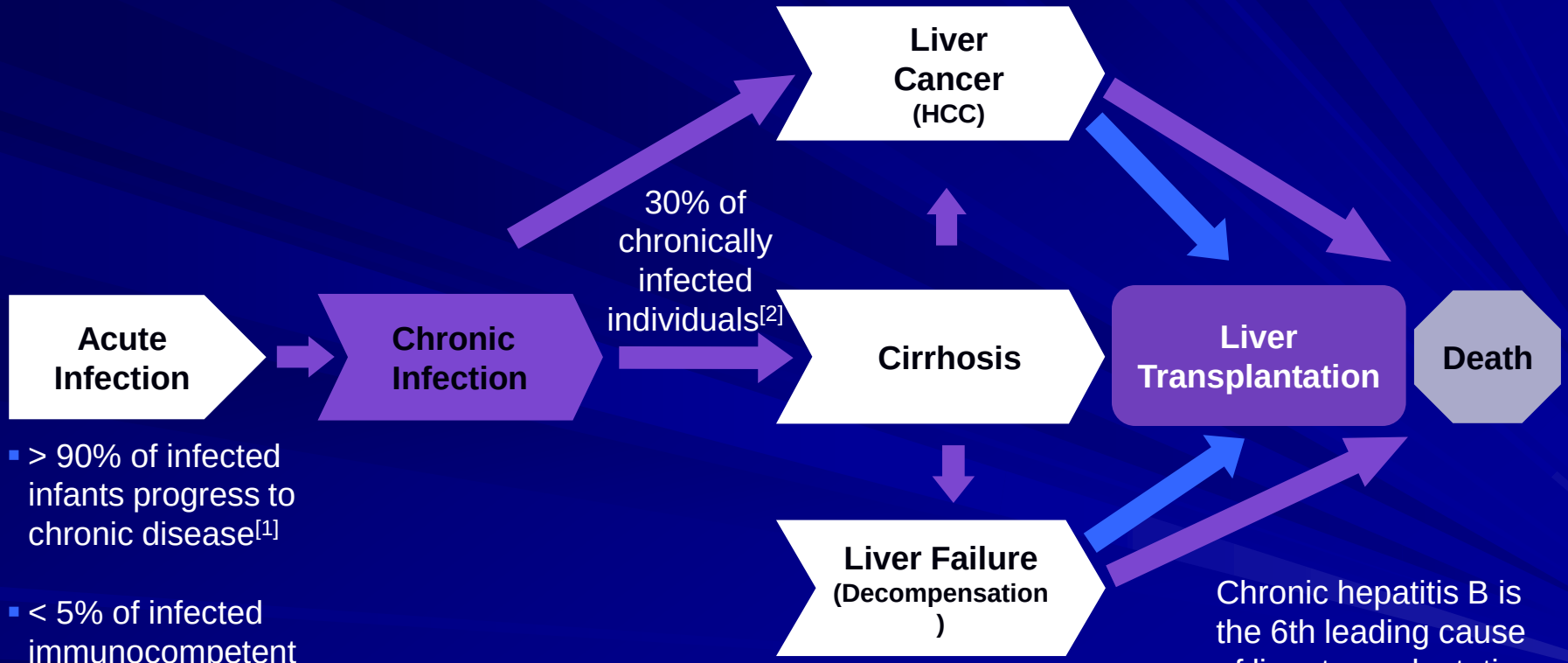
† More than one risk exposure/behavior may be indicated on each case-report.

§ No risk data reported.

¶A total of 1,957 acute hepatitis B cases were reported among males in 2016.

Source: National Notifiable Diseases Surveillance System (NNDSS)

Hepatitis B Disease Progression

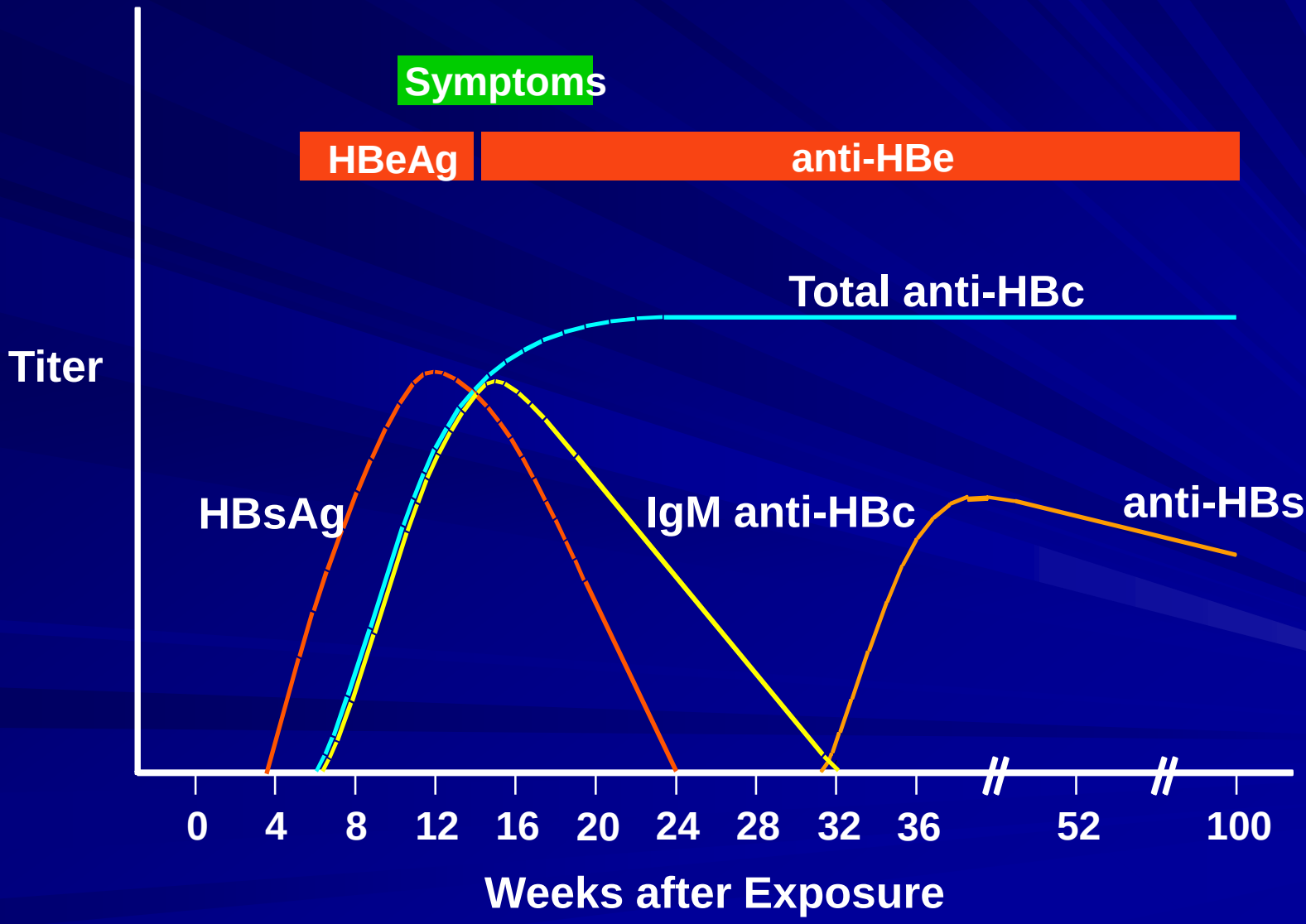


- > 90% of infected infants progress to chronic disease[1]
- < 5% of infected immunocompetent adults progress to chronic disease[1]

