Hepatitis B and Hepatitis C for the Non-specialist

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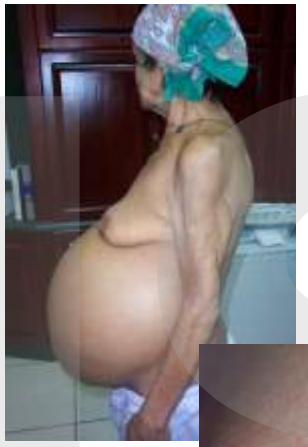
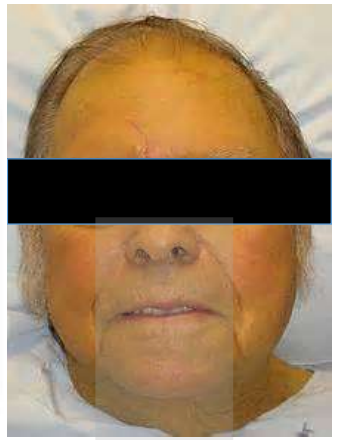
Case #1

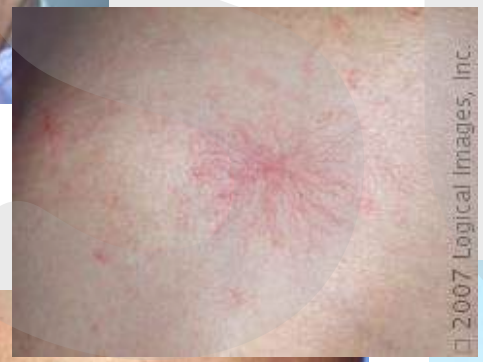
- You are seeing a 55yo male as a new patient in your clinic
- He has a history of hepatitis C
- No current EtOH, quit 2 years ago
  - Prior to that he was drinking 6 beers a day
- He also reports that he was once told he might have had hepatitis B
- Next steps?

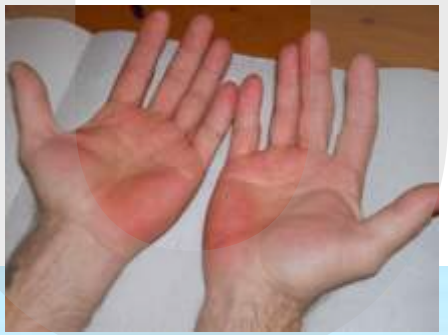
First things first…Does the patient have cirrhosis?

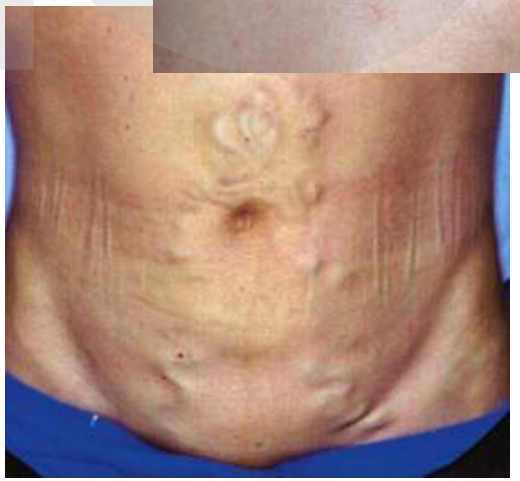
- Exam- muscle wasting, spider angiomata, palmar erythema, hyperestrogenemic findings
- Laboratory Data- PLT, INR, **flip-flop in the AST/ALT ratio**
- Imaging (U/S, CT)- nodular liver, caudate hypertrophy, splenomegaly, signs of portal hypertension (varices)
- This hepatologist's approach, choice of 1st imaging test
  - Mild disease suspected → U/S liver
  - Cirrhosis suspected → Multiphase CT of the liver (liver morphology and evaluate for HCC at time of diagnosis of cirrhosis)

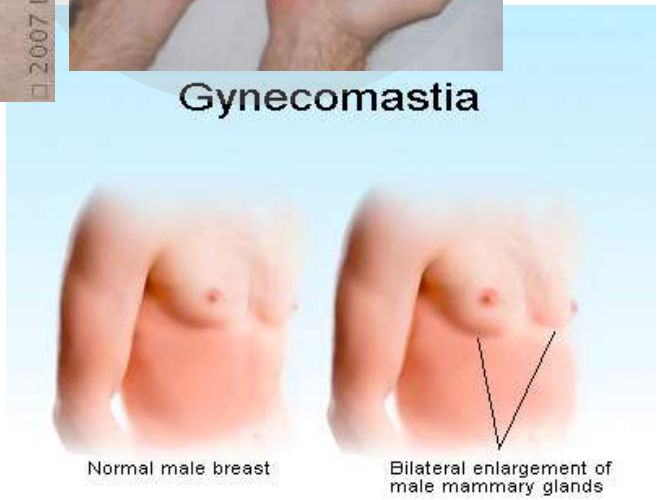




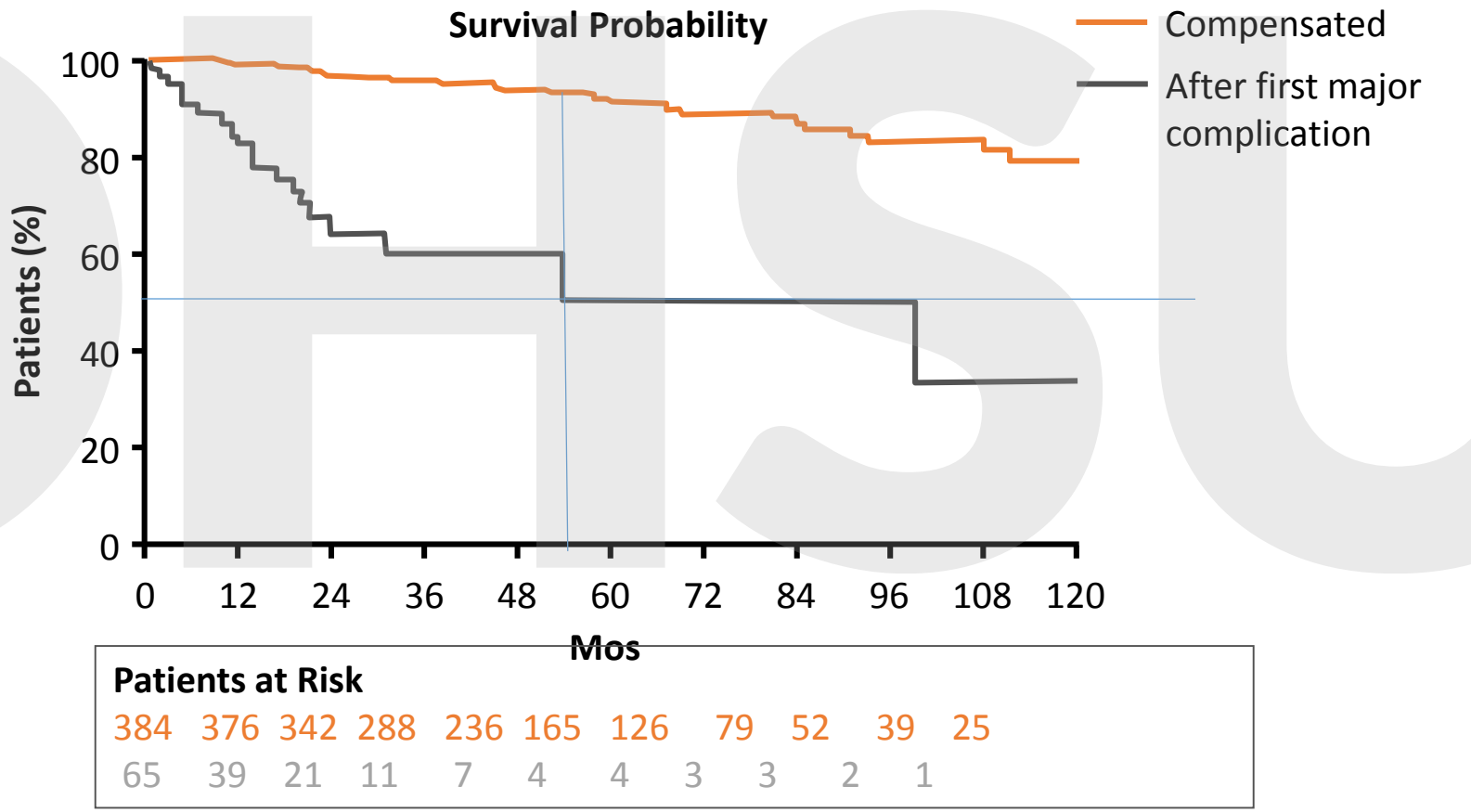








First decompensation of liver disease is a poor prognosticator



Fattovich G, et al. Gastro1997; 112: 463-472

Fibrosis Assessment: Liver Biopsy

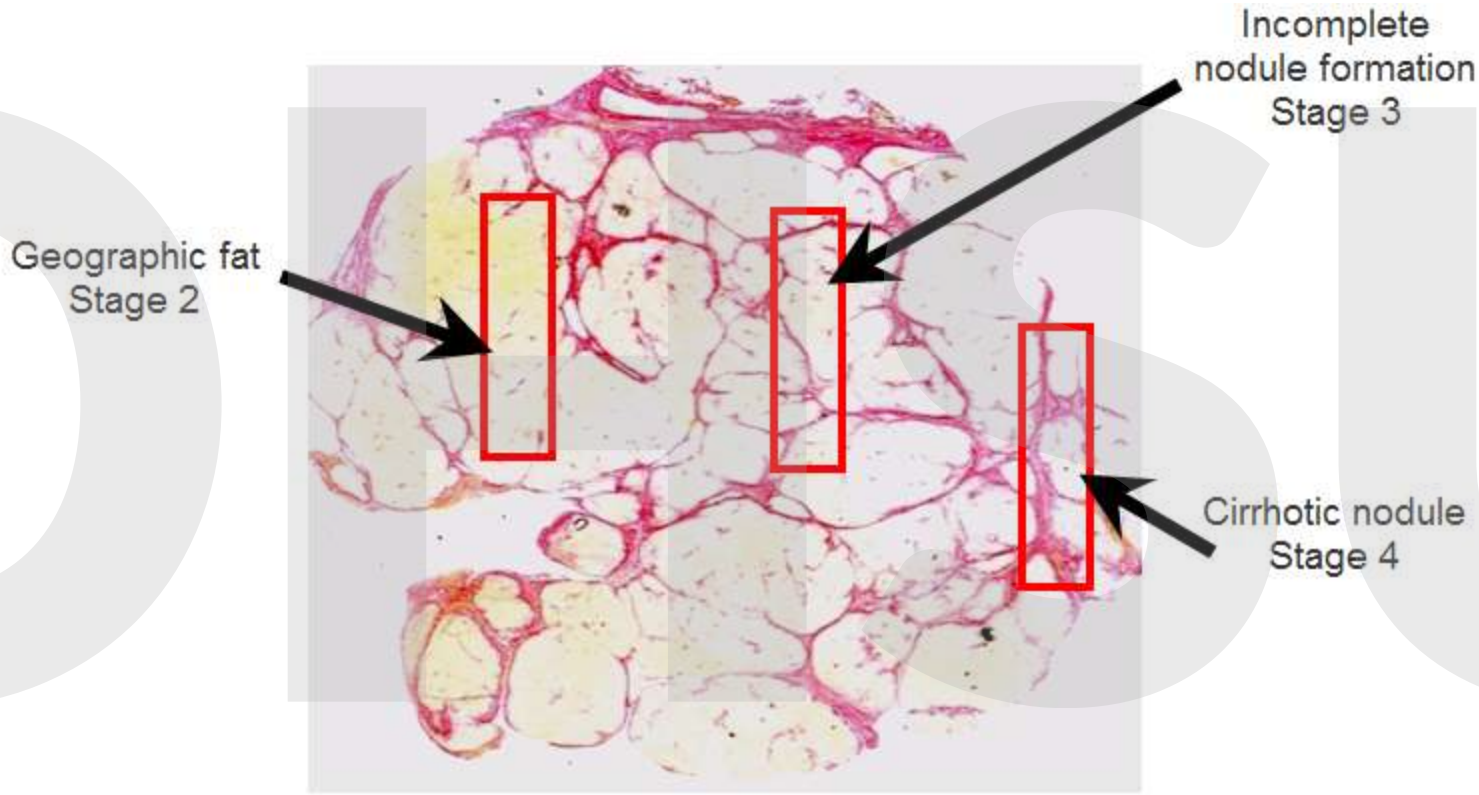
PRO

- Provides greatest amount of information compared to other methods of assessment
- Can assist in
  - Defining etiology of liver disease
  - Fibrosis stage
  - Inflammatory grade
- May assist in determining prognosis (disease activity, recovery from injury)

