A Primer on Viral Hepatitis

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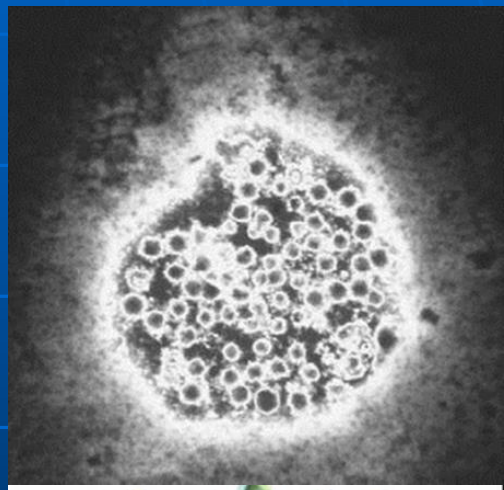
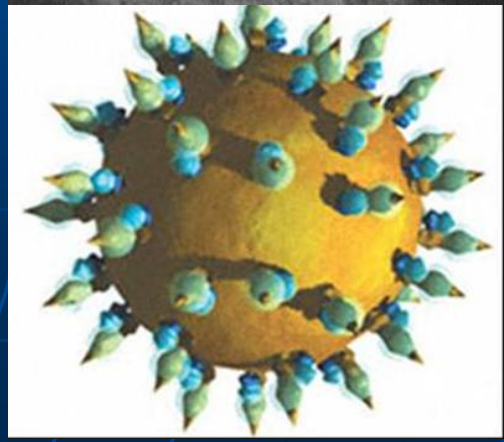
Objectives

- Describe various types of viral hepatitis, their routes of transmission and presentations.
- Interpretation of the various serological tests for acute and chronic viral hepatitis
- Current management in light of the AASLD and IDSA guidelines.

Introduction

- Classic acute viral hepatitis is caused by one of the five etiologic agents:
  - Hepatitis A Virus
  - Hepatitis B Virus
  - Hepatitis C Virus
  - Hepatitis D Virus
  - Hepatitis E Virus
    - Rare viral infection—CMV, HSV





Case history

- 45 yrs old prisoner admitted with nausea, vomiting and fever for 3 days. No h/o IVDU, no tattoos. On exam, he has jaundice and tenderness in RUQ. Conscious and oriented.
- Labs: CBC: Normal, Bili: 10→19mg/dl, ALT: 3434→3510IU, AST: 2326→1428 IU, AP: 156, INR: 2.5→3.6.
- What is the diagnosis
- What serological tests will you order?
  - HAV- IgM and IgG
  - HEV-IgM and IgG
  - HBsAg, HbCore IgM &IgG, HBeAg, HBeAb, HDV Ab IgM and IgG
  - HCV AB and HCV RNA PCR

Hepatitis A and E – Important Features

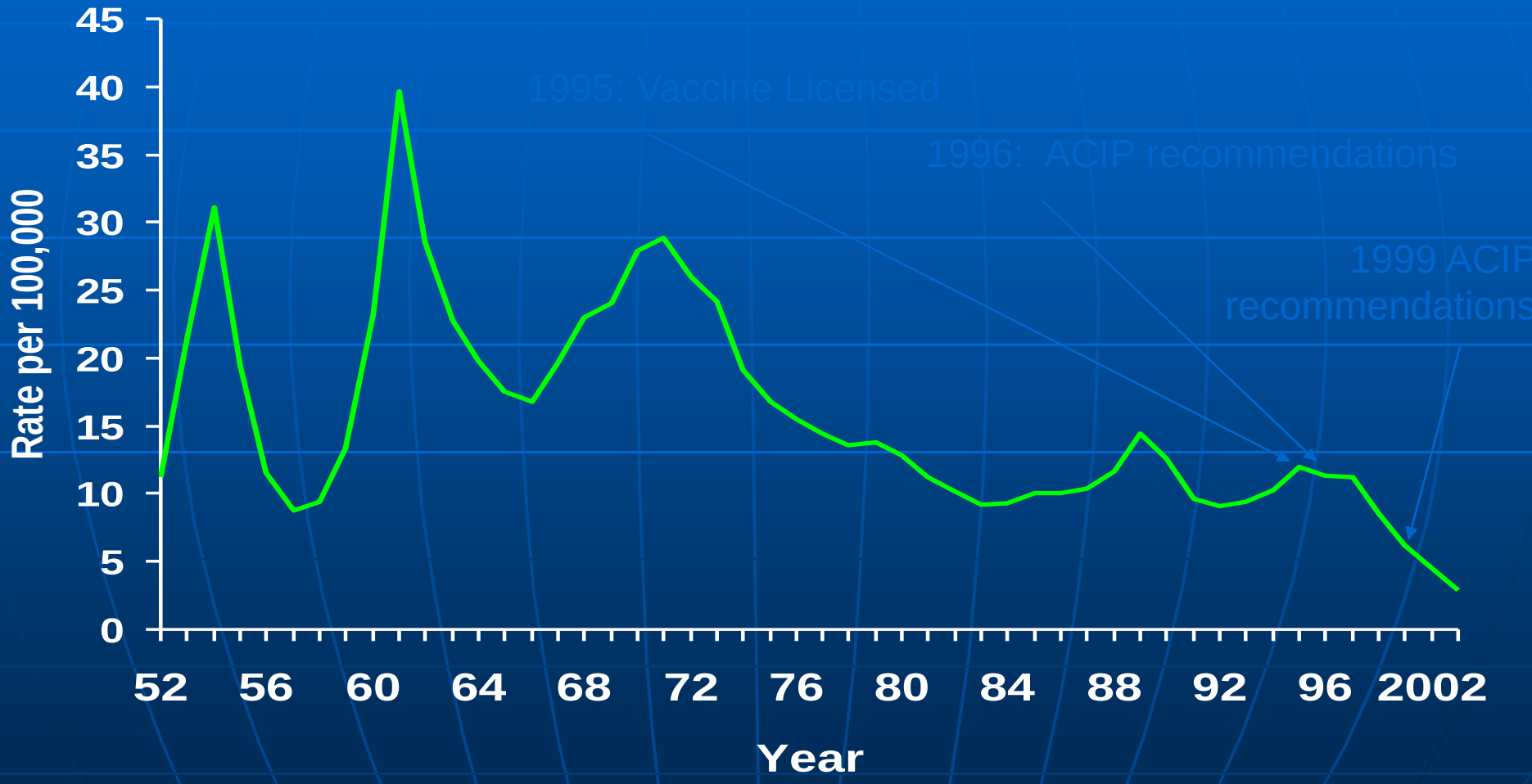
- **Transmission:** Oro-fecal route
- **Incubation period:** Average 40 days
  Range 15-60 days
- **Jaundice by age group:**
  - < 6 yrs: <10%
  - 6 – 14 yrs: 40 - 50%
  - > 14 yrs: 70 - 80%
- **Illness severity:** Increased with age
- **Case-fatality rate:** Overall- 1%-3%
  Pregnant women-15%-25% **(HEV)**.
- **Rare Complications:** Fulminant hepatitis
- Cholestatic hepatitis **(more with HEV)**
- Relapsing hepatitis
- **Chronic sequelae:** None identified