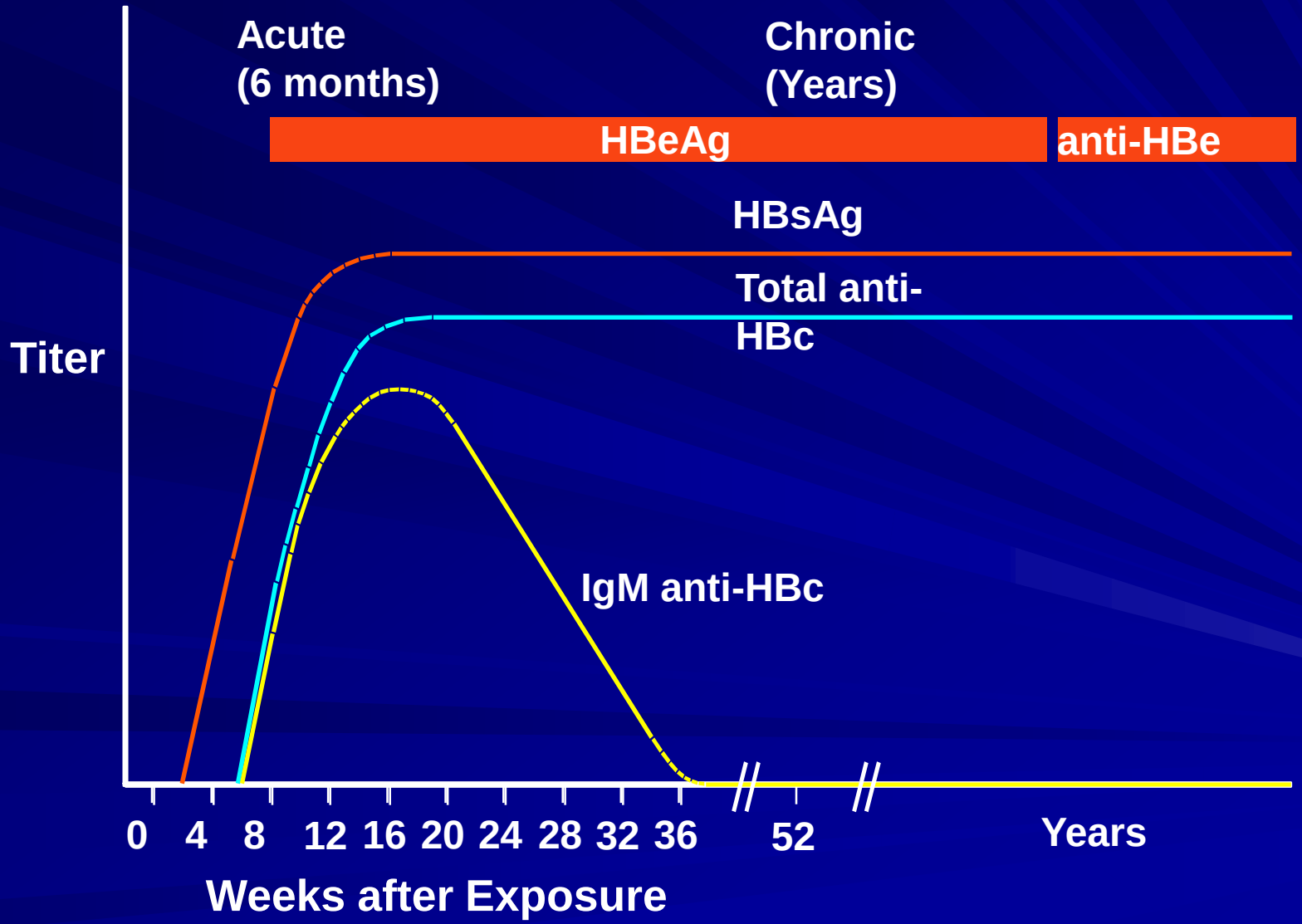
23% of patients decompensate within 5 yrs of developing cirrhosis[3]

Chronic hepatitis B is the 6th leading cause of liver transplantation in the US[4]

Acute HBV Infection with Recovery



Progression to Chronic HBV Infection



Complications of Chronic Hepatitis B

- Many patients are asymptomatic
- Hepatic complications
  - Cirrhosis, decompensated disease, hypersplenism
- Extrahepatic manifestations:
  - Seen in 10-20% of patients ; Thought to be due to circulating immune complexes
  - Polyarteritis nodosa
  - Membranous nephropathy

Interpretation of Serologic Results

HBsAg	Total Anti-HBc	IgM Anti-HBc	Anti-HBs	Interpretation
Negative	Negative	--	Negative	Susceptible; offer vaccination
Negative	Positive	--	Positive	Immune due to natural infection
Negative	Negative	--	Positive	Immune due to hepatitis B vaccination
Positive	Positive	Negative	Negative	Chronic HBV infection
Positive	Positive	Positive	Negative	Acute HBV infection
Negative	Positive	--	Negative	Unclear; could be any one of the following: 1. Resolved infection (most common) 2. False-positive anti-HBc; susceptible 3. “Low-level” chronic infection 4. Resolving acute infection

CDC. Hepatitis B FAQs for Health Professionals.

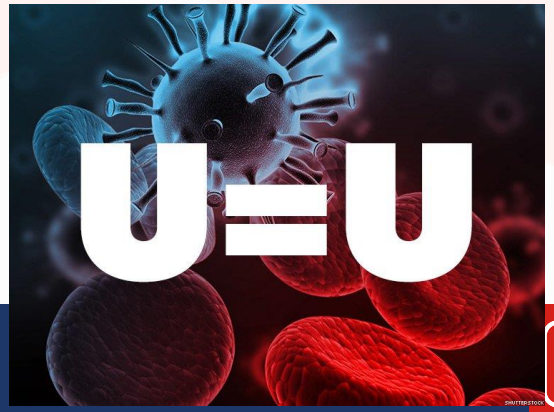
Volume 25, Number 1

Estimated HIV Incidence and Prevalence in the United States 2014–2018

- US population- 330 million
- HIV -estimated 1.2 million aged 13 and older
- Thus HIV prevalence **>1/330 Americans**
  - Males- 0.7% (1/150 male Americans)
  - Females-0.2%

Recommendations for Initiating ART for an HIV infected person

- ART (Antiretroviral therapy or HIV medications) is recommended for all HIV-infected individuals to reduce the risk of disease progression.
- Effective ART reduces transmission to almost **“0”**
- HIV is easier to treat than Diabetes, COPD, CHF
- Undetectable= Untransmissible



DHHS Guidelines: Recommended Regimens for **First-line HIV Antiretroviral Therapy**

Class	Regimen
INSTI	▪ BIC/TAF/FTC (Biktarvy®) ▪ DTG/ABC/3TC (Triumeq®) ▪ DTG + (TAF or TDF)/FTC (Tivicay®+ Descovy® or Truvada®) ▪ RAL + (TAF or TDF)/FTC (Isentress®+Descovy® or Truvada®)

IAS-USA now lists EVG/COBI/TAF/FTC and RAL + TAF/FTC as alternative regimens owing to their lower resistance barriers and, respectively, more drug interactions and higher pill burden

DHHS Guidelines. 2019.

HIV/HBV co-infection

- HIV-HBV co-infection
  - Approximately 5% -10% of people with HIV in the US
- Patients with chronic HBV should be evaluated to assess the severity of HBV infection
- Progression to cirrhosis, end-stage liver disease, or hepatocellular carcinoma is more rapid in persons with HBV/HIV coinfection than in persons with chronic HBV monoinfection

Thio CL, Lancet. Dec 14 2002;360(9349):1921-1926.