CON

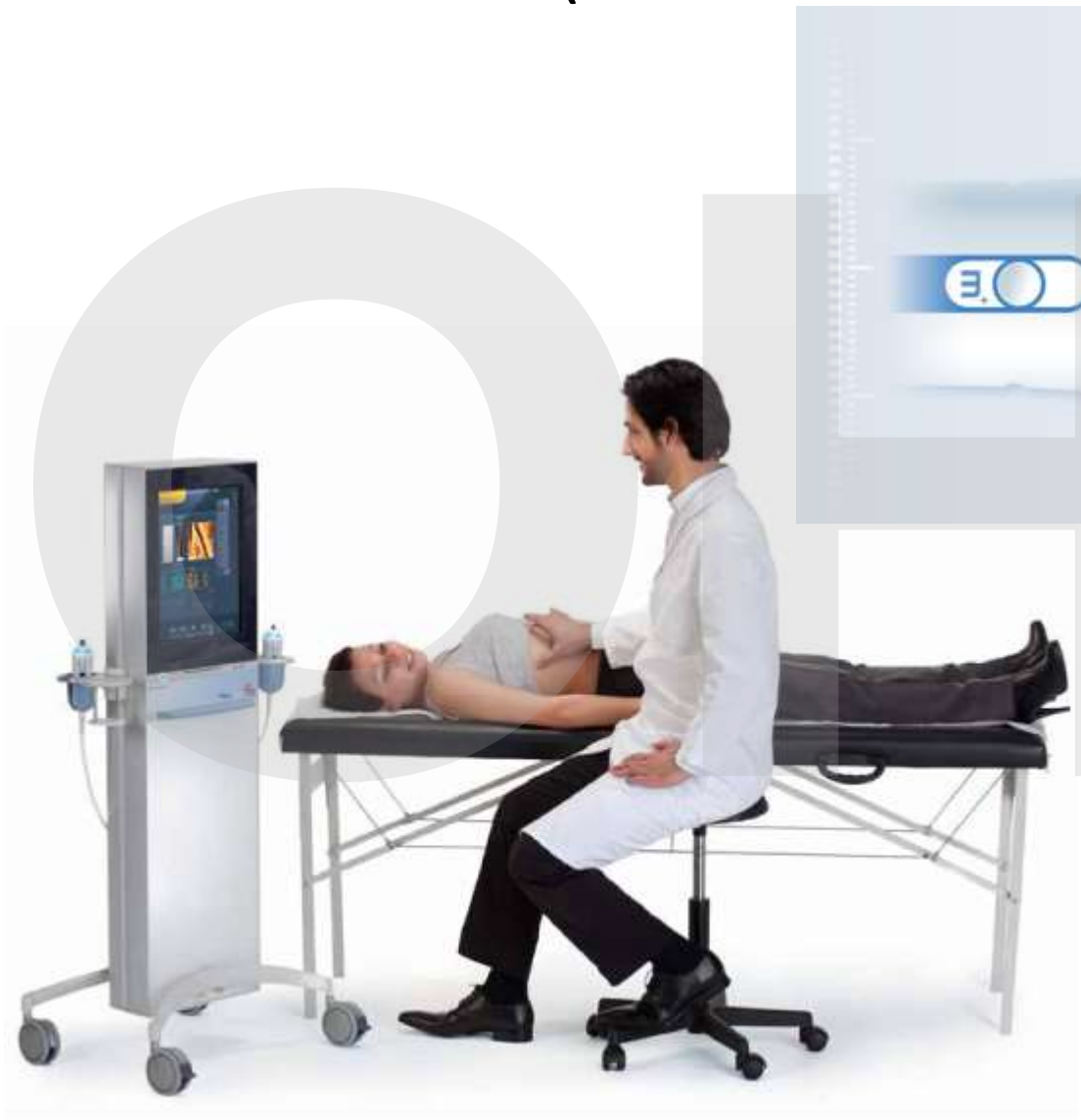
- Risk
  - 1:1000 risk of bleeding
  - 1:2000 risk of infection
  - 1:2000 risk of injury to adjacent organ
  - 1:10,000 chance of death
- Sampling Error
  - Geographic variation in fibrosis and fat
  - Up to a 30% chance of sampling error
  - “Inter-observer” variation
- Result is often descriptive rather than clearly diagnostic

Potential for Sampling Error in Liver Biopsies



Bedossa P, et al. Hepatology. 2003;38:1449-1457.

Fibroscan (Transient Elastography)



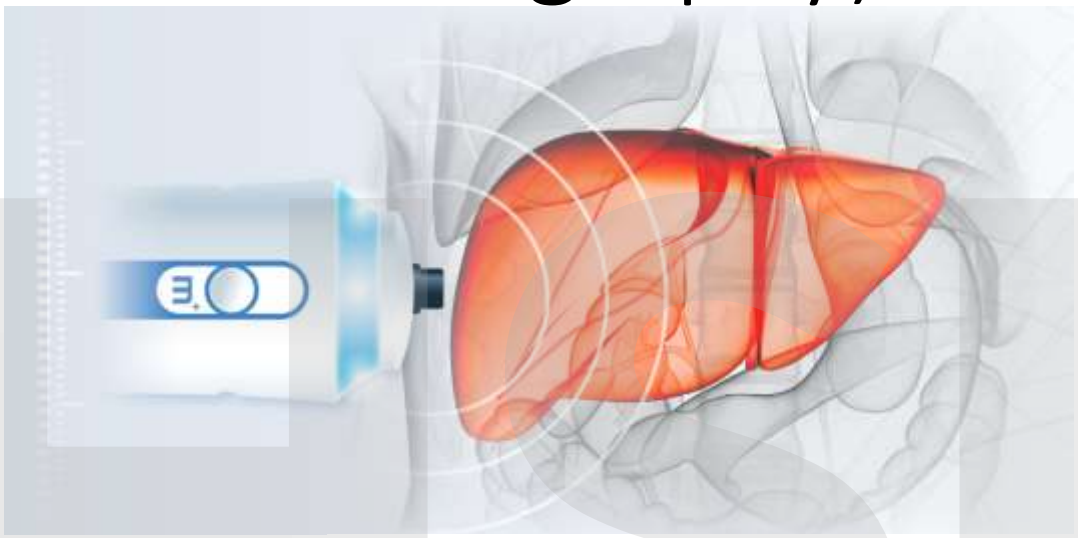


Table 1 Recommended values for different stage of fibrosis

Disease	F0–F1 (Kpa)	F2 (Kpa)	F3 (kpa)	F4 (kpa)
Hepatitis B	≤6.0	≥6.0	≥9.0	≥12.0
Hepatitis C	≤7.0	≥7.0	≥9.5	≥12.0
HCV–HIV coinfection	≤7.0	≤10	≥11.0	≥14.0
Cholestatic liver disease	≤7.0	≥7.5	≥10.0	≥17.0
NAFLD/NASH	≤7.0	≥7.5	≤10	≥14.0

Bonder A, Afdhal N, Curr Gastroenterol Rep (2014) 16:372

FIB-4 (Fibrosis-4)

- **Formula :**

  (Age x AST) / (Platelets x (sqr (ALT))

- **Explanation of Result**
  - **NASH :**
    - Fib4 score < 1.30 = F0-F1
    - Fib4 score > 2.67 = F3-F4
  - **HCV :**
    - Fib4 score < 1.45 = F0-F1
    - Fib4 score > 3.25 = F3-F4

Martínez SM1et al. Noninvasive assessment of liver fibrosis. Hepatology. 2011

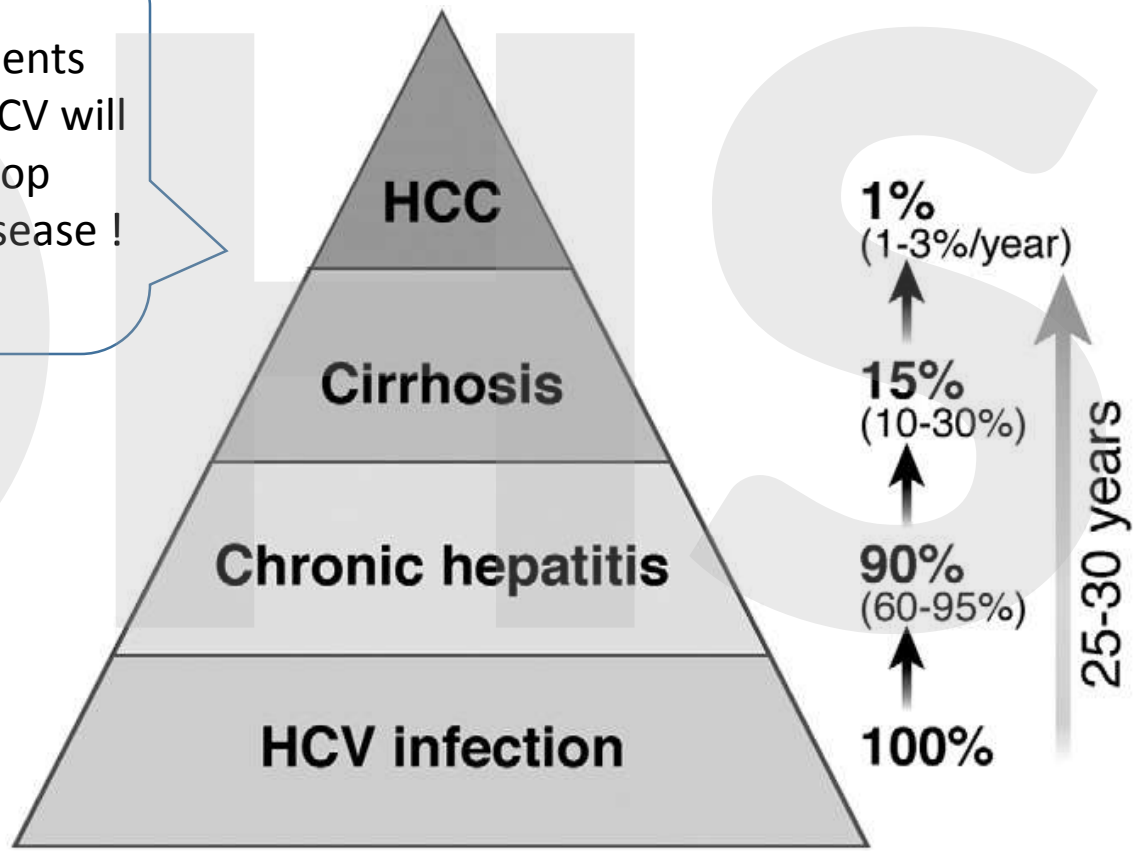
Bottom Lines…

- Clinical/Lab/Imaging all support diagnosis of cirrhosis
  - Diagnosis made!
  - HCC surveillance- regardless of etiology of liver disease
    - U/S of the liver with or without AFP every 6 months
  - EGD for variceal screening
- Making the diagnosis of cirrhosis is potentially the most important component of the initial evaluation of a patient with chronic liver disease
- If no evidence of cirrhosis with clinical data/labs/imaging, risk stratify by assessing degree of fibrosis:
  - Fibroscan
  - Fib-4
  - (Liver biopsy)

Hepatitis C

Natural History

75% of patients exposed to HCV will not develop significant disease !



El Serag, Gastro 2007

HCV Screening Guidelines

HCV Screening Guidelines From AASLD/IDSA/IAS-USA, CDC, and USPSTF

Age-based	• One-time screening for adults born between 1945 and 1965[1-3]
Risk-based	• Past or current injection drug use[1-3] or intranasal drug use[1,3]
	• Long-term kidney dialysis[1-3]
	• Recipients of: transfusion of blood or blood component, organ transplant before July 1992,[1-3] clotting factor concentrate before 1987;[1,2] blood from a donor who later tested HCV-positive[1,2]
	• Healthcare worker exposed to HCV-infected blood[1-3]
	• Receipt of an unsterile/unregulated tattoo[1,3]
	• Children born to HCV-infected mothers[1-3]
	• Incarceration[1,3]
Other medical conditions	• HIV infection[1,2]
	• Unexplained chronic liver disease, including persistently elevated ALT[1,2]

ALT = alanine aminotransferase; AASLD, IDSA, IAS-USA = The American Association for the Study of Liver Diseases, the Infectious Diseases Society of America, and the International Antiviral Society-USA; CDC = Centers for Disease Control and Prevention; HIV = human immunodeficiency virus; USPSTF = US Preventive Services Task Force.

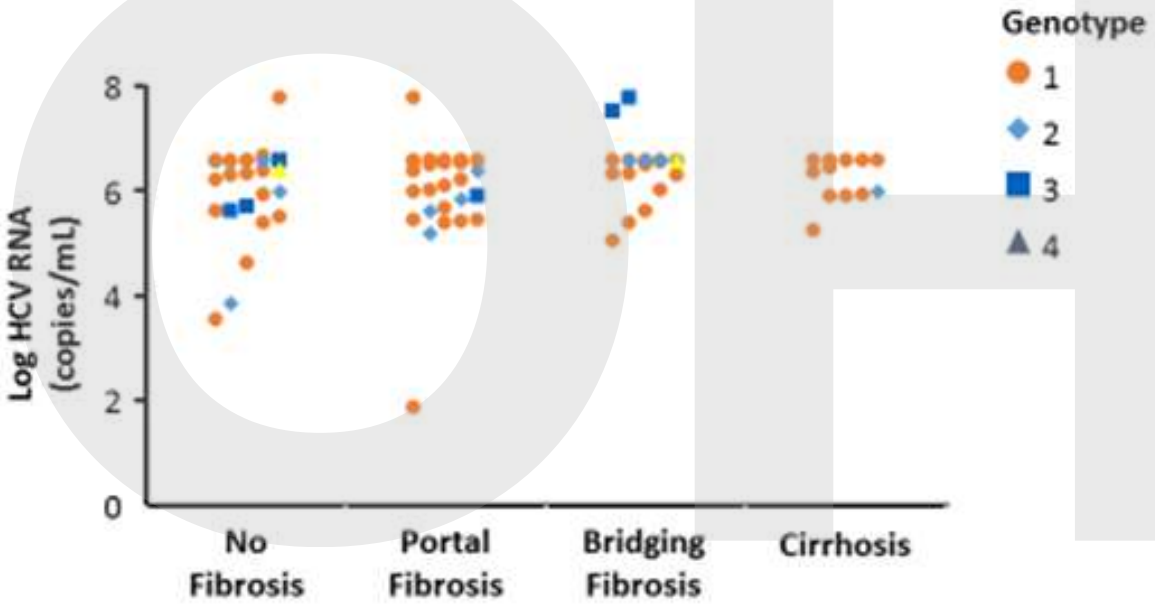
1. AASLD, IDSA, IAS-USA. Recommendations for testing, managing, and treating hepatitis C. 2014. www.hcvguidelines.org. Accessed May 27, 2014; 2. CDC Testing Recommendations for Chronic Hepatitis C Virus Infection. January 17, 2012. www.cdc.gov/hepatitis/hcv/guidelinesc.htm. Accessed April 22, 2014; 3. Moyer VA, et al. *Ann Intern Med.* 2013;159:349-357.