Geographic Distribution of HAV Infection

Geographic Distribution of Hepatitis E

Low sero-prevalence in US: 6%

Reported Cases of Hepatitis A and E, United States

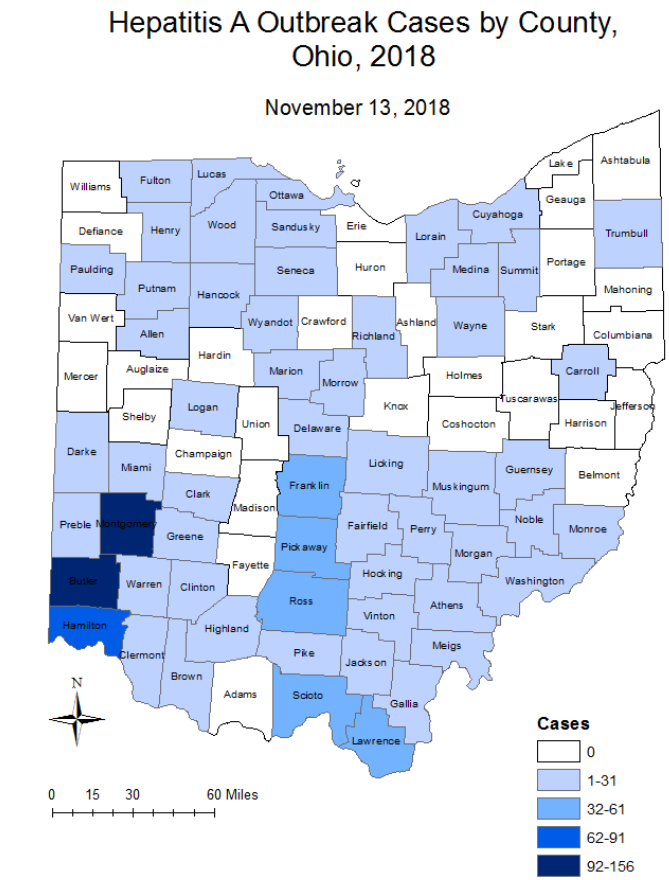


Source: NNDSS, CDC

Who are at risk of HAV & HEV?

- Children who go to day-care centers.
- Troops living under crowded conditions at military camps or in the field.
- Anyone living in heavily populated and unsanitary conditions.
- U.S. cases usually have h/o travel to HAV or HEV-endemic areas.
- **Ohio residents!**

Recent Outbreak of HAV in Ohio



Data analyzed 11/13/2018, Outbreak Response and Bioterrorism Investigation Team, Bureau of Infectious Diseases, Ohio Department of Health, 2018.

- **Hepatitis A Outbreak Summary (11/13/18):**
- **Number of cases: 865**
- Illness onset range: 01/05/2018 – 11/07/2018
- Age range: 3-81 years
- Gender: 60% male
- No. of hospitalizations: 551 (64%)
- No. of counties with cases: 58 (66%)
- **No. of deaths: 1**

Severity of acute viral Hepatitis

King's College Criteria

- **Non-acetaminophen**:
- INR > 6.5 OR
- Any 3 of the following 5:
  - Age < 10 or > 40
  - Serum bilirubin > 18
  - Jaundice to encephalopathy interval > 7 days
  - INR > 3.5
  - Unfavorable Etiology
    - Non-A, non-B hepatitis, halothane, idiosyncratic drug reaction, Wilson's

- 45 yrs
- Bili: 10→19mg/dl,
- INR: 2.5→3.6
- Etiology:
  - HAV- IgM and IgG
  - HEV-IgM and IgG
- No HE

For identifying patients with poor prognosis who needs LT
Sensitivity: 72 %
Specificity: 98 %
PPV: 89 %

Management HAV & HEV

- No specific Rx
- Hospitalization depends on severity of symptoms and LFTs
- Treatment is aimed toward identifying small group who may develop ALF
  - Role of N-acetylcysteine (NAC) in severe Acute HAV and HEV

Hepatol Int (2009) 3:563–570
DOI 10.1007/s12072-009-9151-0

ORIGINAL ARTICLE

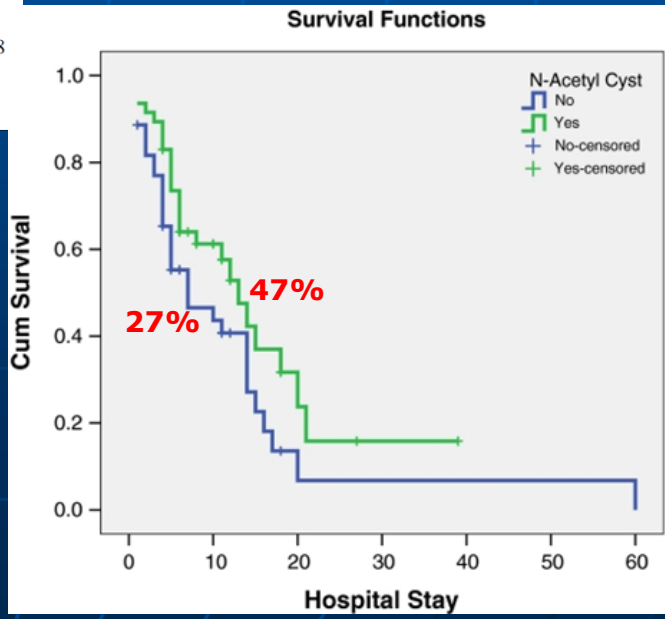
Role of *N*-acetylcysteine in adults with non-acetaminophen-induced acute liver failure in a center without the facility of liver transplantation