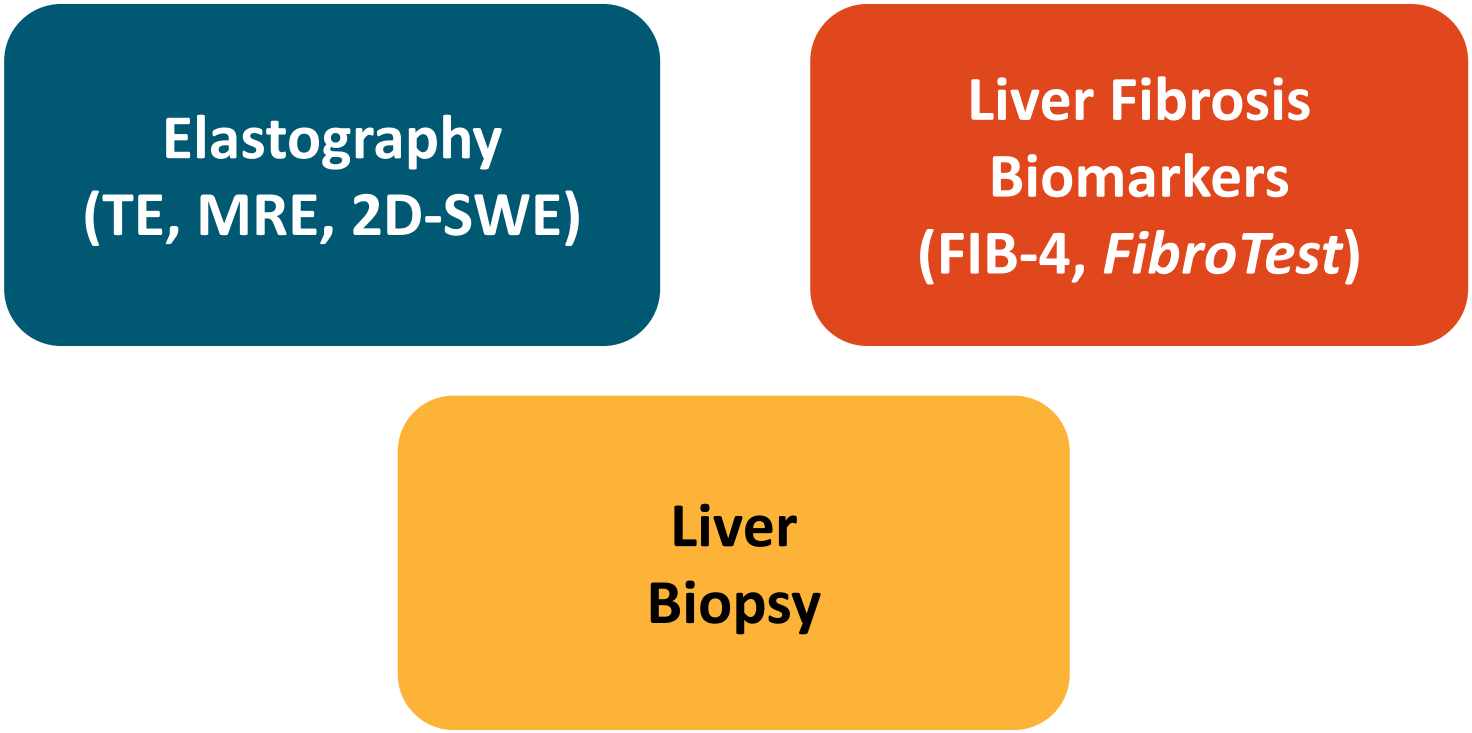
ART initiation in HIV-HBV co-infection

- Before ART initiation
- All persons who are hepatitis B surface antigen (HBsAg) should be tested with a quantitative assay for HBV DNA
- HBV DNA PCR should be repeated every 3 - 6 months to ensure effective HBV suppression.

Decision to initiate HBV treatment

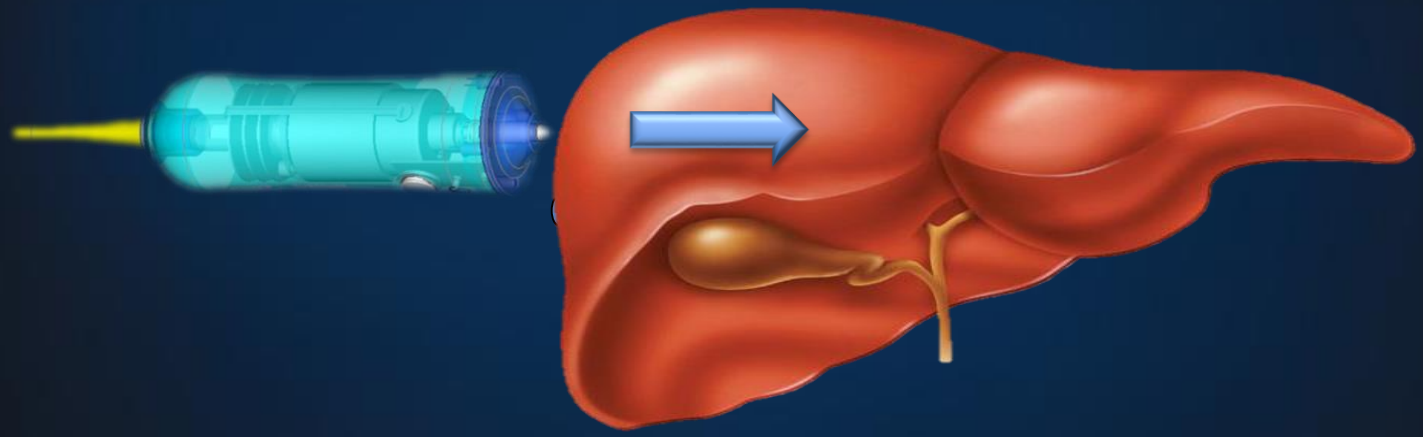
- Based upon
  - Cirrhosis
  - ALT level
  - HBV DNA level
  - Also, fulminant acute HBV, severe exacerbation of chronic HBV, decompensated cirrhosis and a detectable HBV DNA by polymerase chain reaction
- Elevated HBV DNA
  - HBeAg negative patients- >2000 international units/mL (10^4 copies/mL)
  - HBeAg positive patients- >20,000 international units/mL (>10^5 copies/mL)

Noninvasive Methods to Evaluate Fibrosis and/or Inflammation



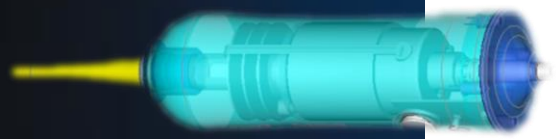
Terrault. Hepatology. 2018;67:1560. EASL. J Hepatol. 2017;67:370. EASL. J Hepatol. 2015;63:237.

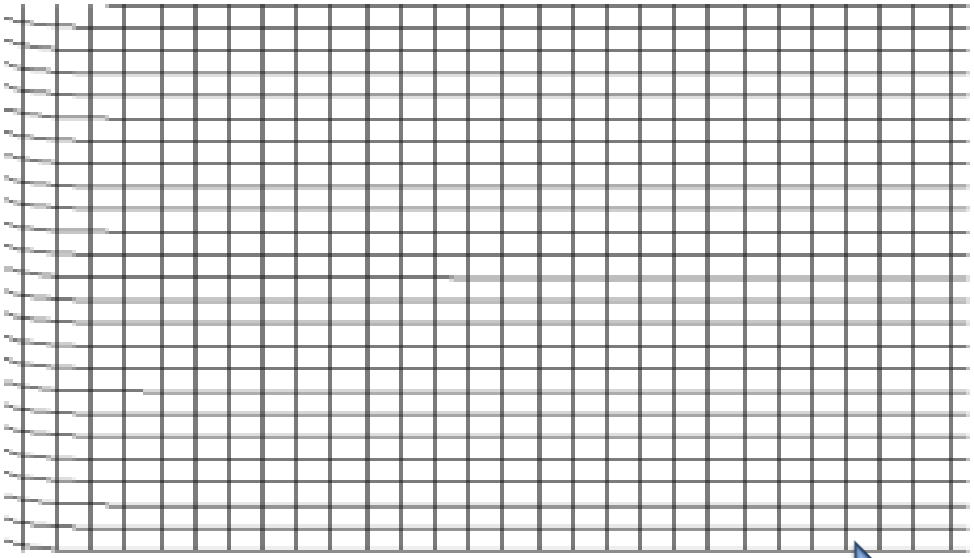
Mechanical Shear Wave Induction



SANDHILL SCIENTIFIC
a medovations company

Shear Wave Movement





Quantitative HBsAg

- Quantitative HBsAg is a valuable tool in evaluating patients in the gray zone, particularly in determining if they are true inactive carriers
  - Can guide treatment decision and indicate HCC screening
- qHBsAg < 1000 IU/mL and HBV DNA < 2000 IU/mL: inactive carrier with decreased risk for HCC
- Can also help in determining when to stop therapy
- HCC:
  - HBV DNA < 2000 IU/mL and qHBsAg < 1000 IU/mL: lower risk of HCC and progression