HCV Tests: What the Results Mean

TEST	NOTES
HCV Antibody	Exposure to virus Does not confer immunity
HCV RNA PCR (QUANT)	Amount of virus in the blood Confirms presence of infection
HCV QUAL	Mostly an antiquated test Detectable virus below the limit of detection
HCV genotype	Impacts treatment regimen

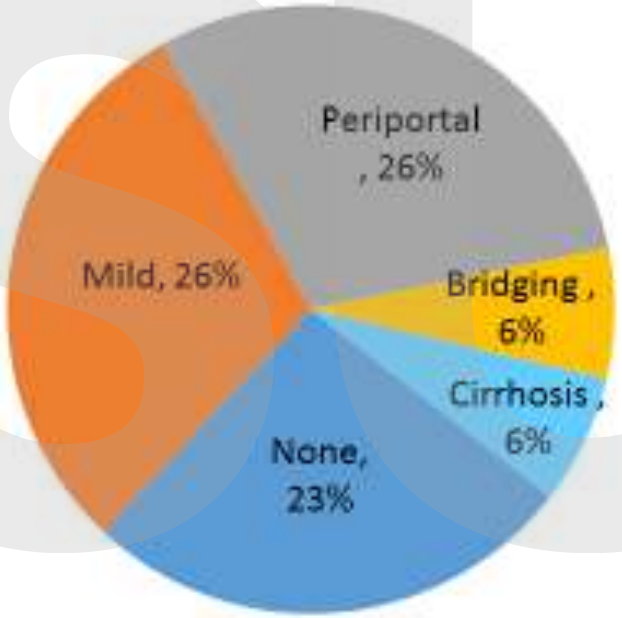
Anti-HCV	HCV RNA	Interpretation
+	+	Acute or chronic HCV depending on the clinical context
+	–	False positive HCV antibody Resolved infection (Low-level intermittent viremia)
–	+	Early acute HCV infection Chronic HCV in setting of immunosuppressed state False positive HCV RNA test
–	–	Absence of HCV infection

HCV viral load does *not* predict fibrosis



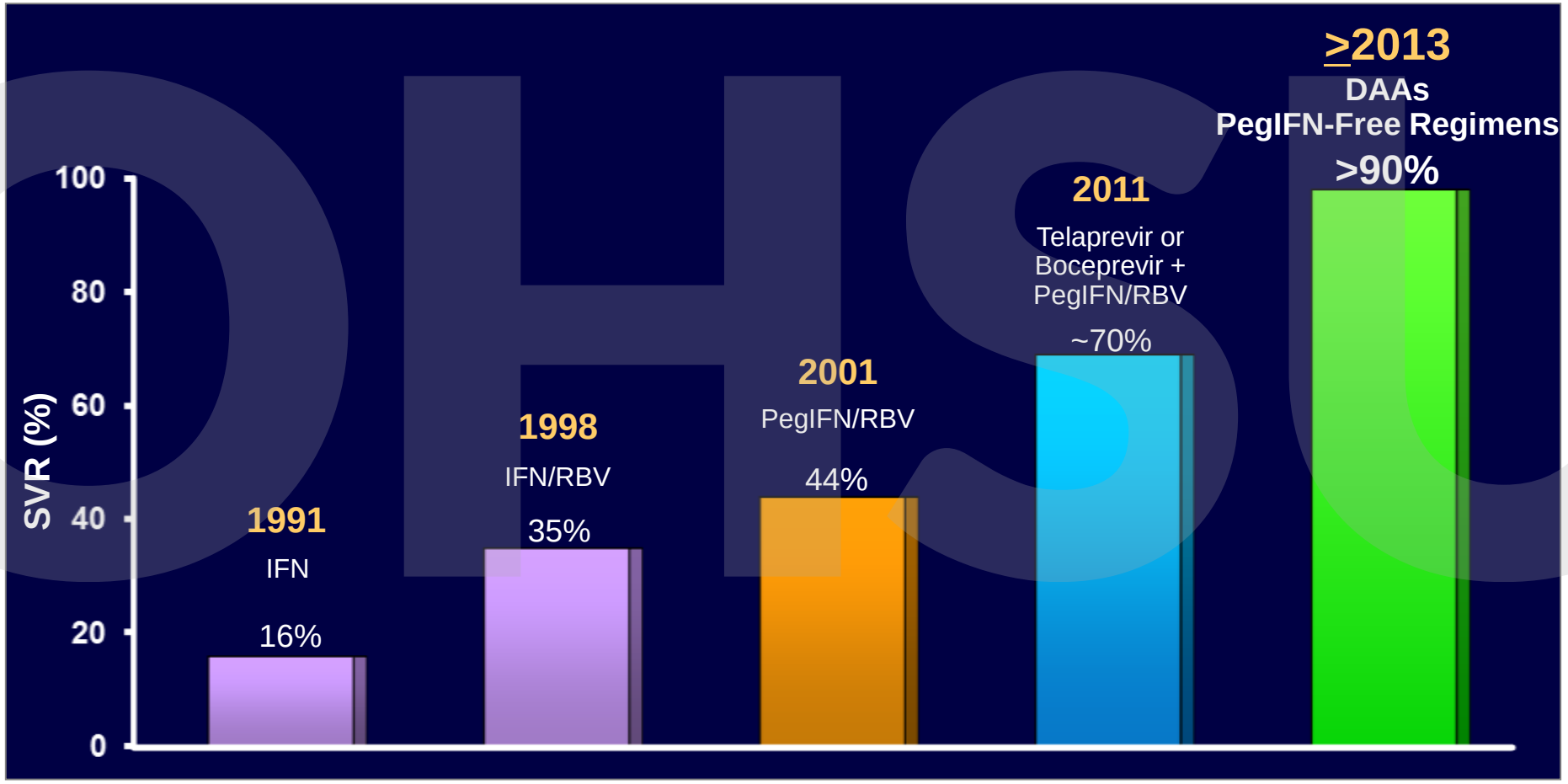
Ferreira-Gonzalez A, et al. Semin Liver Dis. 2004;24(Suppl 2):9-18.

Fibrosis can be present despite normal liver tests



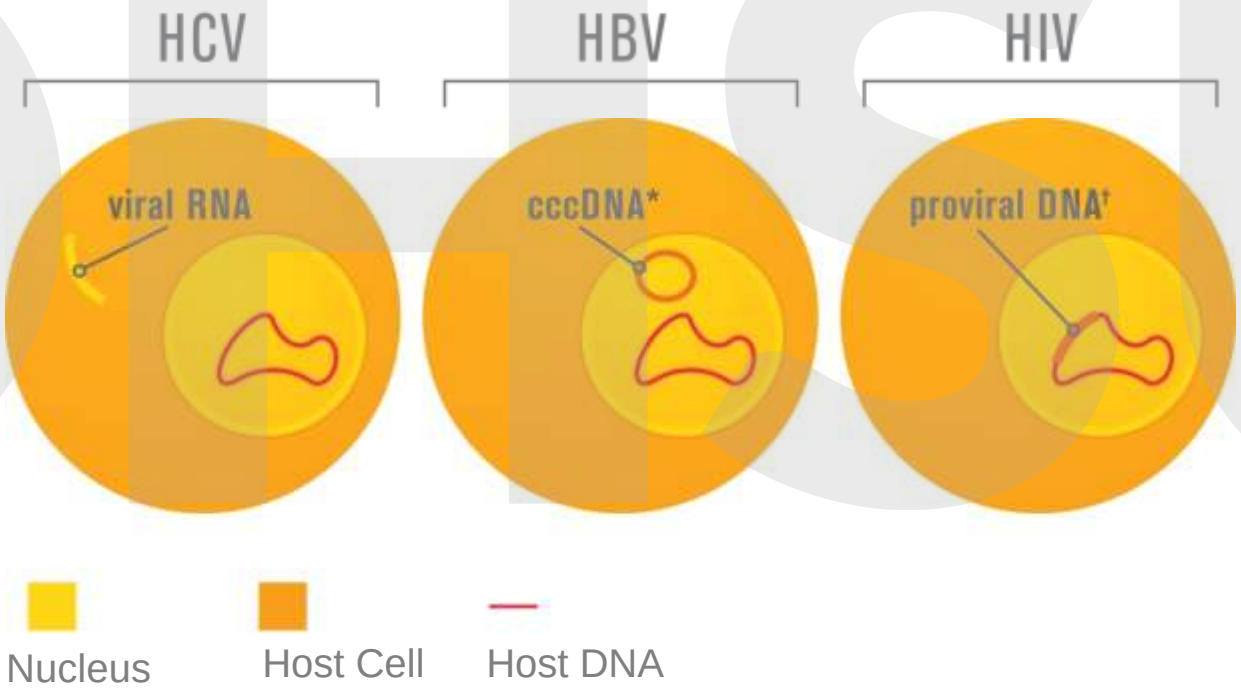
Schiffman et al. J Infect Dis. 2000; 182: 1595-1601

Chronic HCV Therapy: Presently High Cure Rates with Direct Acting Antivirals



Why Is Cure Possible?

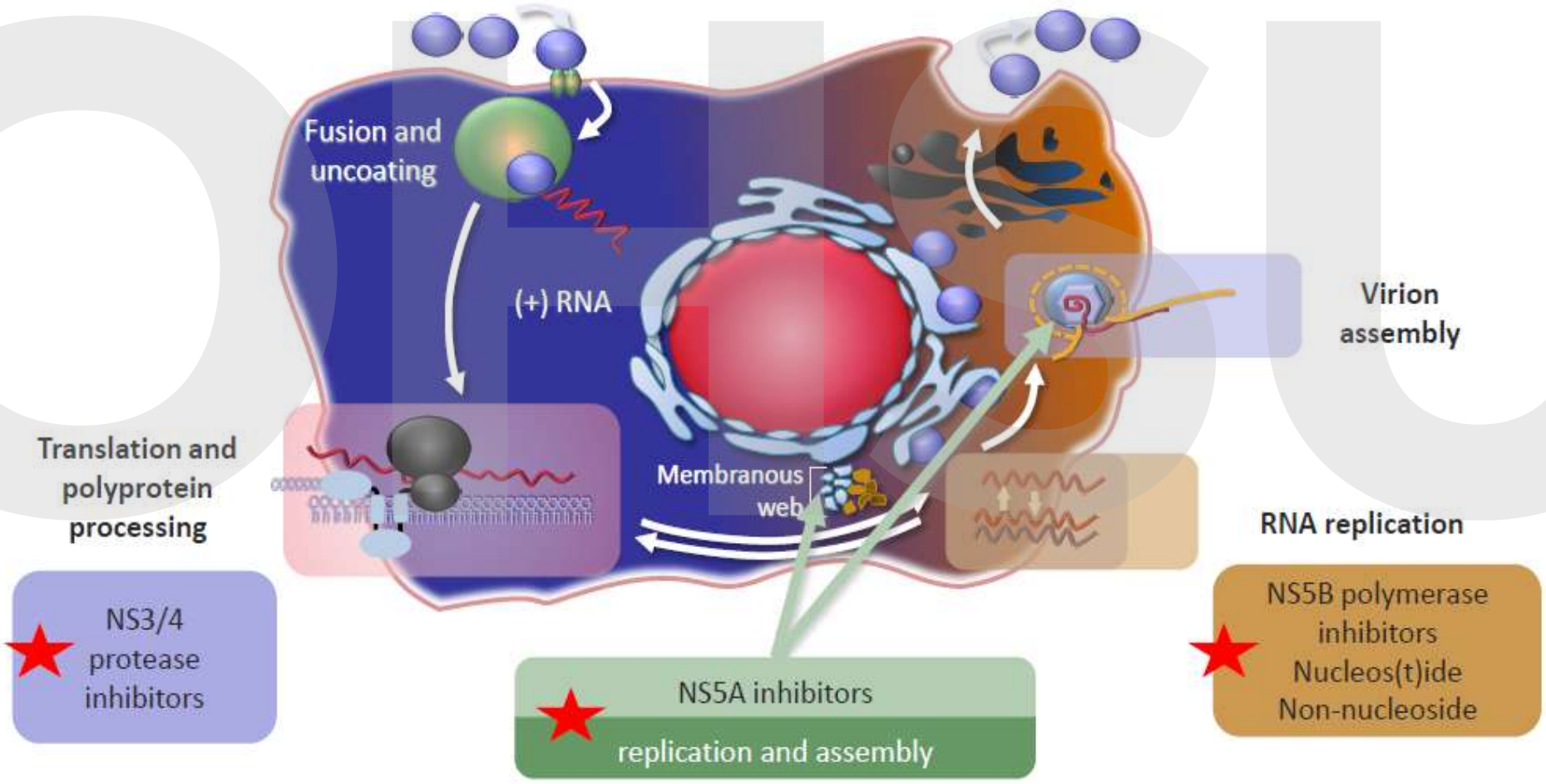
- HCV does not integrate into the nuclei of infected cells, while HBV and HIV DNA are incorporated into the nucleus of the cell



*HBV cccDNA (covalently closed circular DNA): accumulates in hepatocyte nuclei, acting as a template for viral messenger RNA transcription.
†HIV proviral DNA: integrates into the chromatin of infected cells, acting as the template for the transcription of viral genes.

Soriano V et al. *J Antimicrob Chemother.* 2008;62(1):1-4.