Khalid Mumtaz · Zahid Azam · Saeed Hamid · Shahab Abid · Sadik Memon · Hasnain Ali Shah · Wasim Jafri

Table 1 Baseline characteristics of study subjects in the two treatment groups

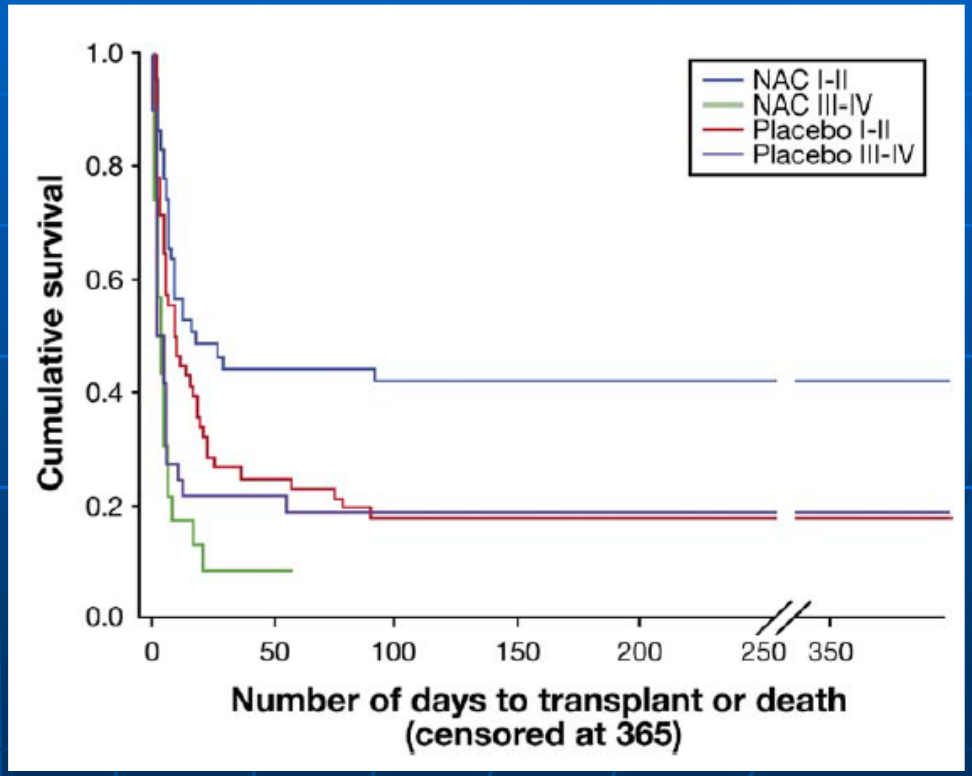
Characteristics	*N*-Acetylcysteine group (group 1, $n = 47$)	Control group (group 2, $n = 44$)	*P*
Male gender	26 (55.3%)	24 (54.5%)	0.941
Age (years)	27.74 ± 11.79	37.52 ± 18.82	0.004
Prothrombin time (s)	59.55 ± 36.07	53.05 ± 30.57	0.357
Bilirubin (mg/dl)	20.63 ± 11.03	14.36 ± 8.90	0.004
Serum albumin (mg/dl)	2.73 ± 0.55	2.70 ± 0.75	0.820
Alanine aminotransferase (mg/dl)	1926 ± 1374.2	1457.2 ± 1467.8	0.342
Interval between jaundice and hepatitis E (days)	8.87 ± 9.47	13 ± 18.24	0.175
Creatinine at admission (mg/dl)	1.39 ± 0.82	1.57 ± 0.90	0.312
Presence of ascites	10 (21.3%)	16 (36.4%)	0.111
Pregnancy with acute hepatitis E	8 (17%)	1 (2.3%)	0.031[a]
Hepatic encephalopathy			
Grade I	6 (12.8%)	6 (13.6%)	
Grade II	9 (19.1%)	18 (40.9%)	0.128
Grade III	15 (31.9%)	9 (20.5%)	
Grade IV	17 (36.2%)	11 (25.0%)	

Factors	Adjusted odds ratio	95% confidence interval for adjusted odds ratio	Wald *P*
Age (years)			
≤40[a]			
>40	10.3	2.0–52.3	0.005
N-Acetylcysteine			
Given[a]			
Not given	10.3	1.6–65.7	0.014
Type of FHF			
Hyperacute liver failure[a]			
Acute liver failure	5.03	3.1–130.3	0.018
Prothrombin time group (s)			
≤50[a]			
>50	15.6	3.6–67.9	<0.001
Requirement of ventilator			
Not ventilated[a]			
Ventilated	20.1	3.1–130.2	0.002



N-acetylcysteine improves transplant-free survival in non-acetaminophen ALF
ALFSG group. Gastroenterology 2009

- 173 patients enrolled;
  - NAC (n:81) or placebo (n:92).
- **Overall survival** at 3 weeks:
  - NAC group: 70%
  - Placebo: 66%; (p-value:0.28).
- **Transplant free survival:**
  - NAC patients: 40%
  - Placebo: 27%; p-value:0.04.