2018 AASLD Guidance: Whom to Treat

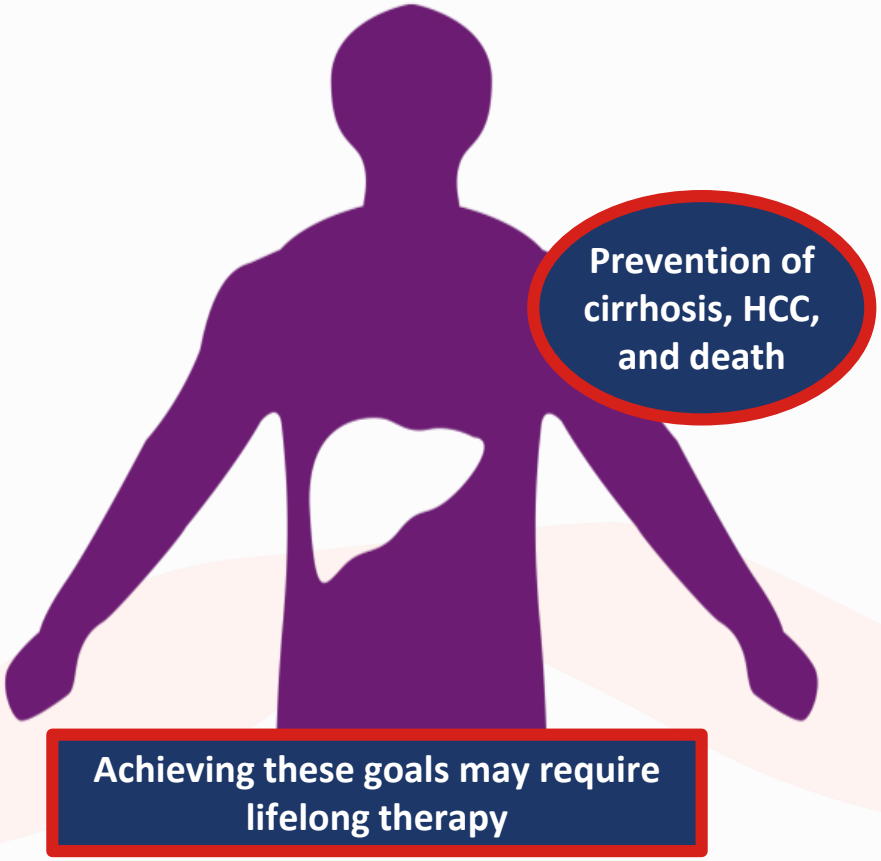
- AASLD recommendations for antiviral therapy
  - Adults with immune-active CHB (HBeAg negative or HBeAg positive) to decrease the risk of liver-related complications
    - Additional factors: age, family history of HCC or cirrhosis, previous treatment history, presence of extrahepatic manifestations, presence of cirrhosis
  - Select group of immune-tolerant adults older than 40 yrs of age with normal ALT and elevated HBV DNA (1,000,000 IU/mL) and liver biopsy specimen showing significant necroinflammation or fibrosis

If treatment is not indicated, actively monitor as candidacy may change with disease progression

Terrault. Hepatology. 2018;67:1560. www.aasld.org.

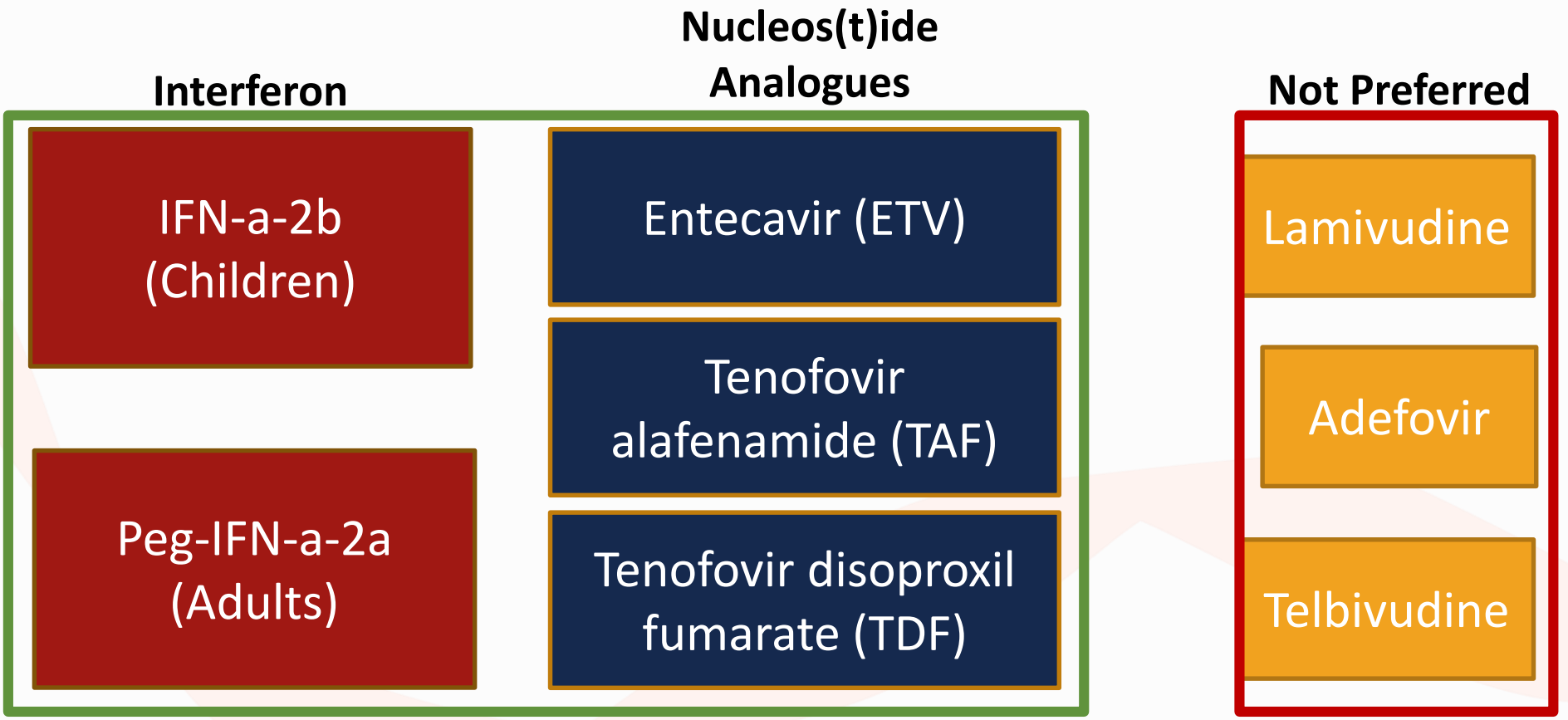
Goals of Therapy for HBV

- Liver Histology Improves
- Seroconversion (HBeAg ↓, anti-HBe ↑, HBsAg ↓)
- Serum HBV DNA ↓
- ALT Normalization



Options for HBV Treatment

Dual therapy in HIV/HBV Co-infection



EASL. J Hepatol. 2017;67:370. Terrault. Hepatology. 2018;67:1560.