Current Treatments for HCV

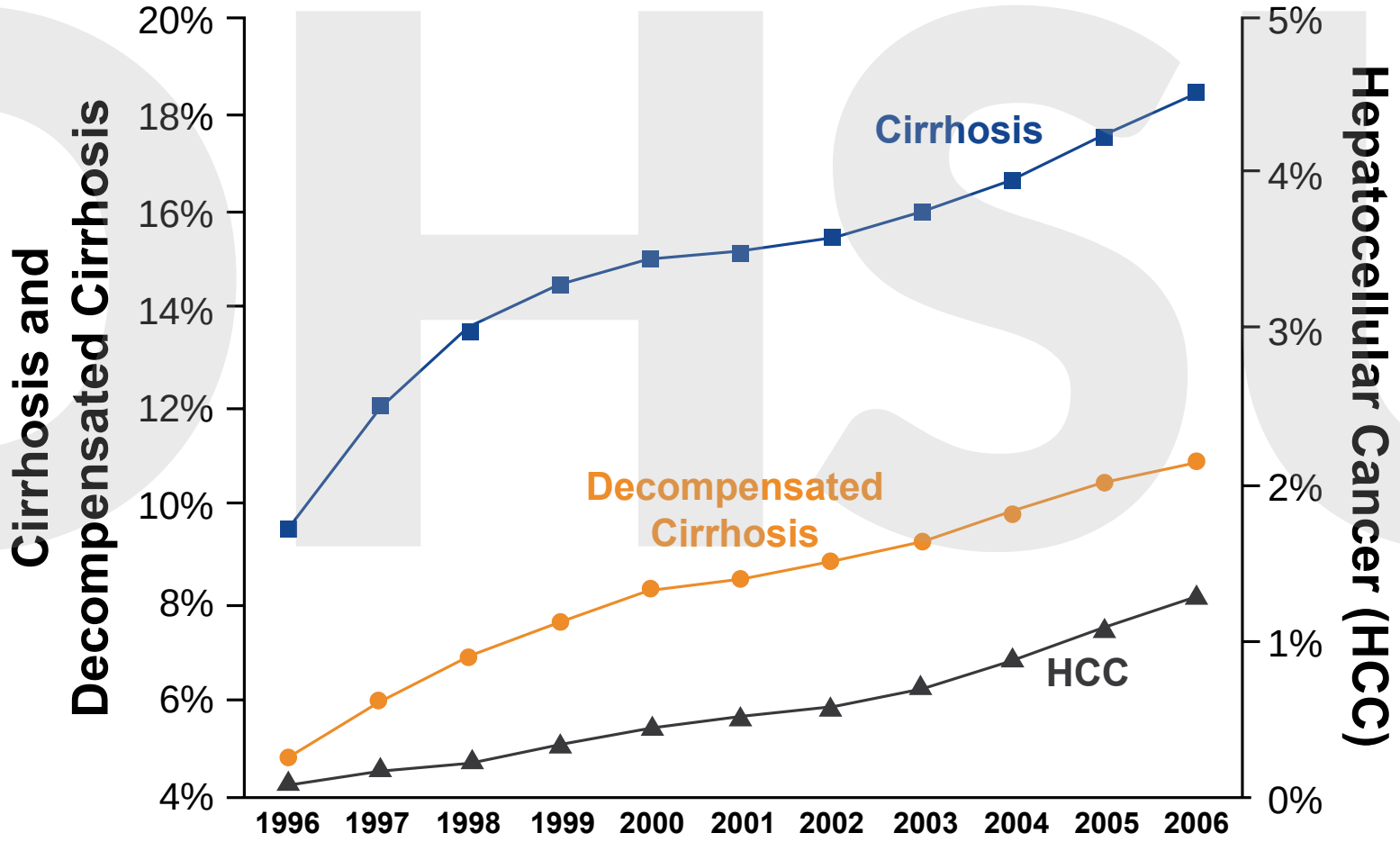


HCV Treatment

- Sustained Virologic Response (SVR)
  - Durable- 99% stay HCV negative for >10 years
  - SVR = undetectable HCV RNA in patient's blood 3-6 months after stopping treatment
- Benefits of achieving SVR
  - Delays liver disease progression
  - Decreases risk of liver cancer
  - Reduces need for liver transplant
  - Reduces transmission

Progressive Increase in Incidence of HCV-Related Cirrhosis and HCC in US

Annual Prevalence Rates Between 1996 and 2006 Among HCV-Infected Veterans



El-Serag HB. *Gastroenterology* 2012;142:1264–1273.

Treatment of Hepatitis C

- No more interferon! (And practically no ribavirin)
- Regimen choice often made in conjunction with gastroenterologist/hepatologist
- ECHO program

Current Treatment Options- Comparisons

	Mavyret™[1] (glecaprevir/pibrentasvir)	Zepatier®[2] (elbasvir/grazoprevir)	Harvoni®[3] (ledipasvir/sofosbuvir)	Epclusa®[4] (sofosbuvir/velpatasvir)	Vosevi®[5,a] (sofosbuvir/velpatasvir/voxilaprevir)
Manufacturer	AbbVie	Merck	Gilead	Gilead	Gilead
MOA	PI + NS5A	NS5A + PI	NS5A + NS5B	NS5B + NS5A	NS5B + NS5A + PI
Genotype coverage	**1 2 3 4 5 6**	**1** 2 3 **4** 5 6	**1** 2 3 **4 5 6**	**1 2 3 4 5 6**	**1 2 3 4 5 6**
Dosing of DAAs	Once daily (3-pill blister pack)	Once daily (1 pill)	Once daily (1 pill)	Once daily (1 pill)	Once daily (1 pill)
8-week duration	**1 2 3 4 5 6**	1 2 3 4 5 6	**1**[b] 2 3 4 5 6	1 2 3 4 5 6	1 2 3 4 5 6
Data in NS5A-inhibitor failures	Yes[c]	No	No	No	Yes
Concomitant ribavirin	Not indicated for any populations	GT1a with resistance and GT1 and 4 P/R-experienced	Treatment- experienced cirrhotics, decompensated cirrhosis	Decompensated cirrhosis	Not indicated for any populations
Use in decompensated cirrhosis	No	No	Yes	Yes	No
Use in severe renal impairment	Yes	Yes	No dose recommendation in severe CKD	No dose recommendation in severe CKD	No dose recommendation in severe CKD

Cost of HCV Medications

Estimated Wholesale Acquisition Cost (WAC)	
Recommended Regimens for GT1a HCV, without Cirrhosis	
Regimens and Duration of Therapy	Cost of Regimen
*Elbasvir-Grazoprevir x 12 weeks	$54,600
Glecaprevir-Pibrentasvir x 8 weeks	$26,400
^Ledipasvir-Sofosbuvir x 8 weeks	$63,000
Ledipasvir-Sofosbuvir x 12 weeks	$94,500
Sofosbuvir-Velpatasvir x 12 weeks	$74,760

*This 12-week regimen is for patients without baseline NS5A resistance-associated substitutions (at amino acid positions 28, 30, 31, or 93) for elbasvir
^This 8-week regimen is appropriate only for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL

http://www.hepatitisc.uw.edu

Current Treatment Options- Comparisons

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Manufacturer	AbbVie	Merck	Gilead	Gilead	Gilead
MOA	PI + NS5A	NS5A + PI	NS5A + NS5B	NS5B + NS5A	NS5B + NS5A + PI
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Use in severe renal impairment	Yes	Yes	No dose recommendation in severe CKD	No dose recommendation in severe CKD	No dose recommendation in severe CKD

Harvoni (LED/SOF)

- High cure rate across many previously difficult to treat population
  - Decompensated cirrhosis
  - HIV
  - Post liver transplant
  - Treatment experienced
- Duration of treatment: 8*, 12, or 24 weeks
- Very well tolerated: headaches, nausea, fatigue

*Must be HCV treatment naïve, non-cirrhotic, with baseline viral load <6 million IU/mL

Epclusa (VEL/SOF)

- More “potent” version of Harvoni
  - Works on all genotypes
  - More resistant to NS5A mutations
- Duration of treatment: 12 weeks
- Very well tolerated: Headaches, nausea, fatigue

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Mavyret (GLE/PIB)

Next Generation Direct-Acting Antivirals

Glecaprevir
(formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Collectively: G/P

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A inhibitor

In vitro:[1,2]

- High barrier to resistance
- Potent against common NS3 polymorphisms (e.g., positions 80, 155, and 168) and NS5A polymorphisms (e.g., positions 28, 30, 31 and 93)
- Additive/synergistic antiviral activity

Clinical PK & metabolism:

- Once-daily oral dosing
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg
Glecaprevir was identified by AbbVie and Enanta.

1. Ng TI, et al. Abstract 636. CROI, 2014. 2. Ng TI, et al. Abstract 639. CROI, 2014.

Mavyret (GLE/PIB)

- FDA indications:
  - Treatment of chronic HCV in GT 1-6
  - Treatment of GT 1 patients who previously failed a regimen containing an HCV NS5A inhibitor OR an NS3/4A PI, BUT NOT BOTH
- Dosing
  - 3 tablets (100mg/40mg) daily X 8 to 16 weeks
  - Comes in 4 or 8 weeks package

Mavyret Prescribing Information 2017

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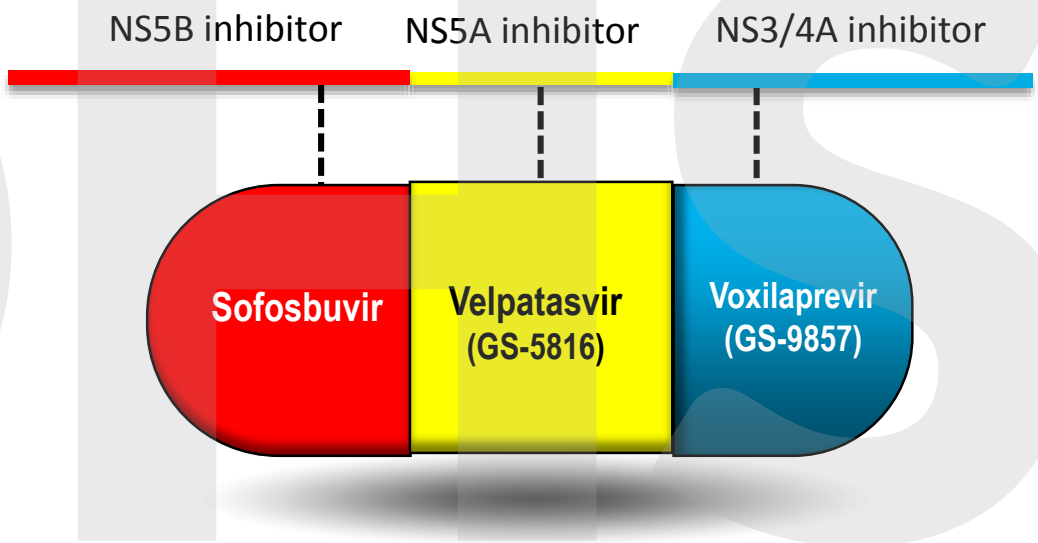
Vosevi (SOF/VEL/VOX)



- Broad genotypic activity
- Retains activity against almost all clinically relevant resistance associated substitutions (RAS)
- All-oral, once-daily regimen with food

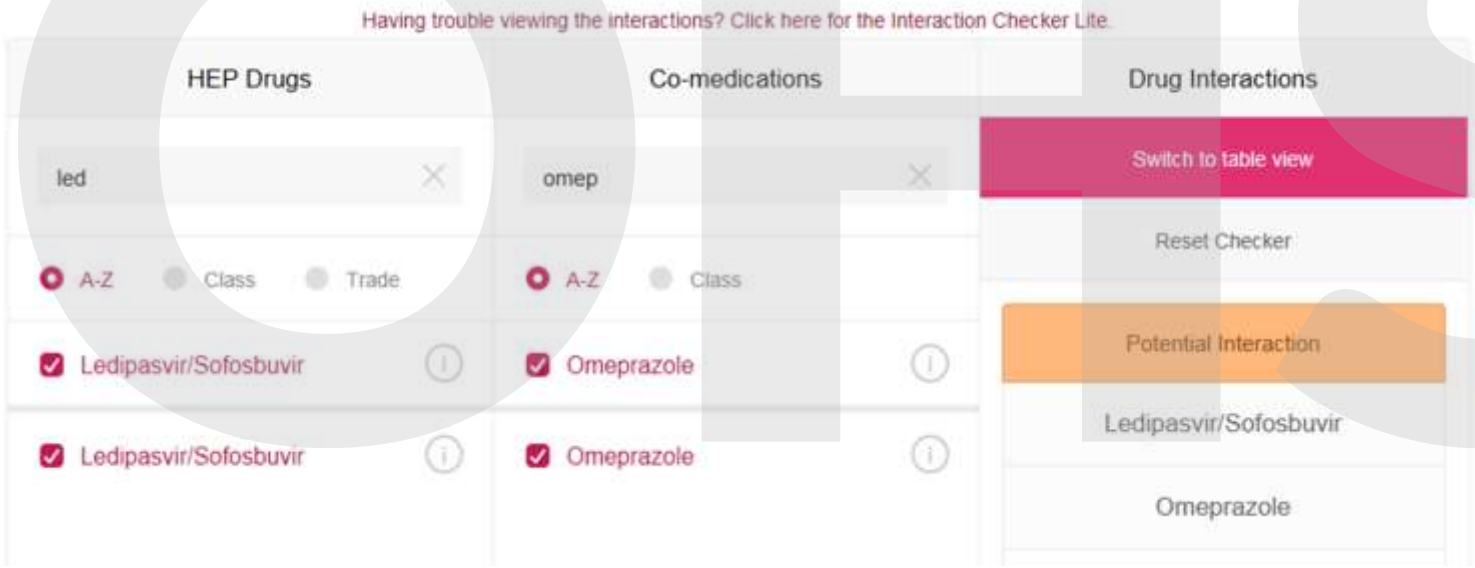
FDA indications:

-Genotype 1-6 who have previously been treated with an HCV regimen containing an NS5A inhibitor