Vaccination for HAV and HEV

Vaccination for HAV

- HAV vaccine: Havrix ,Vaqta
  - Formalin inactivated virus
    - Greater than 2 years of age
    - 2 doses, 6-12 months apart

  Candidates for vaccine
    - Children living in endemic area
    - Increased risk of HAV
      - **People more than 30 year of age with CLD**
      - Staff of day care centers
      - Staff of NICU
      - **All residing in OHIO**

Vaccine for HEV

- HEV 239 vaccine, Hecolin® is a promising vaccine
- Recommended for use in 16–65 year-old healthy subjects in China.
- Not FDA approved

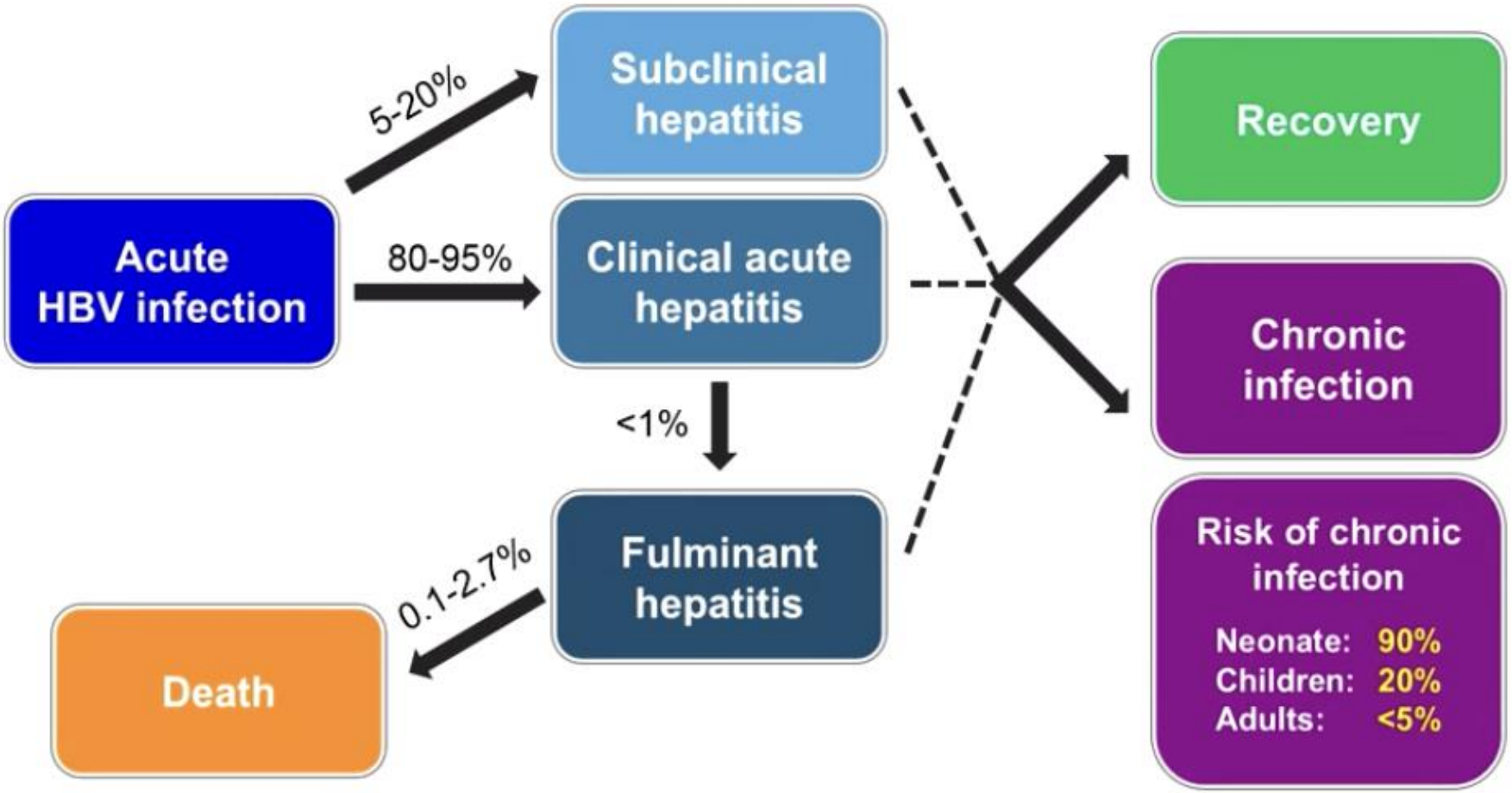
Case of Acute hepatitis B/C

- 32 yrs old male with h/o IVDU and multiple tattoos. Admitted with unwell feeling and jaundice. Exam confirms jaundice and RUQ tenderness.
- Labs: CBC: N; Bili: 7 mg/dl, ALT: 726, AST:660 IU, AP> 100. INR: 1.5.
- US shows altered echotexture of liver.
- **HCV AB: negative; HCV PCR: 325,000copies/ml**
- HBsAg: Negative, HBcIgM: Negative; HBsAB: negative; Hbcore IgG: positive
- HAV IgM and IgG: negative: HEV: negative
- What is the diagnosis?
- What are the risk of progression to chronic phase?
- How will you manage it?

Hepatitis B and C

- Both are blood borne viral infections.
- Sources of transmission in US are:
  - IVDU
  - Sexual transmission—HBV 15-20%
  - Tattoos
  - Vertical transmission—HBV 20-25%
- Sources of transmission in developing world:
  - Unscreened Blood and product tx
  - Therapeutic injection
  - Contaminated surgical instruments

Outcomes of Acute HBV Infection Vary by Age of Exposure



Hyams KC. *Clin Infect Dis* 1995;20:992-1000;
J Liang. *Hepatology* 2009;49(5 Suppl): S13-21.

When to treat Acute Hepatitis B

- AVT is usually not indicated as >90% spontaneously resolve infection.
- Patients with severe acute liver injury or ALF due to HBV may benefit from entecavir or tenofovir.
- Duration of treatment is not certain. However, 3-6 months post HBSAg seroconversion is generally advised

A randomized controlled trial of lamivudine to treat acute hepatitis B. Kumar M et al. Hepatology 2007

- Most cases resolve spontaneously without therapy
- Can lead to severe hepatitis and ALF in 0.5-2% of patients
- Do patients with acute HBV require antiviral therapy?