Preferred First-line Monotherapies for Chronic Hepatitis B

No Cirrhosis or Compensated Cirrhosis	Decompensated Cirrhosis†
Entecavir 0.5 mg/day	Entecavir 1 mg/day
Tenofovir Alafenamide (TAF)	TDF (TAF)
Tenofovir Disoproxil fumarate(TDF)	
PegIFN*	

*Considered less safe than NA therapy;

Terrault. Hepatology. 2018;67:1560. EASL. J Hepatol. 2017;67:370. Martin. Clin Gastroenterol Hepatol. 2015;13:2071. Entecavir PI.

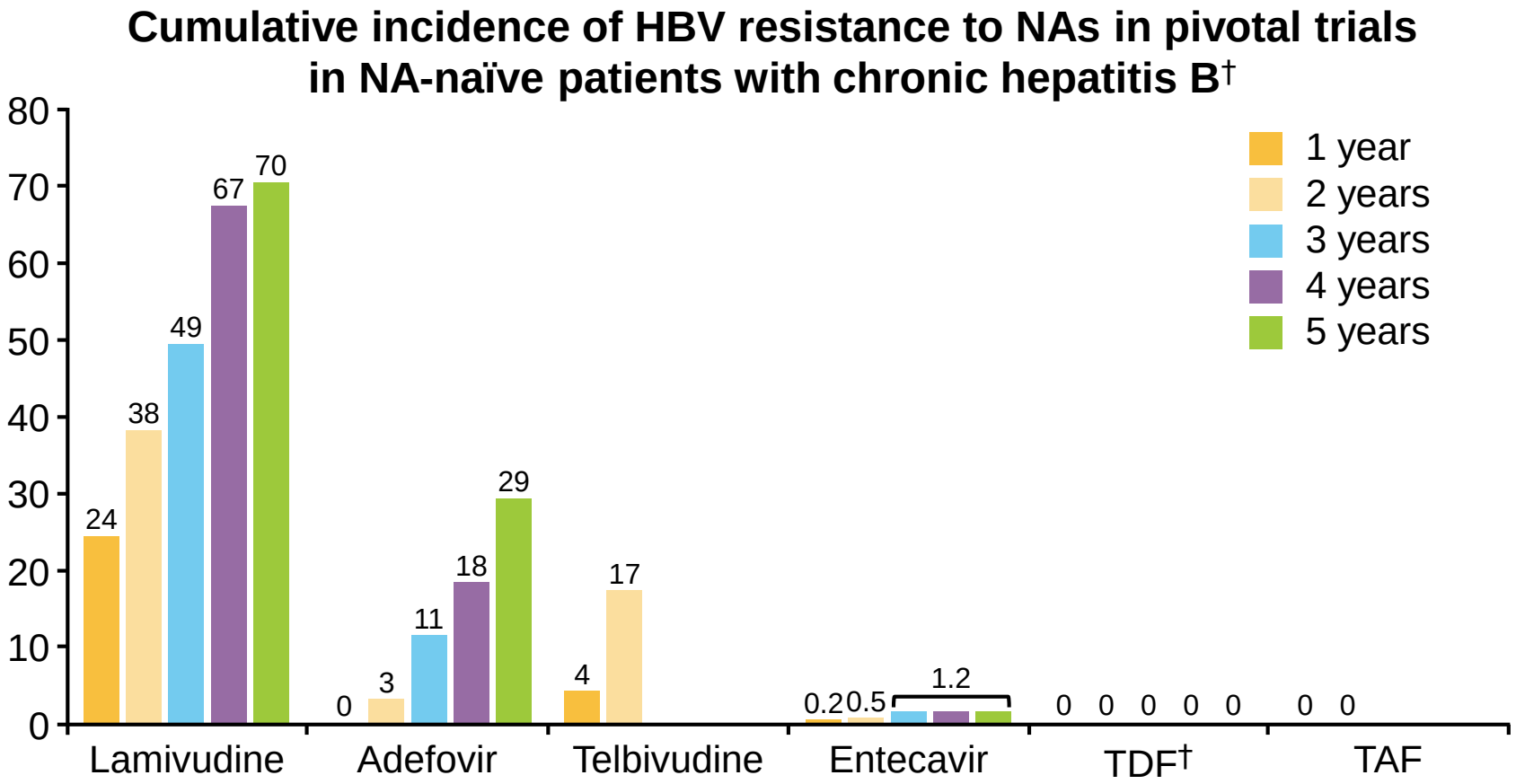
ART and HBV treatment- crossover

- ARVs approved to treat HIV that are also active against HBV.
  - Emtricitabine (FTC)
  - Lamivudine (3TC)
  - Tenofovir disoproxil fumarate (TDF)
  - Tenofovir alafenamide (TAF)

When 3TC or FTC are the only active drugs used to treat chronic HBV, 3TC-resistant HBV emerges in >90% of patients by year 5

- Discontinuation of these drugs may potentially cause serious hepatocellular damage resulting from reactivation of HBV
- Anti-HBV drug entecavir has activity against HIV.
  - If given as monotherapy for HBV in an HIV positive patient it may select for the M184V mutation in HIV
  - This confers HIV resistance to 3TC and FTC

Prevention of resistance should rely on the use of first-line NAs with a high barrier to resistance*



*Evidence level I, grade of recommendation 1; †Collation of currently available data – not from head-to-head studies;
‡No evidence of resistance has been shown after 8 years of TDF treatment
EASL CPG HBV. J Hepatol 2017;67:370–98

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TAF vs TDF for treatment of HBV

- **Efficacy in getting to HBV DNA levels <29 IU/mL at 48 weeks of therapy**
- HBeAg-negative, chronic hepatitis B
  - TAF -94%
  - TDF-93%

  Buti M, EASL International Liver Conference. 2016. Barcelona, Spain.
- HBeAg-positive patients
  - TAF – 64%
  - TDF- 67%

    Chan HLY, EASL International Liver Conference. 2016. Barcelona, Spain.

Results of HepB therapy

- On Treatment:
  - HepB eAg seroconversion is seen in -20-25%
  - HepB sAg seroconversion to HBsAb only in -<3%
  - Undetectable Viral Load in upto -90%

First-line Treatment Options for CHB

Status	Treatment	Notes
Preferred	ETV, TAF,* or TDF†	▪ High potency, high genetic barrier to resistance
	PegIFN	▪ Less safe with cirrhosis (reserve for mild CHB), contraindicated with decompensated cirrhosis
Not preferred	LAM, ADV, or TBV	▪ Low genetic barrier to resistance

*Efficacy and safety of TAF have not been established for CHB in patients with decompensated cirrhosis, pregnant women, or children; recommendations for these populations are subsequently limited. †If TDF is chosen, monitor renal function and BMD in at-risk patients.

ETV, TAF, and TDF have very favorable safety and resistance profiles

Terrault. Hepatology. 2018;67:1560. EASL. J Hepatol. 2017;67:370.

Guidelines: HBV Infection and Pregnancy

- All pregnant women should be screened for HBV[1]
- Risk of chronic HBV infection linked to age of exposure; ~ 90% infants, 5% adults[2]
- HBIG and HBV vaccine should be administered to newborns of HBsAg-positive mothers < 12 hrs after delivery
- **Expectant mothers**
  - Treat for HBV as indicated for nonpregnant persons
  - Women who do not meet standard treatment indications should be considered for antiviral prophylaxis in the third trimester if HBV DNA > 200,000 IU/mL