-GT 1a or 3 who have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor

HCV Treatment: Drug Interactions

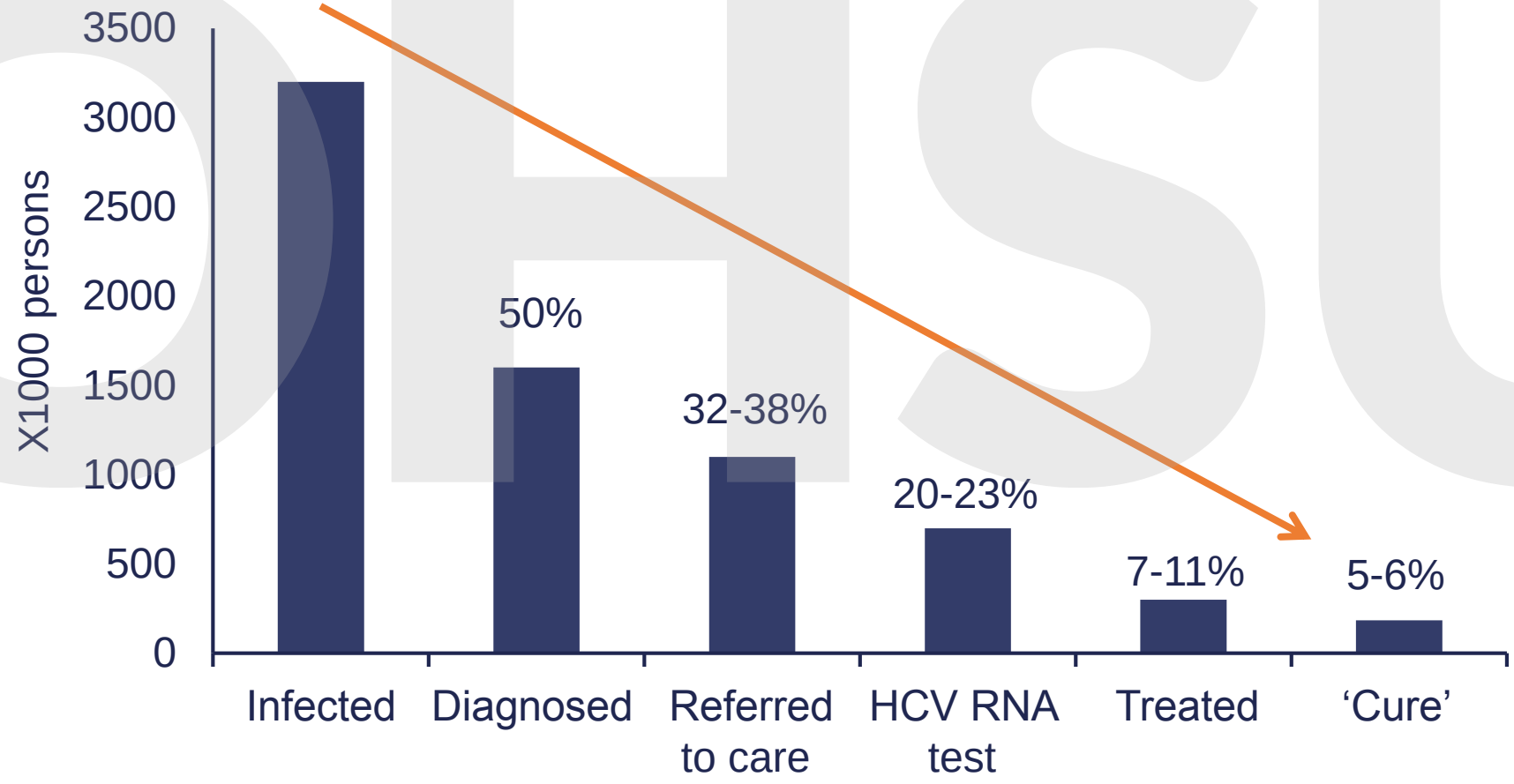
Liverpool Hep C Interactions



- Common Drug Interactions:
  - Acid Reducers
  - Statins
  - Amiodarone
  - CYP and PGP inducers
  - CYP inhibitors

HCV-Infected Persons in the US: Estimated Rates of Detection, Referral to Care and Cure

CDC & USPSTF recommend 1-time testing of baby boomers (born 1945-1965)



Holmberg S, N Engl J Med 2013; 368: 1859

Case #1

- You are seeing a 55yo male as a new patient in your clinic
- He has a history of hepatitis C
- No current EtOH, quit 2 years ago
  - Prior to that he was drinking 6 beers a day
- He also reports that he was once told he might have had hepatitis B
- Next steps?
  - Liver panel, INR, CBC
  - Fibrosis assessment- Fibroscan
  - Treat HCV
  - History of HBV….stay tuned

Resources

- HCV guidelines
  - http://www.hcvguidelines.org/
- HCV resources
  - www.**hepatitisc**.**uw**.edu/
- AASLD website
  - www.aasld.org
- Liverpool HCV Interactions
  - https://www.hep-druginteractions.org/

- OHSU Consult Line 503-494-4567

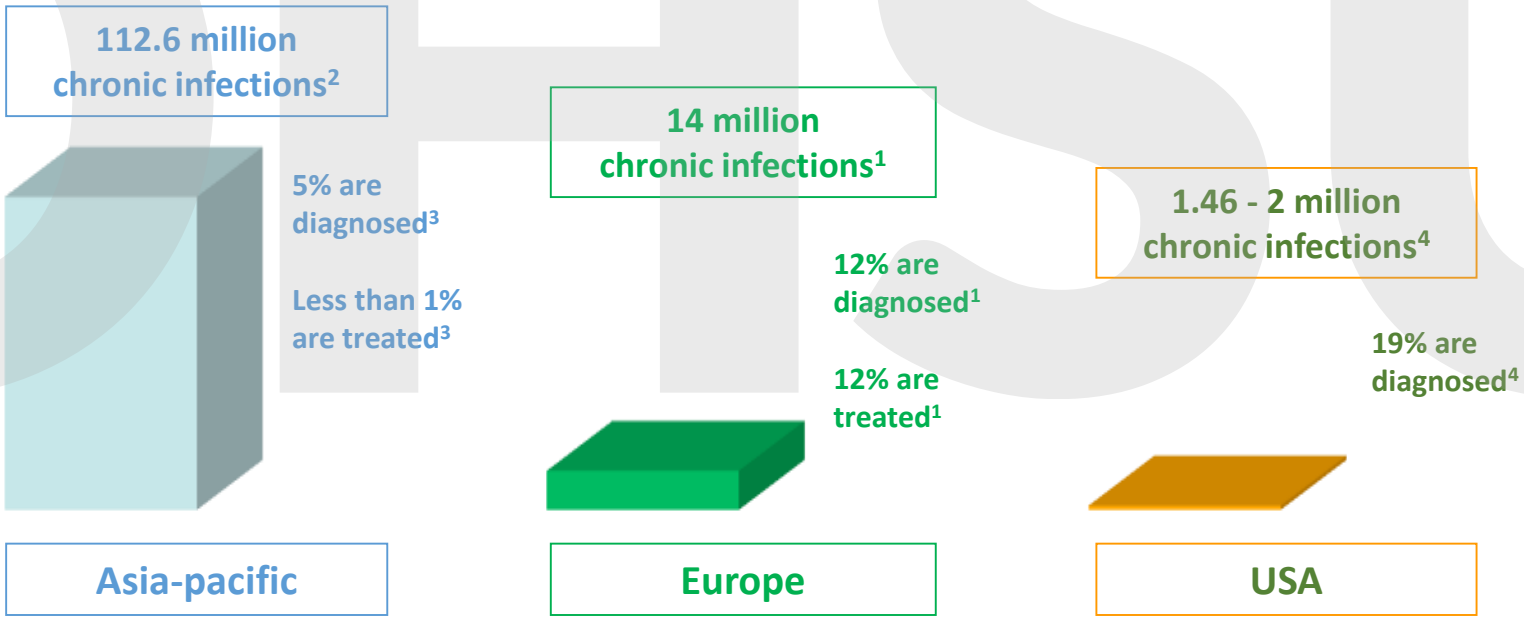
Take home points: HCV treatment

- Revolutionary!
- Need to be aware of drug-drug interactions- close partnership with pharmacy
- For those on the front lines
  - Identify chronic HCV- Birth cohort screening
  - Identify HCV cirrhosis, refer if needed
  - Those without cirrhosis or prior DAA failure can be treated safely in the primary care setting
  - More and more HCV being treated by PCP's
- All patients with HCV should be considered for treatment
  - Underinsured
  - Insurance pre-authorization *
- Compensated cirrhosis
  - Ensure that there is no evidence of HCC with multiphase CT scan
  - Child's A cirrhosis patients tolerate treatment well

Hepatitis B

Hepatitis B- An Unmet Medical Need

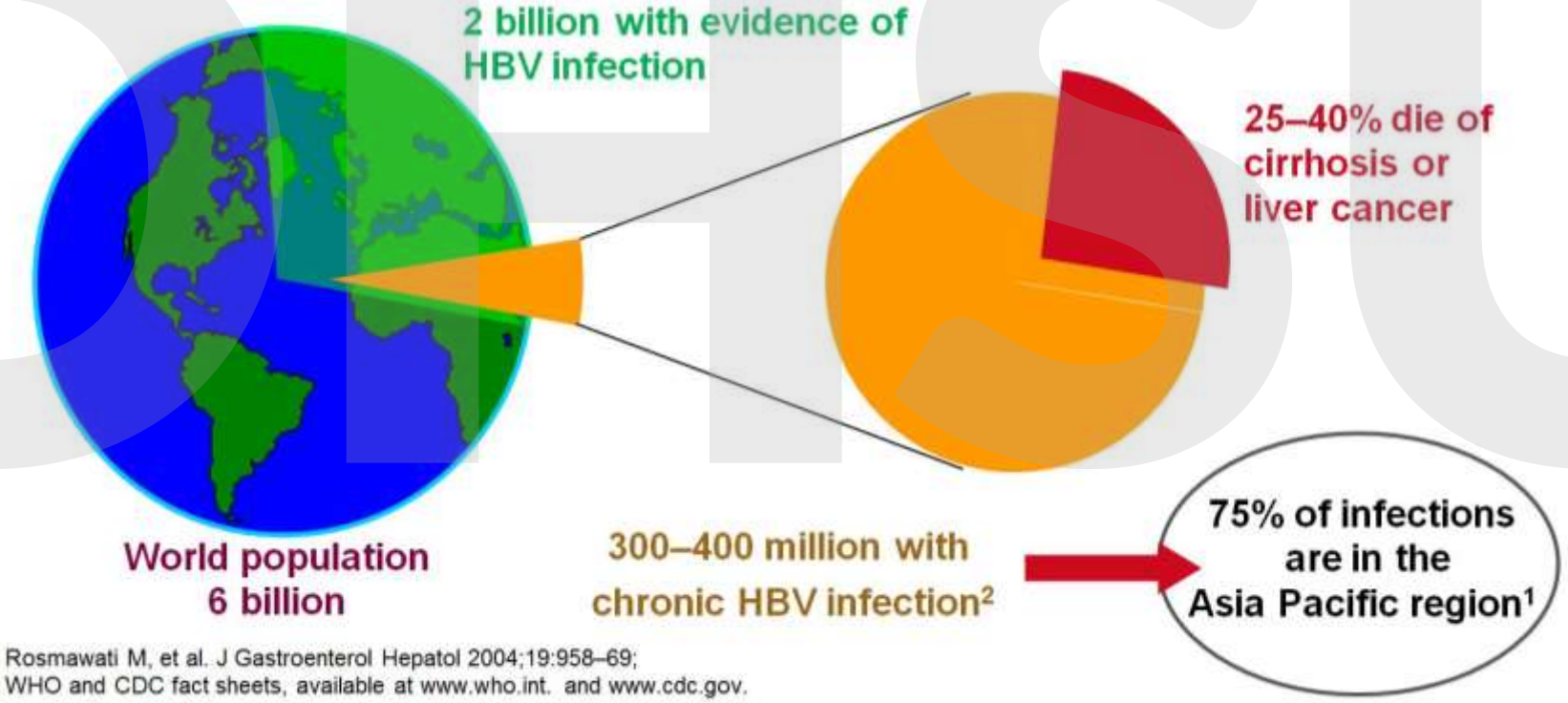
- Under-diagnosed
- Under-treated



1. BMS Market Research. Information available upon request from Bristol-Myers Squibb;
2. Mohamed R, et al. J Gastroenterol Hepatol 2004;19:958-69;
3. Decision Resources. Hepatitis B virus in China – Emerging markets study #5; 4. BMS Market Research.

Global Impact of HBV

- Due to its high incidence and risk of liver injury, CHB constitutes a significant health and economic burden within the Asia Pacific region[1]



1. Rosmawati M, et al. J Gastroenterol Hepatol 2004;19:958–69;
2. WHO and CDC fact sheets, available at www.who.int. and www.cdc.gov. (accessed March 2015)

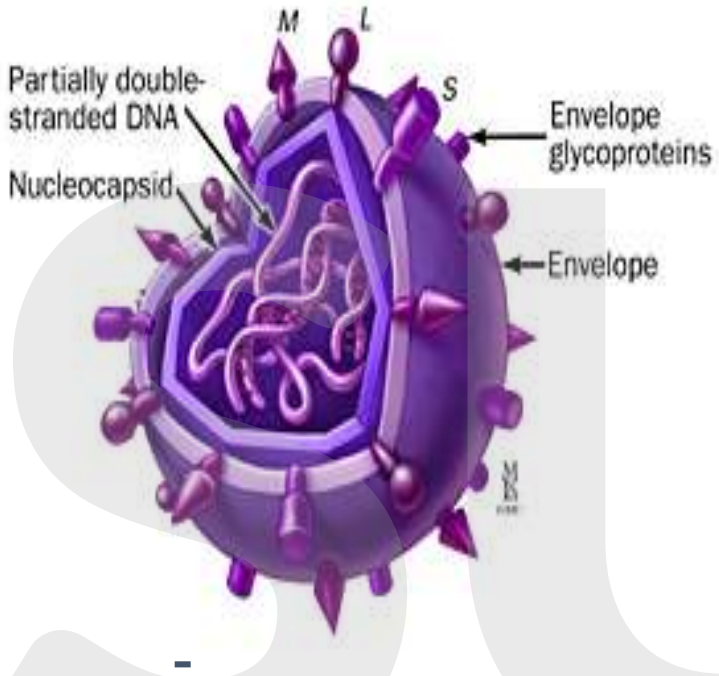
HBV Virology

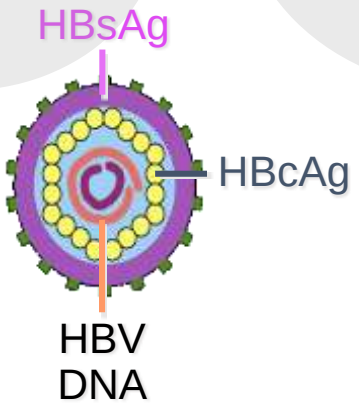
Spherical particle comprised of:

- Outer Envelope (**HBsAg**) protein
- Inner Nucleocapsid (**HBcAg**) protein
- Within nucleocapsid is the partially double stranded circular molecule of **HBV DNA**

cccDNA = viral RNA template

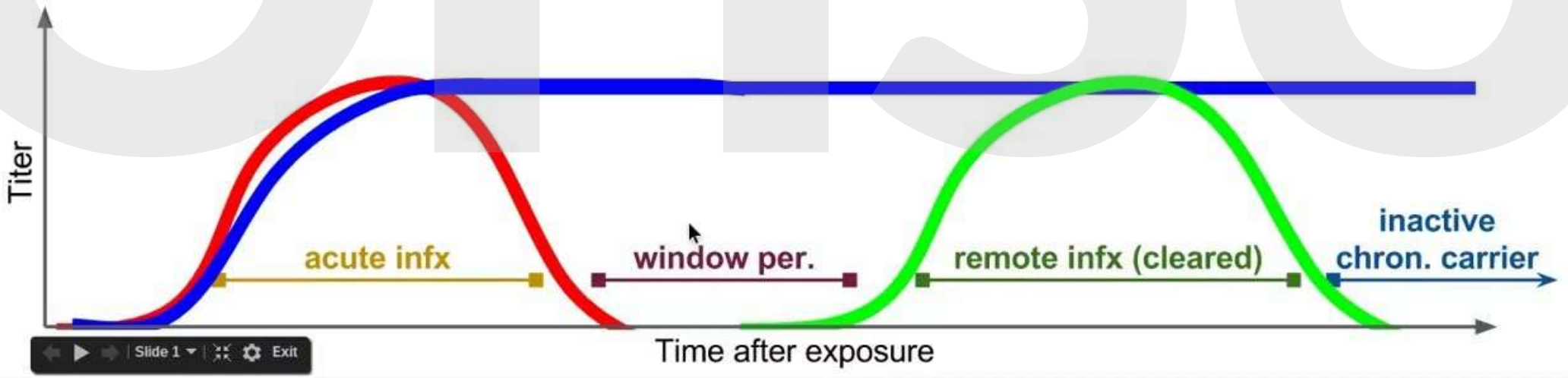
- Stable
- Resistant to host immune response
- Resistant to antiviral therapy
- Stuck in hepatocyte DNA permanently
- Stimulates oncogenesis





Hepatitis B serologies

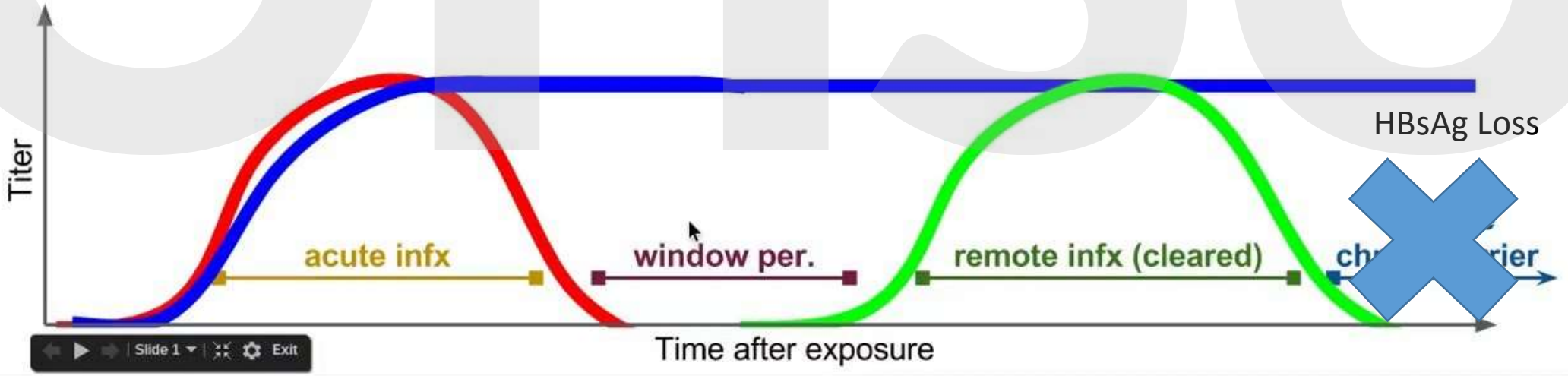
Marker	Meaning	Acute infection	Window period	Chronic infection	Remote infection (cleared)	Immun-ization	Inactive chronic carrier
HBcAb	Exposure	+	+	+	+	-	+
HBsAg	Infection	+	-	+	-	-	-
HBsAb	Immunity	-	-	-	+	+	-

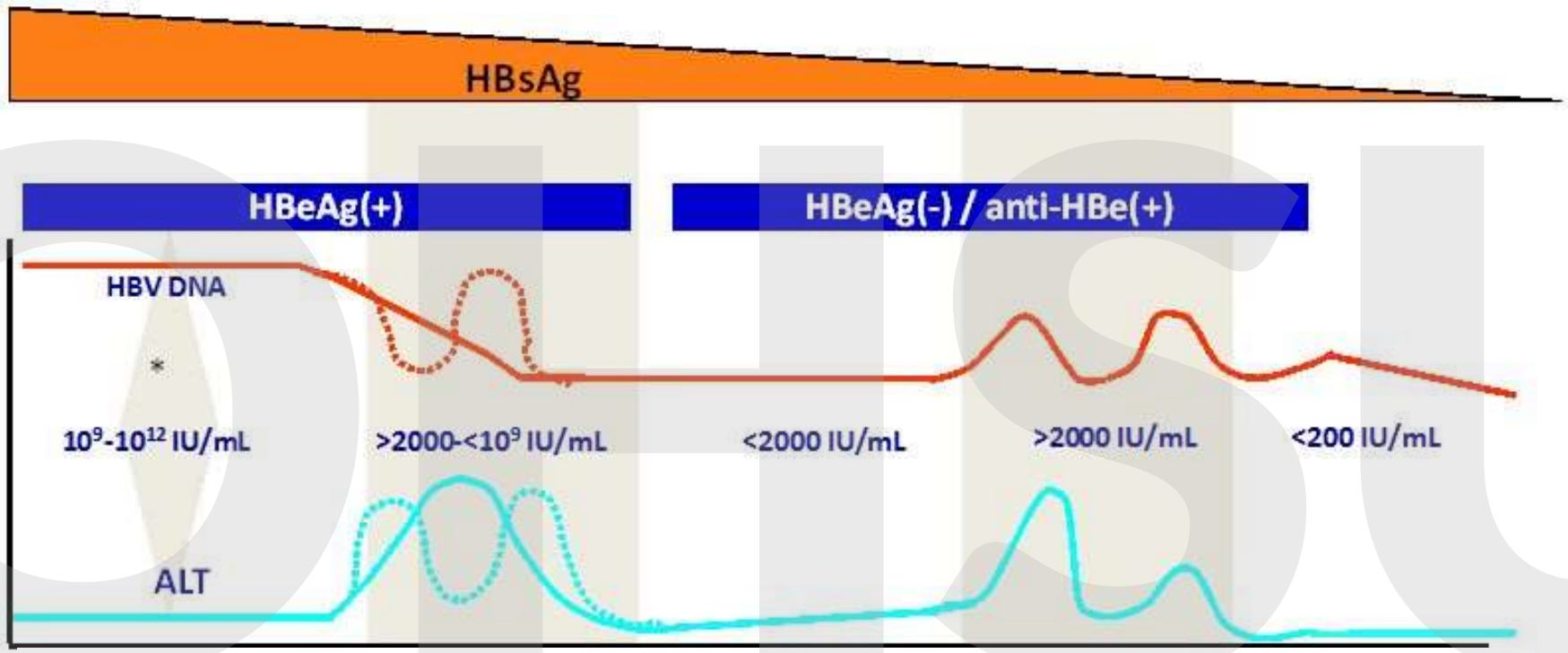


Hepatitis B serologies

HBsAg Loss

Marker	Meaning	Acute infection	Window period	Chronic infection	Remote infection (cleared)	Immun-ization	[illegible]
HBcAb	Exposure	+	+	+	+	-	+
HBsAg	Infection	+	-	+	-	-	-
HBsAb	Immunity	-	-	-	+	+	-

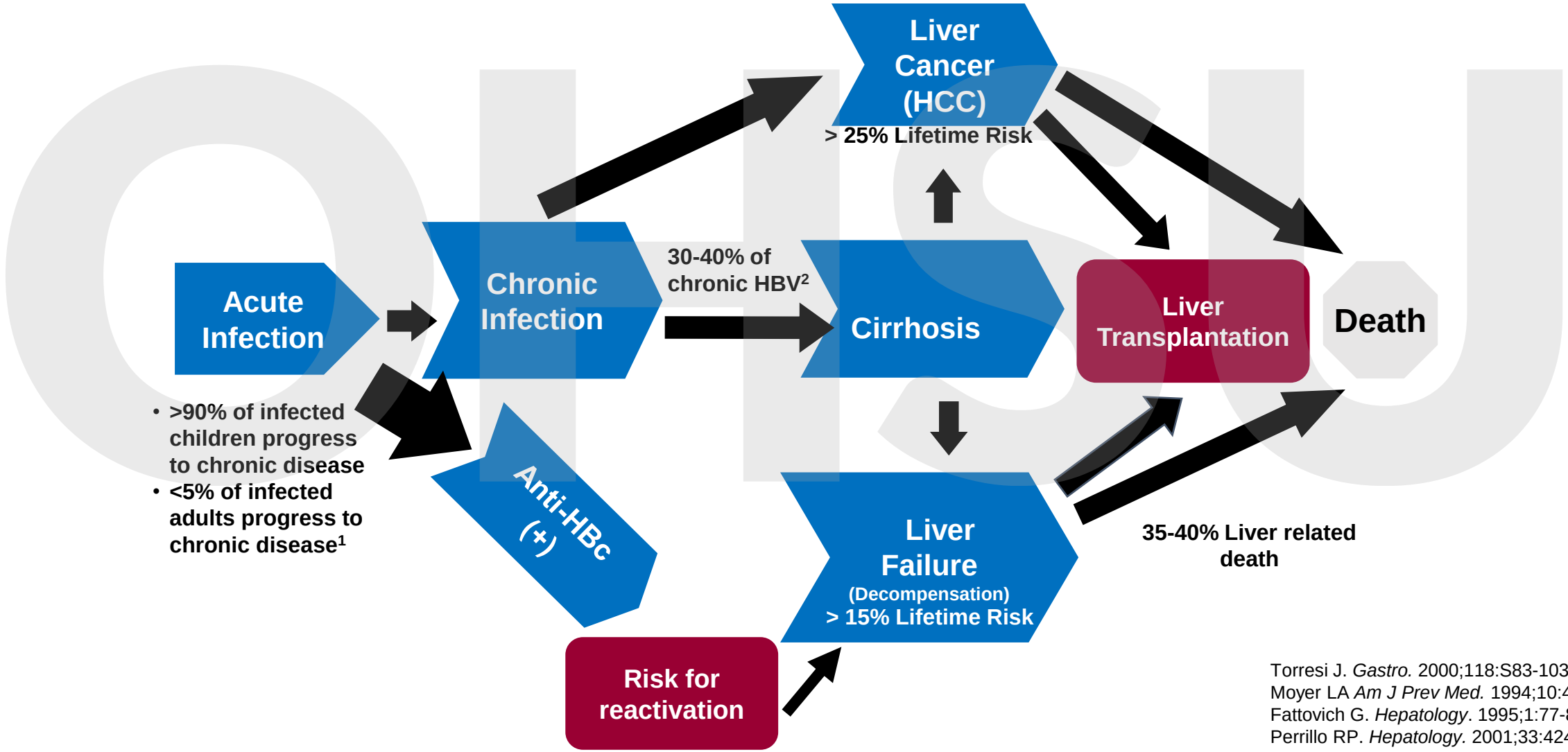




Immune-tolerant	Immune-reactive	Immune-control	Immune-reactive or Immune escape	Immune- control

Phases of Infection

Natural History of HBV



Torresi J. *Gastro.* 2000;118:S83-103[1];
Moyer LA *Am J Prev Med.* 1994;10:45-55[2];
Fattovich G. *Hepatology*. 1995;1:77-82[3];
Perrillo RP. *Hepatology.* 2001;33:424-432.[4]

Surveillance for HCC in HBV

- Who should receive HCC surveillance?
  - Chronic HBV with or without cirrhosis
- How?