Lamivudine for acute HBV

Entry criteria

- ALT>2.5xULN
- Bil >2.5x ULN
- HBcIgM+

Exclusions

- Co-infections
- Alcohol>20g/d
- Hepatotoxic drugs
- Chronic HBV

- RCT 1:1 – LAM vs placebo
- Lamivudine was given for 3 m
- Severe HBV:
  - Encephalopathy
  - Bil≥10mg/dL
  - INR ≥ 1.6
- FU 12 m

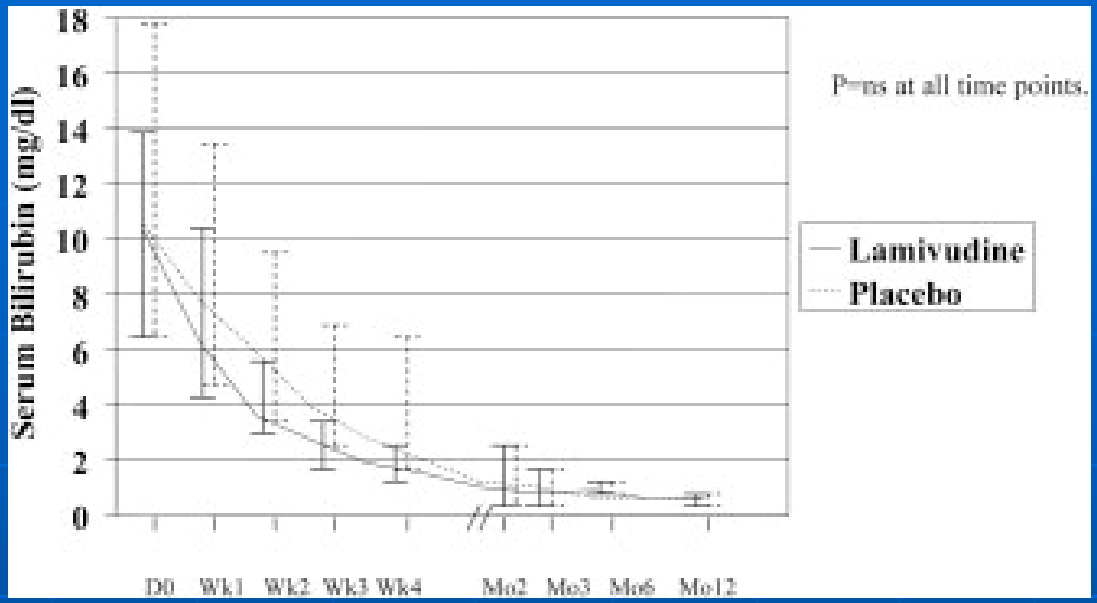
Kumar, Hepatology 2007

Baseline characteristics

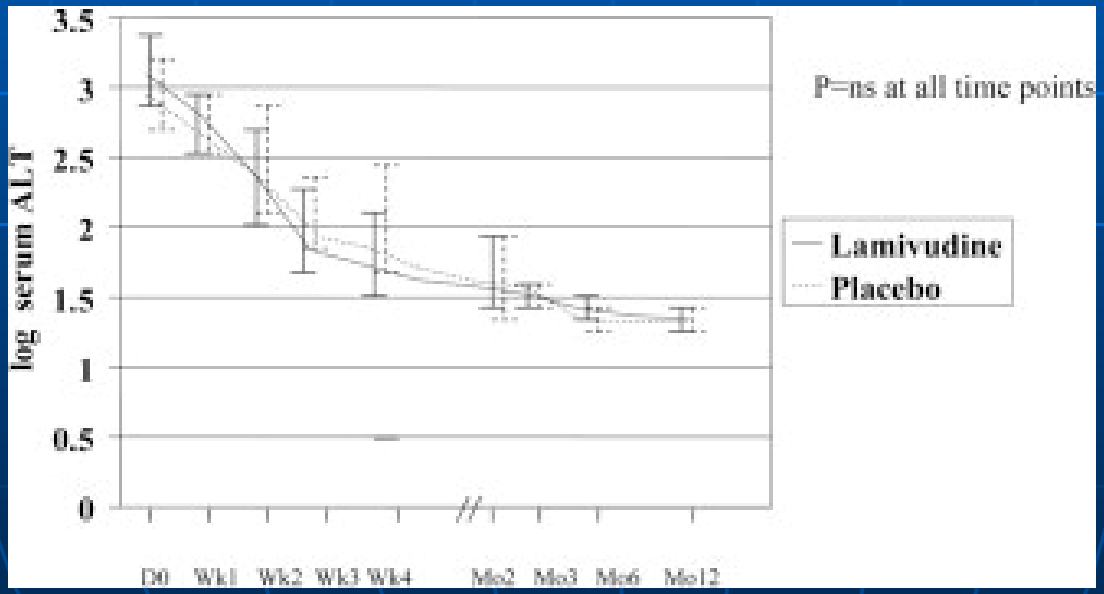
	LAM	PLB
Total no of patients	31	40
Age	37	36
Severe HBV	71%	62.5%
Bilirubin	**10.9**	**12.3**
ALT	1658	1253
INR	2.0	1.89
HBeAg+	83.9%	85%
HBV DNA (log cpm)	5.53	5.24
Encephalopathy	6.5%	2.5%
Deaths	0	0

Kumar, Hepatology 2007

Bilirubin



ALT



Kumar, Hepatology 2007

Clinical outcomes

	LAM	PLB
Total no of patients	31	40
HBsAg-ve>12m	93.5%	92.5%
Decompensation	0	0
Deaths	0	0

Kumar, Hepatology 2007

Conclusions

- Lamivudine did not confer any clinical benefits in patients with acute HBV
- Lamivudine also did not decrease the prevalence of chronic hepatitis B

Kumar, Hepatology 2007

The Study of Efficacy of Lamivudine in Patients with Severe Acute HBV

Jian-Wu Yu, et al . DDS 2010

Entry criteria

- INR>1.4
- **Bil >13 mg/dl**
- HBsAg+
- ALT flare>5x ULN
- HBcIgM+
- HBV DNA≥10^4 cpm