1. Terrault. Hepatology. 2018;67:1560. 2. Weinbaum. MMWR Recomm Rep. 2008;57:1.

Eradication of HBV is rare

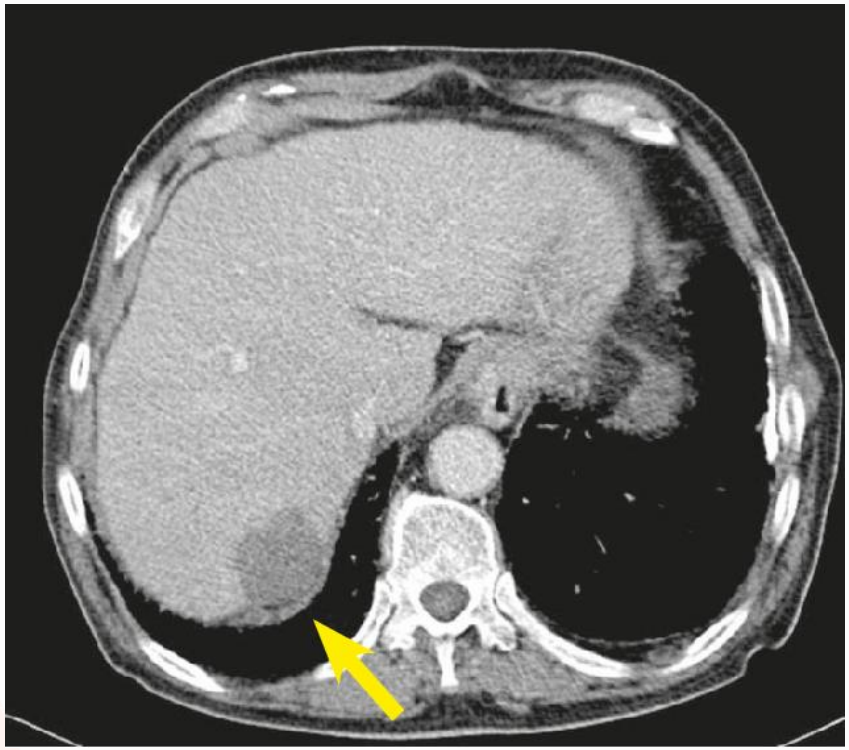
- Even in patients who have cleared hepatitis B
- i.e., HBsAg is negative ; HBsAb- positive
  - Traces of HBV are detectable by serum PCR
  - HBV DNA can be detected in liver tissue
  - HBV specific cytotoxic T cells are present in high numbers suggesting ongoing activation

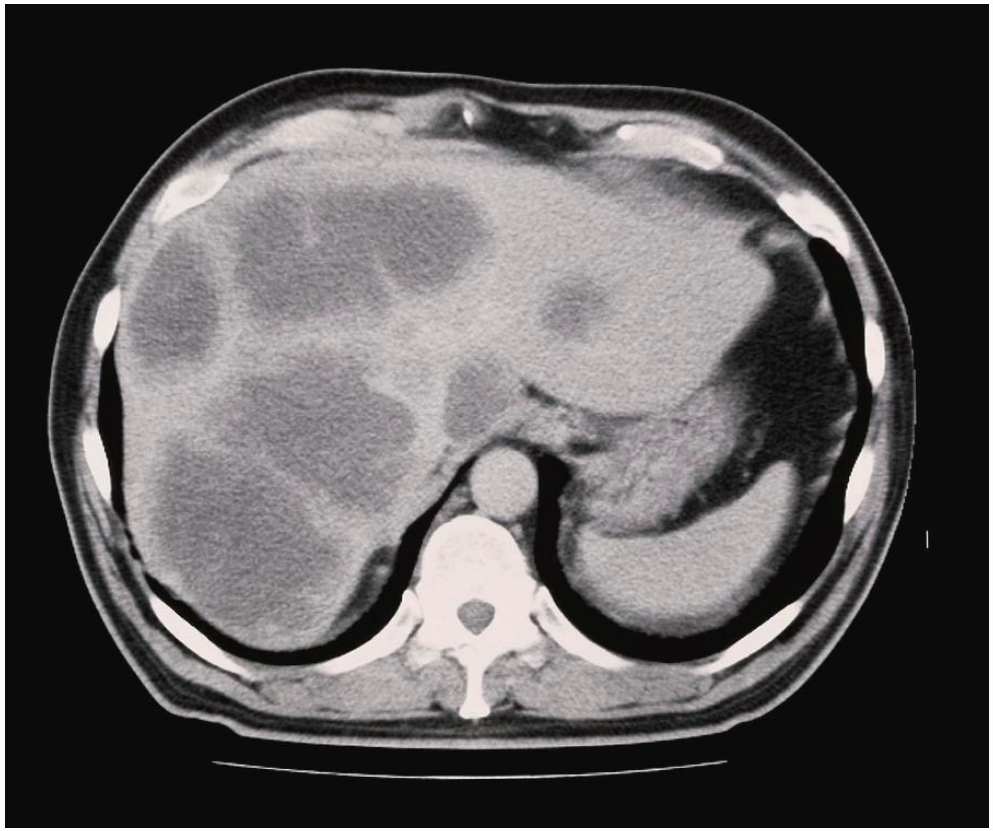
General comments on HepB therapy

- Counsel avoidance of alcohol
- Vaccinate against hepatitis A (if not immune)
- On Treatment:
  - HepB eAg seroconversion is seen in 20-25%
  - HepB sAg seroconversion to HBsAb in <3% (More in Western populations- upto 20%)
  - Complete virological supression (HBV DNA) is seen in upto 90% with oral nucleotid(s)e therapy
  - Improves long term survival

HBV and Hepatocellular carcinoma

- The majority of patients with HBV who develop HCC will have cirrhosis
- In addition to cirrhosis, other HBV-related factors that were associated with HCC risk include
  - High viral load (ie, HBV DNA levels >10^6 copies /mL)
  - HBeAg positivity (an indicator of a prolonged replication phase)
  - HBsAg levels >1000 IU/mL in patients with HBeAg negative chronic HBV with low viral load (ie, inactive chronic HBV)
  - HBV genotype C
  - Male sex (for patients who are HBsAg positive)
  - Viral coinfection (HCV or hepatitis D virus)
  - Blood group B
  - Family history of HCC





- If the imaging characteristics are consistent with HCC and the AFP is >400 ng/mL, a biopsy may not be necessary in all patients,

Who is at Risk for HBV reactivation?

- Patients who test positive for both anti-HBc and HBsAg
- Immunosuppressive therapy
  - Rituximab and other drugs that target B lymphocytes
  - high-dose steroids
  - Anti-TNF agent
  - Chemo
- HIV infected patients who have discontinued therapy with antiretroviral drugs that also have activity against HBV
  - TDF, TAF
- Solid organ or bone marrow transplantation
- **While on treatment for HCV.**

Risk for HBV Reactivation

- All HIV patients starting HCV medications should be assessed for HBV co-infection
  - HBsAg, anti-HBs, and anti-HBc testing
  - Anti-HBs negative → receive anti-HBV vaccination

- Accordingly, persons with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes **two agents** with anti-HBV activity prior to initiating HCV therapy

AASLD/IDSA HCV Guidelines. 2018.

Figure 3.1. Reported number of acute hepatitis B cases— United States, 2001–2016

Source: National Notifiable Diseases Surveillance System (NNDSS)

Hepatitis B Vaccine Approved in 2017

- Recombinant single-antigen formulation with a unique CpG adjuvant is the first new HBV vaccine approved for US adults in > 25 yrs
  - Requires 2 doses (vs 3 doses for previously available vaccines)
  - Can be completed in 1 mo (vs 6 mos for previously available vaccines)
- Other HBV vaccines for adults remain effective
  - 2 single-antigen formulations, 1 combination with hepatitis A

Schillie. MMWR Morb Mortal Wkly Rep. 2018;67:455. Schillie. MMWR Recomm Rep. 2018;67:1.

Hepatitis C Screening Recommendations

Population	Recommendation	Grade (What's This?)
Adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B

One-Time Hepatitis C Testing

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	RATING
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years and older.	I, B
One-time HCV testing should be performed for all persons less than 18 years old with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).	I, B
Periodic repeat HCV testing should be offered to all persons with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).	IIa, C
Annual HCV testing is recommended for all persons who inject drugs and for HIV-infected men who have unprotected sex with men.	IIa, C

Treatment-Naïve Patients: AASLD-IDSA Recommended HCV Regimens

- SVR12 rates for all recommended regimens for HCV genotype 1: ≥95%

		Treatment Duration (weeks)	
Genotype	**Regimen**	**No Cirrhosis**	**Compensated Cirrhosis**
1	Glecaprevir/pibrentasvir	8	8
	Sofosbuvir/velpatasvir	12	12
	Ledipasvir/sofosbuvir	8* or 12	12
	Elbasvir/grazoprevir	12†	12†

*Only for patients who are HIV-uninfected and have a baseline HCV RNA <6M IU/mL.
†Only for genotype 1a patients without baseline NS5A RASs for elbasvir.