  AASLD Guidelines:
  - Liver ultrasound with or without Alpha-fetoprotein (AFP) every 6 months
  - CT/MRI not recommended for HCC surveillance

AASLD Guidelines for HCC 2017

Take home points:
HBV Epidemiology and Testing

- Remains a globally important disease
- This hepatologists' view: avoid using terminology for the phases of HBV without specifically documenting the patient's serologic status
  - HBsAg
  - HBcAb
  - HBsAb
- "Chronic carrier", "inactive carrier" can be ambiguous and confusing
- Risk for HCC in patients with and without cirrhosis in HBV

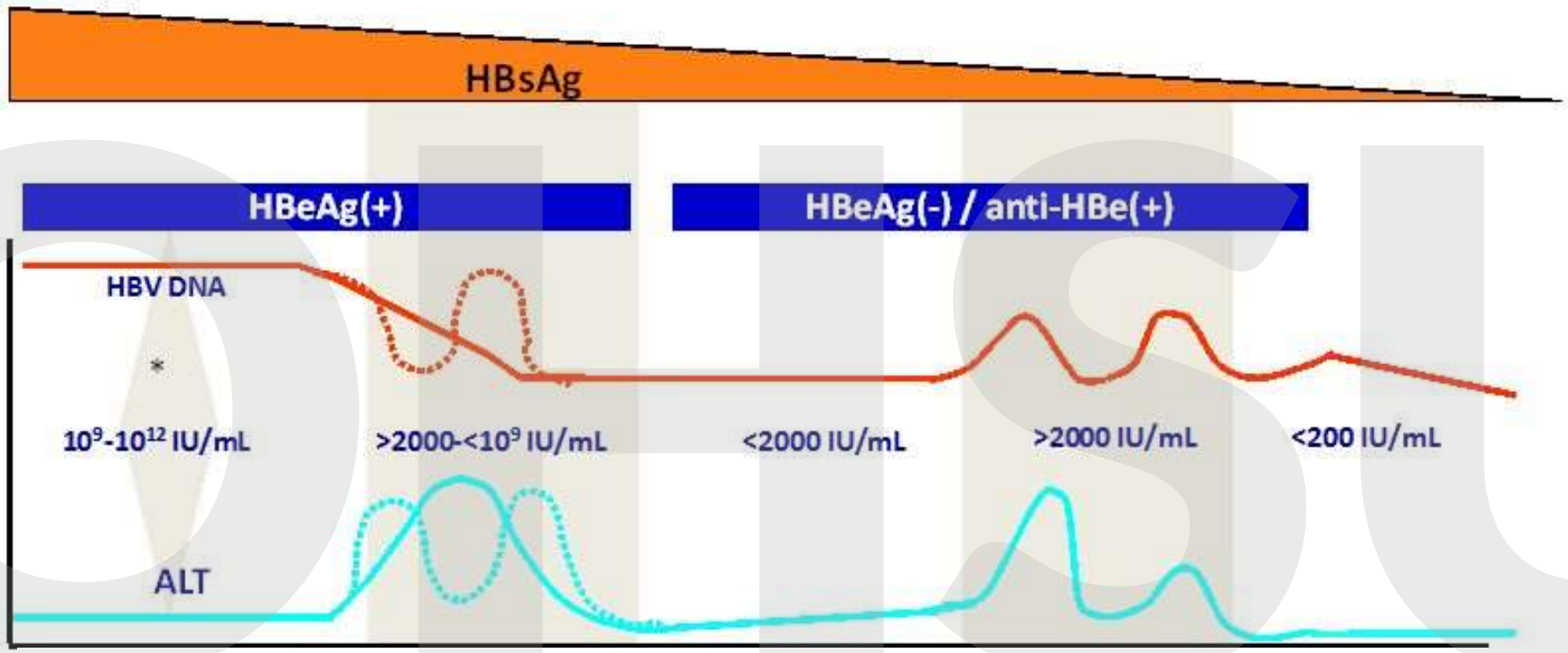
Case #2

- 32yo male presents with a new diagnosis of chronic HBV after giving blood
- He mentions he was once told that he had family members with liver disease
- You check liver tests and ALT 25, AST 22
- HBeAg pos
- HBV DNA 2,000,000 IU/mL
- Should this patient be treated for HCV?

Who should be treated for HBV?

- HBeAg +, ALT >2x ULN, HBV DNA >20,000 IU/ml
- HBeAg -, ALT >2x ULN, HBV DNA>2,000 IU/ml
- Compensated/decompensated cirrhosis
- Prevention of reactivation of HBV in those receiving immune suppression or cytotoxic therapy

Rajbhandari R et al. Clin and Transl Gastro 2016



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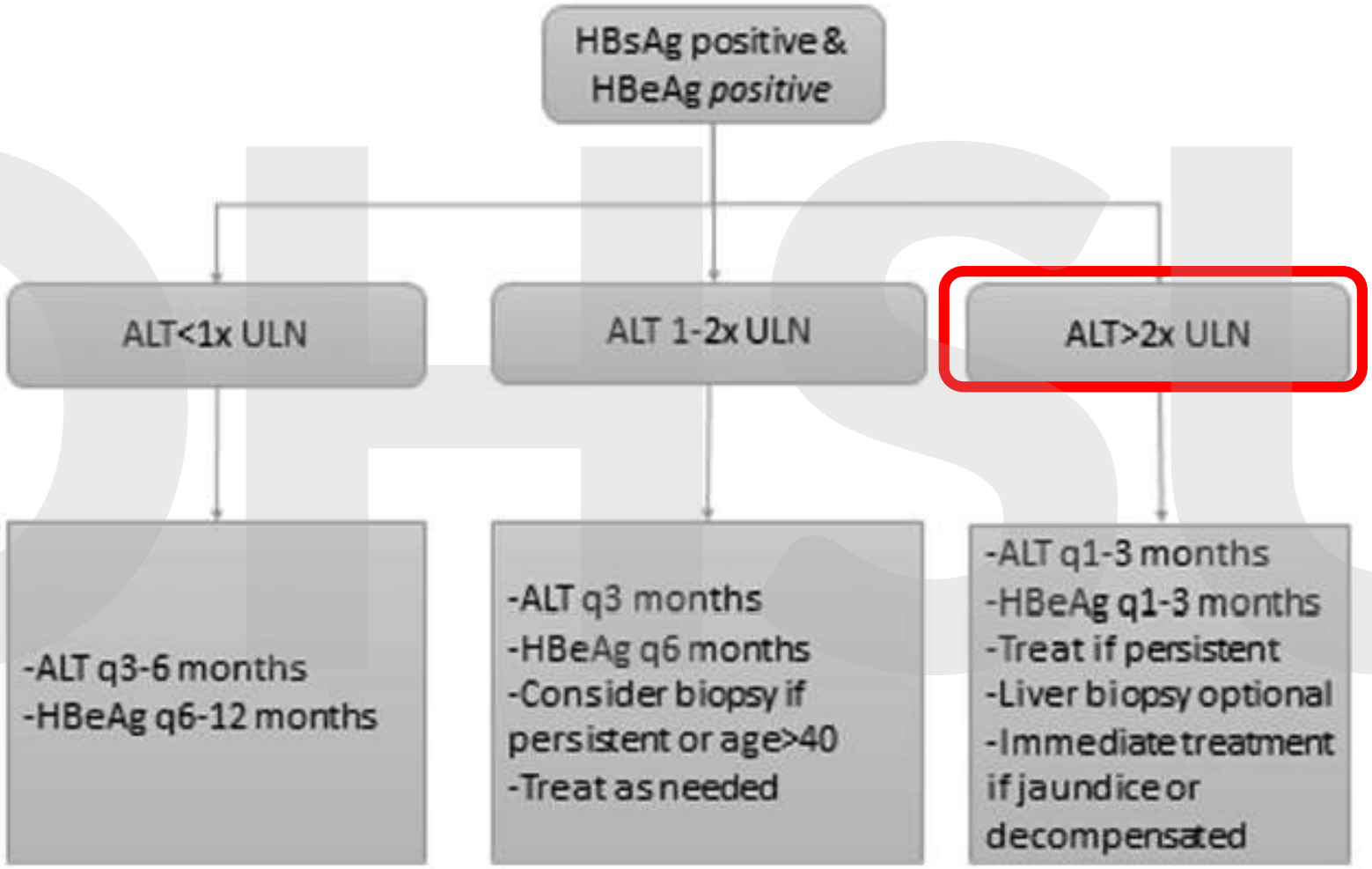
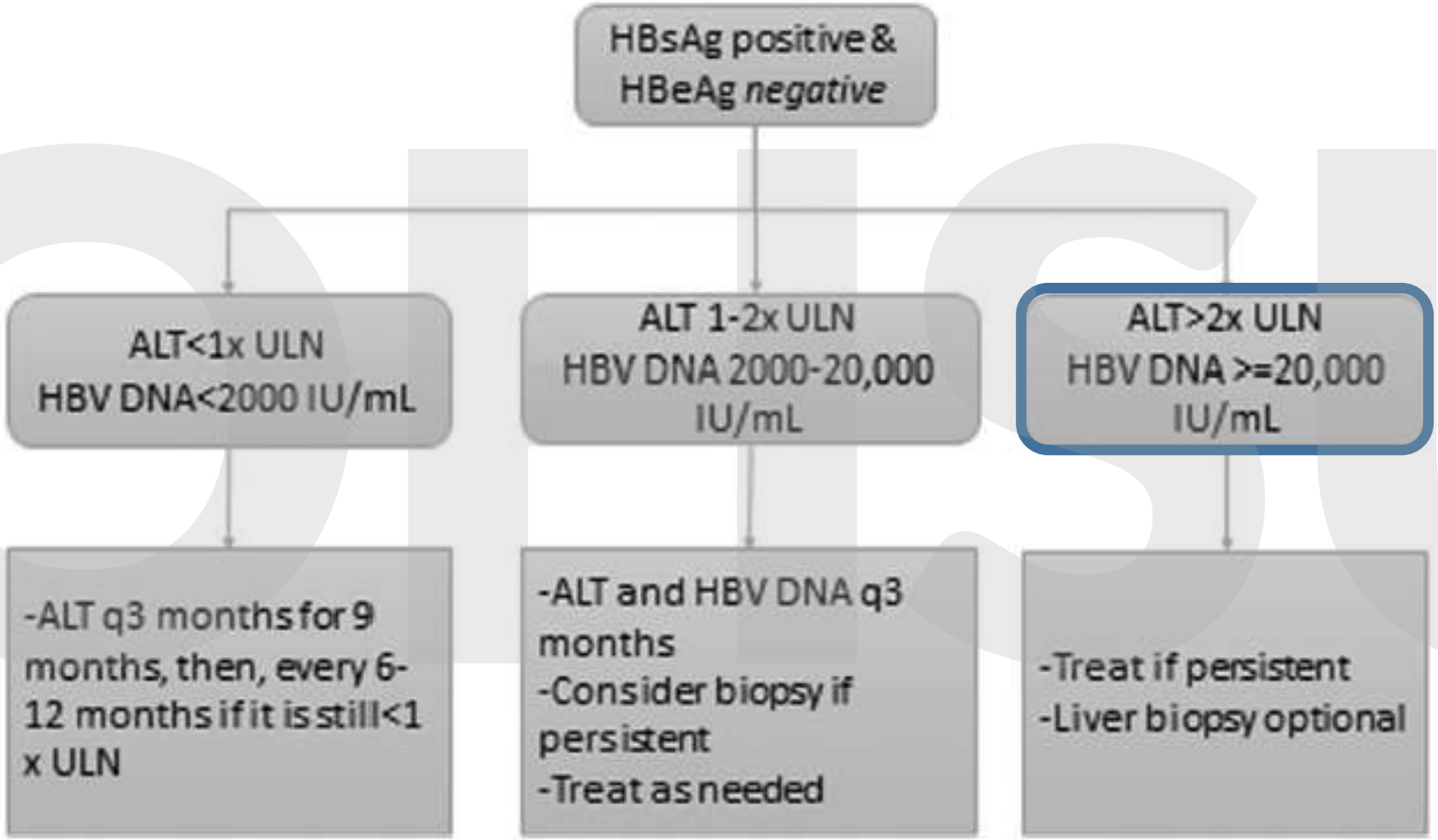
Phases of Infection



Rajbhandari R et al. Clin and Transl Gastro 2016



Rajbhandari R et al. Clin and Transl Gastro 2016

FDA-Approved Treatments for HBV

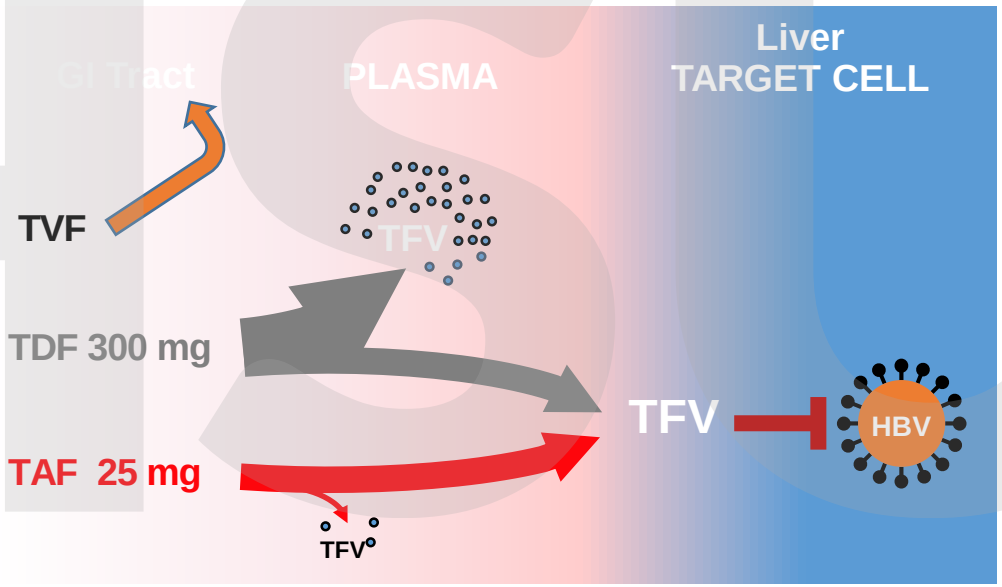
Nucleosides/Nucleotides			
Tenofovir AF	VEMLIDY™	Gilead Sciences	2017
Tenofovir DF	VIREAD®	Gilead Sciences	2008
Telbivudine	TYZEKA™	Idenix / Novartis	2006
Entecavir	BARACLUDE™	Bristol-Myers Squibb	2005
Adefovir dipivoxil	HEPSERA™	Gilead Sciences	2002
Lamivudine	EPIVIR-HBV®	GlaxoSmithKline	1998
Interferons			
Peginterferon alfa-2a	PEGASYS®	Roche	2005
Interferon alfa-2b, recombinant	INTRON® A	Schering / Merck	1992

Preferred regimens

	Potency	Resistance	Disadvantages	Notes
Tenofovir disoproxil fumarate	++	None Effective against LAM, telbivudine and entecavir resistance	Nephrotoxicity with Fanconi's syndrome	Treatment of choice in patients with HBV/HIV co-infection
Entecavir	+	Low Effective against adefovir resistant strains	Can lead to HIV resistance Increased risk of resistance in those who are LAM resistant	Less nephrotoxic than TDF

Tenofovir Alafenamide (TAF)

- Prodrug of tenofovir DF
- Tenofovir AF is more stable in plasma/tissues than tenofovir DF
  - Higher levels in target cells
- Tenofovir DF (but not tenofovir AF) actively enters renal tubular cells via organic anion transporters 1 and 3
- Tenofovir AF has a lesser effect on the proximal renal tubule



90% Lower TFV Levels in Plasma
Minimizes Renal and Bone Effects While
Maintaining High Potency in target cells

DHHS. http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Revision July 14, 2016.

Case #2

- 32yo male presents with a new diagnosis of chronic HBV after giving blood
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- Should this patient be treated for HCV?