Exclusions

- HBcIgG+
- Co-infections
- Alcohol>20g/d
- Hepatotoxic drugs
- Abnormal US

- RCT 1:1 – LAM vs standard medical therapy
- Randomization was by order of admission
- Lamivudine given until HBsAg clearance
- FU 12 m

Yu, Dig Dis Sci 2009

Baseline characteristics

	LAM	med care
Total patients	40	40
Males	30	29
Age	45.8	44.5
Bilirubin	**14.7**	**13.7**
ALT	2456	2507
INR	1.5	1.48
HBV DNA (logs)	6.5	6.7
HBeAg+	33	32

Yu, Dig Dis Sci 2009

Results

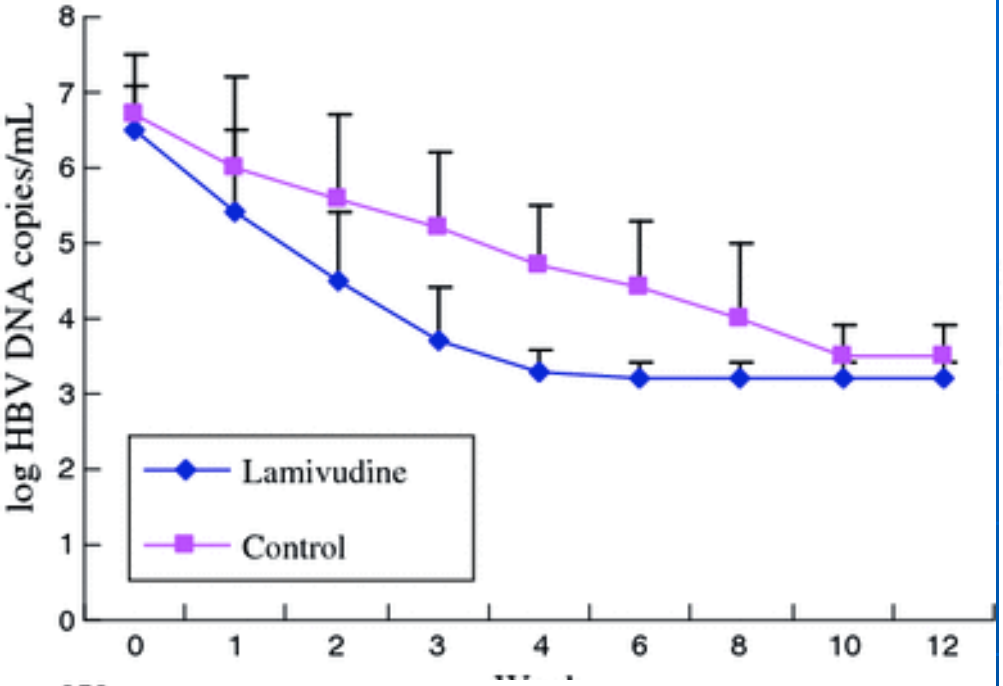
	LAM	med care	p value
Total patients	40	40	
Subac Liver Failure*	**8 (20%)**	**17 (42.5%)**	**0.03**
Mortality @ 3m	**3 (7.5%)**	**10 (25%)**	**0.034**
HBsAg loss @ 3m	39	38	