AASLD-IDSA. http://www.hcvguidelines.org/full-report-view. Version November 6, 2019.

Recommendations for When and in Whom to Initiate HCV Treatment

- Treatment is recommended for all patients with chronic HCV infection, regardless of genotype
  - Exception: life expectancy likely to be short despite treatment or transplantation
- Goal of treatment is SVR
  - Sustained virological response: no HCV detected in the blood 3 months after treatment completion

Benefits of HCV Cure

- Reduction in overall mortality regardless of severity of liver disease
- 84% reduction in incident hepatocellular carcinoma
- Decrease in liver inflammation (reduced AST/ALT)
- Reduction in liver fibrosis progression
- Reduces symptoms and mortality from extra-hepatic manifestations
- Substantially improved quality of life

AASLD-IDSA. http://www.hcvguidelines.org/full-report-view. Version November 6, 2019.
Backus LI, et al. *Hepatology*. 2019;69:487-497.
Backus LI, et al. *Hepatology*. 2018;68:827-838.
Ioannou GN, et al. *Gastroenterology*. 2019;156:446-460.

Pretreatment Laboratory Testing

Within 6 mo of treatment (no cirrhosis) & 3 mo (cirrhosis):

- CBC
- Hepatic function panel
- eGFR
- Cirrhosis (need INR)

Anytime prior to starting antivirals therapy:

- Quantitative HCV RNA
- HIV antigen/antibody
- Hepatitis B surface antigen

Prior to starting antiviral therapy:

- Serum pregnancy test and counseling regarding risk of HCV drugs in pregnancy

CASE PRESENTATIONS

Case 218 – Dr. Adebajo

Baseline Demographics					
Age: 64	**Race:** Black	**Gender:** Female		**Primary Insurance:** Medicaid	
PMH/Comorbidities/Substance Use: None					
Pertinent Clinical Findings: None					
Weight (kg):	Not provided	**Serum Albumin:**	Not provided	**ALT:**	145
Hgb:	14.9	**Total bilirubin:**	0.4	**AST:**	92
PLT:	112	**INR:**	1.1	**SCr/CrCl:**	0.84/----

Case 218 – Dr. Adebajo

HCV Evaluation					
Ultrasound: Pending	**CT:** Not done				**MRI:** Not done
Signs of Cirrhosis:	None				
Staging Modality:	**Results:**	**Interpretation:**		**APRI:**	2.05
Fibroscan/Transient Elastography:	Pending	-----		**FIB-4:**	4.37
Fibrosure:	0.73	F3-F4, severe necroinflammatory activity (0.87)			
Treatment Naïve?:	Yes	**If no, previous treatment:** N/A		**HIV Antibody:**	Negative
HCV Genotype:	**1a**	**HCV RNA:**	18,800,000	**HAV | Total Ab:**	Negative
HBV | sAb:	Positive	**HBV | sAg:**	Negative	**HBV | Total cAb:**	Non-reactive
Requested Regimen:	Epclusa x 12, Mavyret x 8 weeks				

Case 218 – Dr. Adebajo

- **Medication List:**
  - Amlodipine 2.5 mg daily
  - Flonase as needed

- **Clinical considerations:**
  - GT1a
  - Treatment naïve
  - Compensated cirrhosis
    - Platelets 112
  - HBV sAb positive – immune
  - Received 1st dose of HepA vaccine (Havrix® or Vaqta®) – needs 2nd dose 6 months after first dose

Liver Staging Modalities

APRI:	2.05
FIB-4:	4.37

Fibrosure:	0.73	F3-F4, severe necroinflammatory activity (0.87)

APRI; FIB-4

- APRI
  - **<0.5/0.7 Low likelihood of fibrosis**
  - **>1.5 High likelihood of cirrhosis**
- FIB-4
  - **<1.45 Low likelihood of fibrosis**
  - **>3.25 High likelihood of cirrhosis**

FibroSURE™

- Measurement of:
  - Alpha-2 macroglobulin, haptoglobin, GGT, ALT, apolipoprotein A1
  - Fibrosis score and inflammation score
  - **0.72-0.74 consistent with F3-F4**

FibroScan®

- Ultrasound Transient elastography
- Non-invasive
- As accurate in measuring degree of liver inflammation and fibrosis as biopsy
- **>9.5 is considered F3**
- **>12.5 is consistent with cirrhosis (F4)**

Brown et al. *J Hepatol*. 2019;S0168-8278(19)30647-6.

Additional Pretreatment Assessment: Child-Turcotte-Pugh

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	Points		
	1	2	3
Encephalopathy	None	Grade 1 or 2	Grade 3 or 4
Ascites	None	Diuretic Responsive	Diuretic Refractory
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Prothrombin Time Seconds Prolonged or INR	<4 <1.7	4-6 1.7-2.3	>6 >2.3

Albumin not provided

Class A = 5-6 points
Class B = 7-9 points
Class C = 10-15 points

Cirrhosis with CTP Class B and C is considered decompensated

Pugh RN et al. Br J Surg. 1973;60:646-9.

Recommendations

Recommended regimens listed by evidence level and alphabetically for:

Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[b] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c]	8 weeks	I, B

[a] For decompensated cirrhosis, please refer to the appropriate section.

[b] Includes genotype 1a RASs at amino acid position 28, 30, 31, or 93 known to confer antiviral resistance. If 1 or more RASs are present, another recommended regimen should be used.

[c] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information. For patients with HIV/HCV coinfection, a treatment duration of 12 weeks is recommended.

- **GT1a, tx naïve, with compensated cirrhosis**
  - **No drug-drug interactions requiring dosing adjustments**
- *All of the above are valid options*
  - Different payers have different requirements & agents of choice

Recommendations

- GT1a, treatment naïve, compensated cirrhotic
  - Epclusa® (SOF/VEL) x 12 weeks
  - Mayvret ® (GLE/PIB) x 8 weeks
  - Harvoni ® (LDV/SOF) x 12 weeks
  - Zepatier ® (EBV/GZR)- need resistance testing since GT1a

- HAV vaccination series in process

Case 224 – Dr. Christian Reinholz

Baseline Demographics					
Age: 57	**Race:** Black	**Gender:** Female		**Primary Insurance:** Medicaid	
PMH/Comorbidities/Substance Use: Stroke/CVA or TIA					
Pertinent Clinical Findings: None					
Weight (kg):	57.27	**Serum Albumin:**	4	**ALT:**	26
Hgb:	12.6	**Total bilirubin:**	0.4	**AST:**	27
PLT:	263	**INR:**	1.1	**SCr/CrCl:**	0.67/83.8 ml/min

Case 224 – Dr. Christian Reinholz

HCV Evaluation					
Ultrasound: Pending	**CT:** Not done				**MRI:** Not done
Signs of Cirrhosis:	None				
Staging Modality:	**Results:**	**Interpretation:**		**APRI:**	0.26
Fibroscan/Transient Elastography:	Not done	-----		**FIB-4:**	1.15
Fibrosure:	Yes	0.18 F0, severe NI activity (0.11)			
Treatment Naïve?:	Yes	**If no, previous treatment:** N/A		**HIV Antibody:**	Negative
HCV Genotype:	1b	**HCV RNA:**	1,310,000	**HAV | Total Ab:**	Negative
HBV | sAb:	Not provided	**HBV | sAg:**	Negative	**HBV | Total cAb:**	Not provided
Requested Regimen:	Mavyret® x 8 weeks				