Goals of Treatment for HBV

Primary Goals

- Reduction in fibrosis/cirrhosis
- Reduce risk of hepatocellular carcinoma
- Decrease mortality

Surrogate Goals

- Improvement in hepatic inflammation, fibrosis
- Virologic suppression:
  - Undetectable or low HBV DNA level
  - eAg loss/eAb development
- Normalization of serum ALT
- Loss of HBsAg +, appearance of HBsAb (rare but optimal)

Lok ASF. *Hepatology*. 2004;39:857-861.
Keeffe EB. *Clin Gastroenterol Hepatol.* 2006;4:936-962.

Other considerations for HBV treatment

- Liver biopsy to distinguish between immune control and immune reactive/escape phases in HBeAg neg CHB
- Fibroscan can to assess for advanced fibrosis but not inflammation
- Test all “at risk” patients for delta hepatitis (HDV)
  - Advanced liver disease
  - IVDU or sexual transmission as risk for HBV
- Test for HBV mutations if viral breakthrough with treatment
- Entecavir or TAF in renal insufficiency
- Lactic acidosis: class warning with nucleot(s)ide analogues

Take home points:
HBV Treatment Overview

- Is not “curable”
- Loss of HBsAg is a “functional cure”
  - Very uncommon
- In those with an indication for treatment: ETV and TDF preferred
- Counsel patients that indefinite treatment likely

Case #2

- You are seeing the following patient in consultation:

- 65yo female with hx. multiple sclerosis
- Would like to start Ocrelizumab
- HBsAg neg, HBcAb pos, HBsAb neg

- What are your next steps?

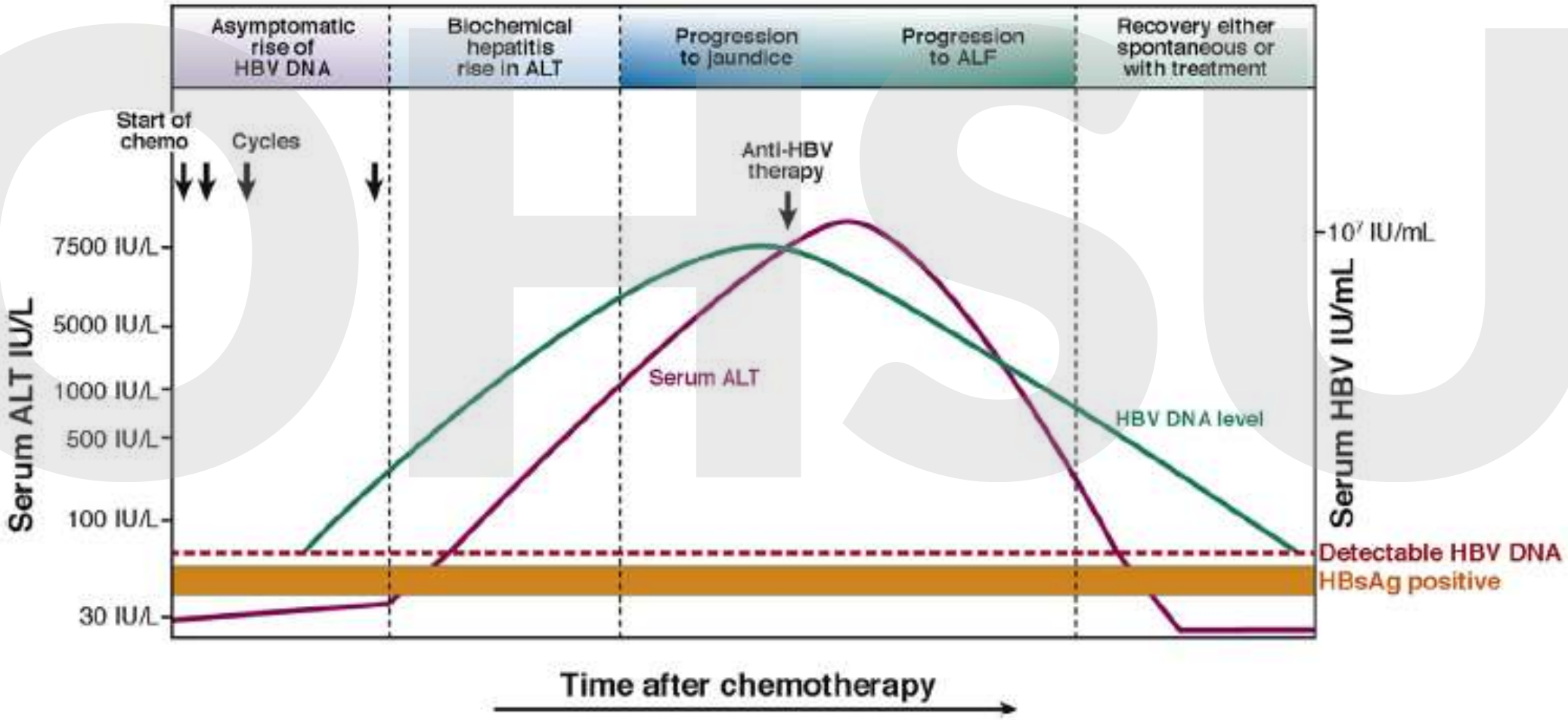
Reactivation of HBV with Immune Suppression and Biologic Therapies

2 categories

- HBV reactivation - patients with HBsAg+ with or without detectable HBV-DNA viremia in the blood
- Reverse seroconversion - reappearance of HBsAg and HBV DNA in individuals who initially are negative for HBsAg and HBV DNA in the serum before immunosuppression and then become positive after exposure to immunosuppressive therapies.
  - Occult HBV
- 25-50% of reactivation can result in severe liver injury/liver failure

Loomba R, Liang JT. Gastroenterology 2017;152:1297-1309

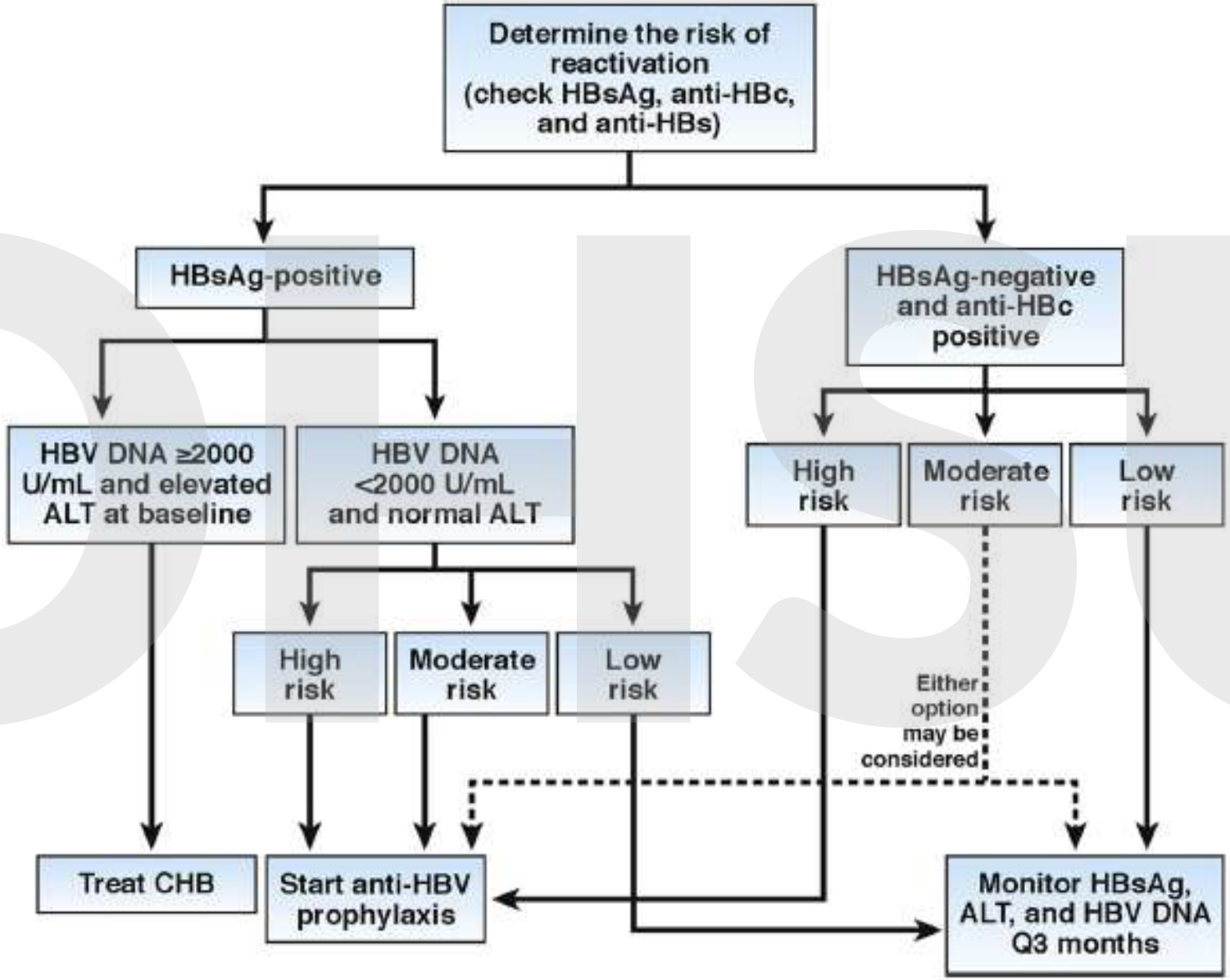
Example course of HBV reactivation



Loomba R, Liang JT. Gastroenterology 2017;152:1297-1309

RISK OF HBV REACTIVATION	**HBsAb +, HBcAb +**	**HBsAb neg, HBcAb +**
Anti-CD 20 (rituximab, ofatumumab, Obinutuzumab)	VERY HIGH (>20% risk)	MODERATE
Hematopoietic stem cell transplantation	VERY HIGH	Low
High dose corticosteroids (>20mg for 4 weeks)	HIGH (11-20% risk)	Low
Other Cytokine Inhibitors (e.g. anti-CD52)	HIGH	Low
Combination Cytotoxic Chemo without corticosteroids (cyclophosphamide, adriamycin, vincristine)	MODERATE (1-10%)	Rare
Anti-TNF inhibitors	MODERATE	Rare
Anti-rejection therapy for solid organ transplant	MODERATE	Rare
Methotrexate, Azathioprine, 6-MP	Low (<1%)	Rare

Di Bisceglie AM et al. Hepatology 2014



Loomba R, Liang JT. Gastroenterology 2017;152:1297-1309

Treatment to prevent HBV reactivation

- Most experience with LAM
- Shift to ETV and TDF
- Can start prophylaxis concurrently with immune suppressive medication
- If viral load is high, could consider starting treatment and then initiating medication if able to wait
- Medications are continued for 6 months post cessation of immune suppression with non B-cell depleting agents
- With B-cell depleting agents, continue for 12 months

Case #2

- 65yo female with hx multiple sclerosis
- Would like to start Ocrelizumab
- HBsAg neg, HBcAb pos, HBsAb neg

- High risk for reactivation → treat with TDF or ETV

Case #1

- You are seeing a 55yo male as a new patient in your clinic
- He has a history of hepatitis C
- No current EtOH, quit 2 years ago
  - Prior to that he was drinking 6 beers a day
- He also reports that he was once told he might have had hepatitis B
- Next steps?
  - Liver panel, INR, CBC
  - Fibrosis assessment- Fibroscan
  - Treat HCV
  - History of HBV….

ORIGINAL RESEARCH

Annals of Internal Medicine

Hepatitis B Virus Reactivation Associated With Direct-Acting Antiviral Therapy for Chronic Hepatitis C Virus: A Review of Cases Reported to the U.S. Food and Drug Administration Adverse Event Reporting System

- N=29 reported to the FDA
- 2 Died and 1 received liver transplantation
- 5 patients hospitalized

Baseline HBV viral characteristics, *n*	
HBsAg	
Positive	13
Negative	4
Not reported	12
HBcAb	
Positive	6
Not reported	23
HBsAb	
Negative	3
Not reported	26
HBV DNA	
Undetectable	16
Detectable	9
Baseline not reported or detectability status unclear	4

AASLD Guidance on HBV Reactivation in Pts Receiving HCV DAA Therapy

- HBV vaccination for all susceptible individuals
- Test for HBV DNA prior to DAA therapy if HBsAg +
- Treatment of active HBV infection at the same time — or before — HCV DAA therapy is started
- Monitoring patients with low or undetectable HBV DNA levels at regular intervals (usually not more frequently than every four weeks) for HBV reactivation during treatment
- Insufficient data to provide recommendations for pts who are HBsAg- and anti-HBc+ or anti-HBs+/anti-HBc+

Version: 11/1/2016

Case #1

- You are seeing a 55yo male as a new patient in your clinic
- He has a history of hepatitis C
- No current EtOH, quit 2 years ago
  - Prior to that he was drinking 6 beers a day
- He also reports that he was once told he might have had hepatitis B
- Next steps?
  - Liver panel, INR, CBC
  - Fibrosis assessment- Fibroscan
  - Treat HCV
  - History of HBV….need to check Hepatitis B serologies and treated based on algorithm

Summary: Who to treat for HBV?

- HBeAg +, ALT >2x ULN, HBV DNA >20,000 IU/ml
- HBeAg -, ALT >2x ULN, HBV DNA>2,000 IU/ml
- Compensated/decompensated cirrhosis
- Prevention of reactivation of HBV in those receiving immune suppression or cytotoxic therapy

Rajbhandari R et al. Clin and Transl Gastro 2016

Summary: HBV in Special Populations

- HBV is never truly cleared even if HBsAg negative
- HBV genome incorporated into the hepatocyte
  - ccc DNA
  - Difficult to quantify risk in occult HBV
- 4 phases of chronic HBV
- Avoid using “carrier” as a descriptor
- Reactivation of HBV
  - Risk stratify based on medication being used and serologic status of patient
  - High risk/Moderate risk → TREAT
  - Low risk→ Observe
  - Steroids!

Questions?

- OHSU Consult Line 503-494-4567