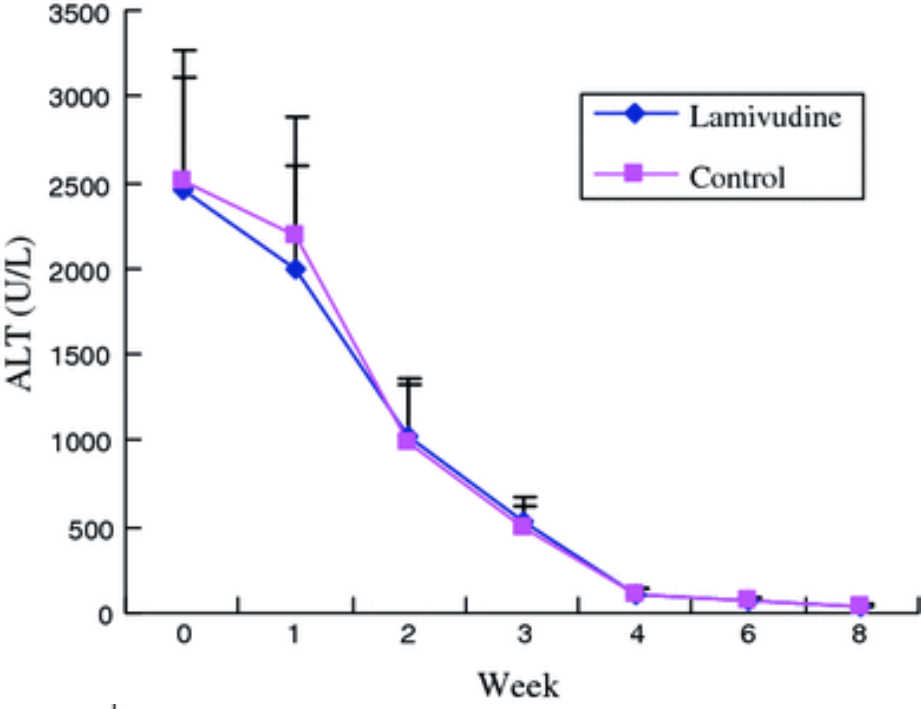
Prognostic markers of mortality

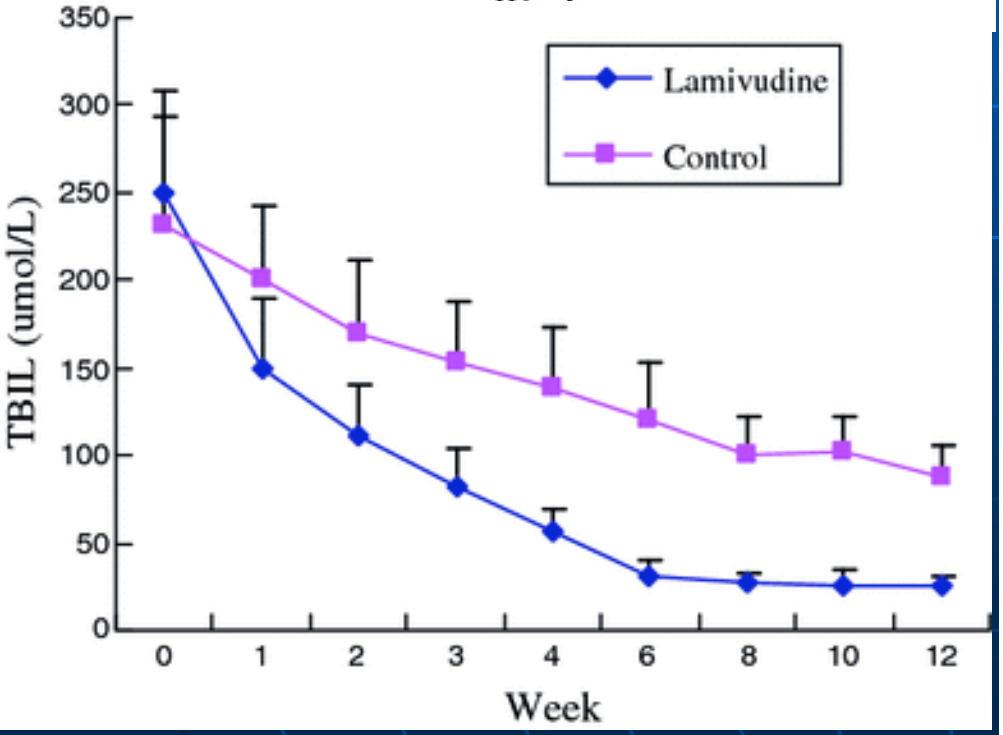
- Age≥ 45
- Lamivudine therapy
- Total: direct bili ratio >2
- Rapid decline HBV DNA
- INR

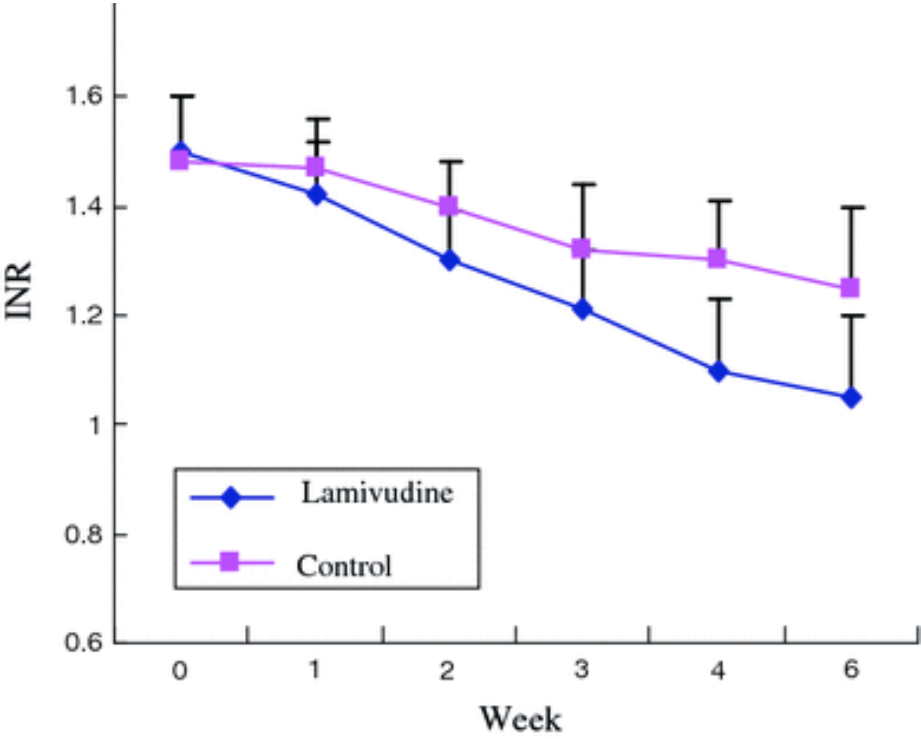
*severe jaundice, INR≥1.6 ± encephalopathy

Yu, Dig Dis Sci 2009


log HBV DNA copies/mL
Lamivudine
Control
0 1 2 3 4 6 8 10 12


ALT (U/L)
Lamivudine
Control
0 500 1000 1500 2000 2500 3000 3500
0 1 2 3 4 6 8
Week


TBIL (umol/L)
Lamivudine
Control
0 50 100 150 200 250 300 350
0 1 2 3 4 6 8 10 12
Week


INR
Lamivudine
Control
0.6 0.8 1 1.2 1.4 1.6
0 1 2 3 4 6
Week

Conclusions

- Lamivudine reduces mortality and liver failure in patients with severe acute HBV
- Differences in enrolment criteria are the likely explanation for differences with Kumar study
- The criteria for starting antiviral therapy in acute HBV is unclear.

Chronic Hepatitis B

Chronic HBV is a Dynamic Disease

- Not curable
  - HBV can be suppressed but not eliminated
- Dynamic disease
  - Life-long monitoring required
  - Best serologic marker of immune control is loss of HBsAg → acquisition of anti-HBs