Case 224 – Dr. Christian Reinholz

- **Medication List:**
  - Baclofen 10 mg q AM & PM, 20 mg QHS
  - Lisinopril 20 mg daily
  - Celexa 40 mg daily
  - Magnesium 400 mg daily
  - Pravastatin 20 mg daily
  - Aspirin 81 mg daily
  - Vitamin D3 1000 units daily

- **Clinical considerations:**
  - GT1b, tx naïve, non-cirrhotic
  - Simplified pathway
  - Drug interactions
  - Vaccination as necessary

Estimated Timing of HCV Elimination: South Region of Appalachia

- Projected HCV elimination achievement in the United States: 2037
  - Diagnosis target (2027), incidence (2037), treatment (2033), HCV-mortality (2020)
- Only 3 states are on track to meet all 4 HCV targets by 2030
  - South Carolina, Connecticut, Washington

Projected Year of Meeting HCV Targets

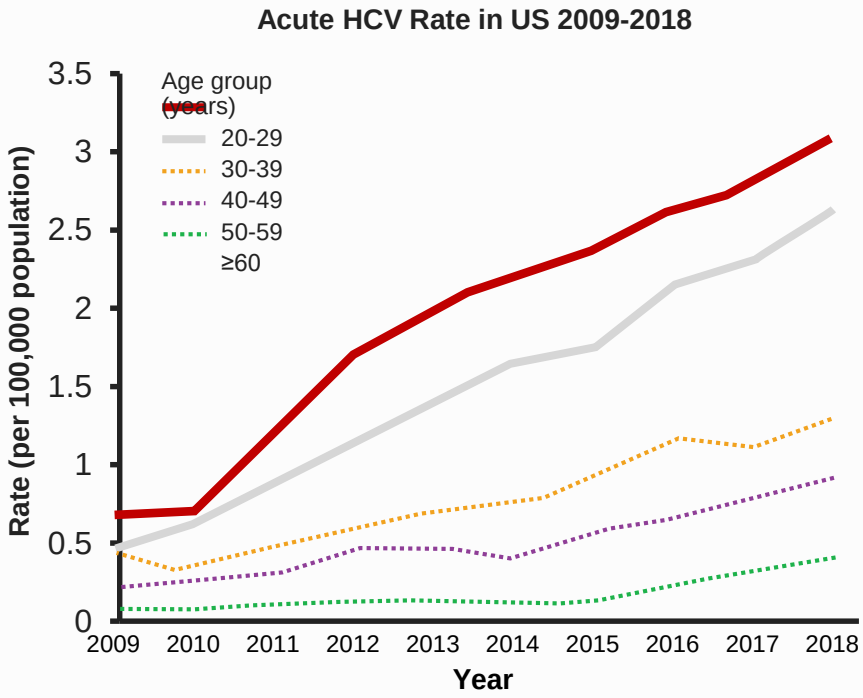
	Alabama	Georgia	Mississippi	South Carolina
Incidence	**2034**	**2039**	**2031**	2030
Liver-related mortality	2020	2019	2019	2019
Diagnosis	2025	2026	2025	2026
Treatment	**2031**	2030	2028	2027
HCV elimination	**2034**	**2039**	**2031**	2030

Markov disease-progression model was used and expanded to simulate HCV progression over time (50 states, Washington, DC, and Puerto Rico).

Sulkowski MS, et al. *J Hepatol.* 2020;73(suppl 1):S323. Abstract THU375.

Changing Trends:
Acute HCV in the United States (2009-2018)

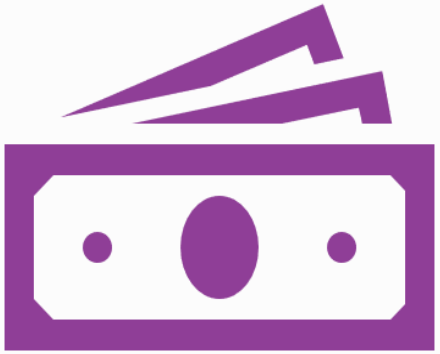
- New acute HCV infections in 2018
  - Reported cases (n=3621)
  - Estimated (n=50,300, adjusted for under-ascertainment and under-reporting)
- 3-fold increase in new cases since 2009
  - Reflects new infections associated with rising rates of injection-drug use
- Most newly acquired acute HCV infections occurred among young, white, PWIDs, who live in non-urban areas (ie, Appalachian, Midwestern, and New England states)



Ryerson AB, et al. *MMWR Morb Mortal Wkly Rep*. 2020;69:399-404.

Barriers to Treatment

- Financial Burden
- Access to Care



Simplified Approach again may assist with limiting visits as well as labs, therefore decreasing costs

On Treatment Monitoring Minimal Requirements

- Monitoring for hypoglycemia - in diabetics.
- Monitoring INR - if on warfarin.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

- **No laboratory monitoring is required for other patients.**
- **This is an update with the Simplified Approach for non-cirrhotic patients**
- **Not universally accepted by payers, requirements may still exist monitoring**
  - **For example, HCV VL**

Which Therapies Can Be Used For All Genotypes?

	GT 1	GT 2	GT 3	GT 4	GT 5	GT 6
GZR/EBR (Zepatier®)	✓			✓		
*GLE/PIB (Mavyret®)	✓	✓	✓	✓	✓	✓
SOF/LDV (Harvoni®)	✓			✓	✓	✓
*SOF/VEL (Epclusa®)	✓	✓	✓	✓	✓	✓
*SOF/VEL/VOX (Vosevi®)	✓	✓	✓	✓	✓	✓

***Pan-genotypic**

HCV Guideline Recommendations

Recommended regimens listed by evidence level and alphabetically for:

Treatment-Naive Patients Genotype 1b Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)	12 weeks[a]	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are HIV-uninfected and whose HCV RNA level is <6 million IU/mL	8 weeks[c]	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A

[a] An 8-week regimen can be considered in those with genotype 1b infection and mild fibrosis (see text for details).

[b] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

[c] For HIV/HCV coinfected patients, a treatment duration of 12 weeks is recommended.

HCV DAA Drug Interactions - HMG-CoA Reductase Inhibitors

	Rosuvastatin	Atorvastatin	Pravastatin	Lovastatin	Simvastatin	Pitavastatin
Ledipasvir	Not recommended	Lowest dose, Monitor	Lowest dose, Monitor	Lowest dose, Monitor	Lowest dose, Monitor	Lowest dose, Monitor
Velpatasvir	Max 10mg	Lowest dose, Monitor	OK	Monitor	Lowest dose, Monitor	Lowest dose, Monitor
Pibrentasvir/ glecaprevir	Max 10mg	Not recommended	Max 20mg Reduce 50%	Not recommended	Not recommended	Monitor
Elbasvir/ grazoprevir	Max 10mg	Max 20mg	OK	Max 20mg	Max 20mg	OK
Velpatasvir/ Voxilaprevir/ Sofosbuvir	Not recommended	Lowest dose, Monitor	Max 40mg	Lowest dose, Monitor	Lowest dose, Monitor	Not recommended

Chauvin et al. Clin Pharmacokinet. 2013 Oct;52(10):815-31.

DAA- Direct-acting Antiviral

Recommendations

- GT1b, treatment naïve, non-cirrhotic, on statin therapy
  - Epclusa® (SOF/VEL) x 12 weeks
  - Harvoni® (LDV/SOF) x 12 weeks
    - 8-week course if HCV RNA <6 million IU/mL
  - Mayvret® (GLE/PIB) x 8 weeks
    - Requested regimen
  - Zepatier® (EBV/GZR) x 8-12 weeks
- HAV/HBV vaccination
  - HBV testing needed

AETC AIDS Education & Training Center Program Southeast

Monthy 1st and 3rd Wednesday and
12:00pm-1:00pm EST
11:00am-12:00pm CST
09:00am-10:00am PST

4th Wednesday
12:00pm-1:00pm CST
01:00pmpm-2:00pm EST
10:00am-11:00am PST

South East Viral Hepatitis Interactive Case Conference