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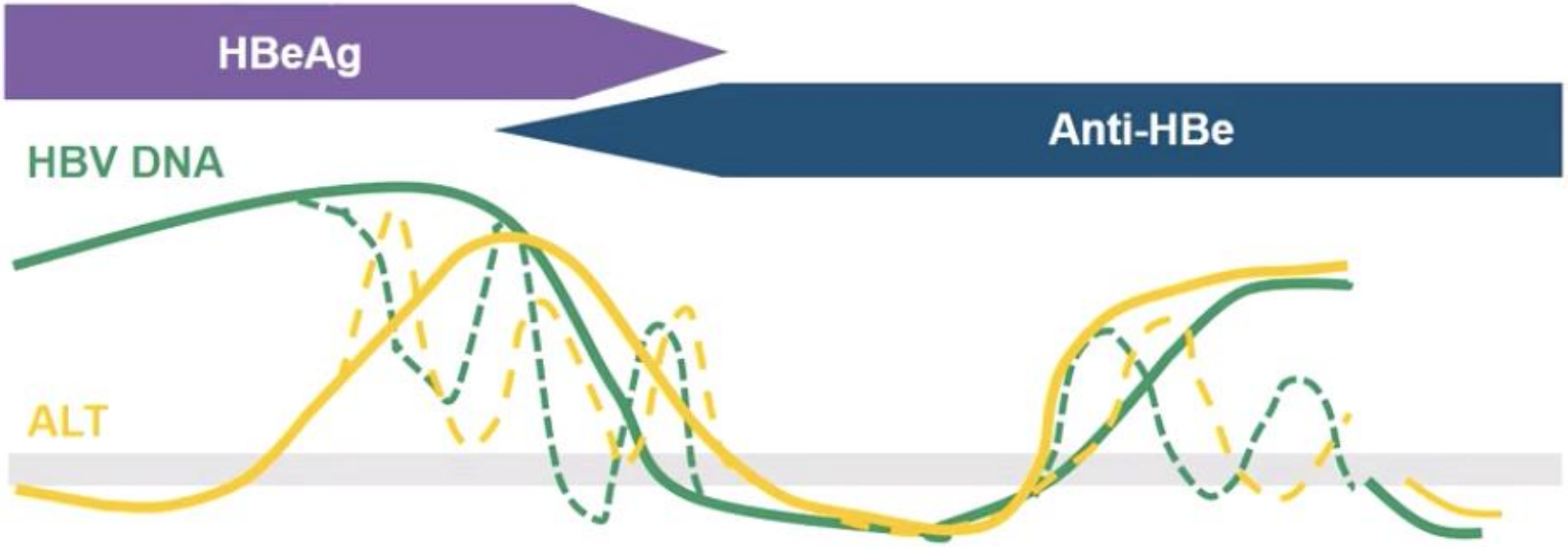
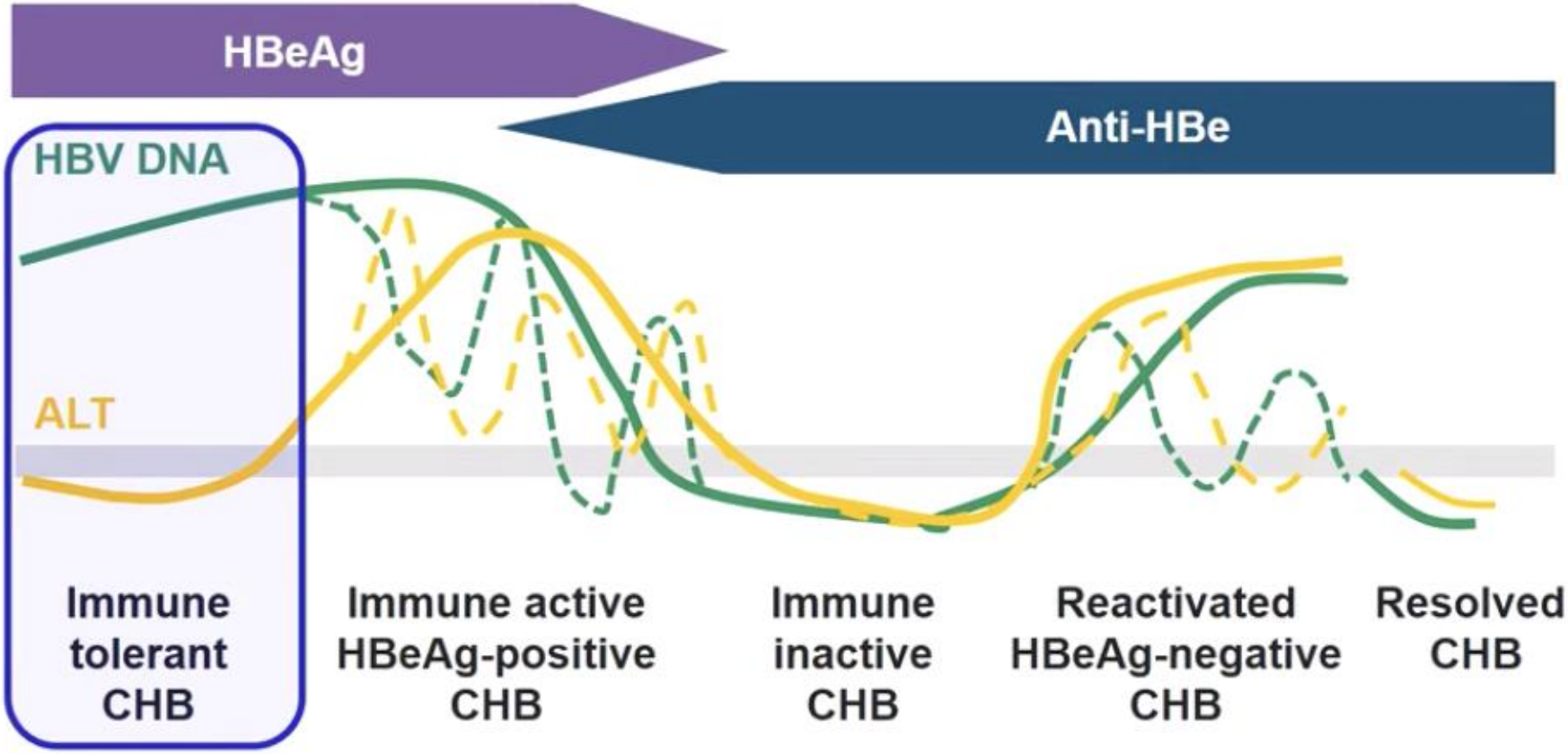
★ ***One normal ALT or low HBV DNA level does NOT imply an absence of long-term problems***

Phases of Chronic Hepatitis B (CHB)



Lok AS, et al. *Arch Intern Med*. 2006;166:9.

Immune Tolerant Chronic Hepatitis B (CHB)



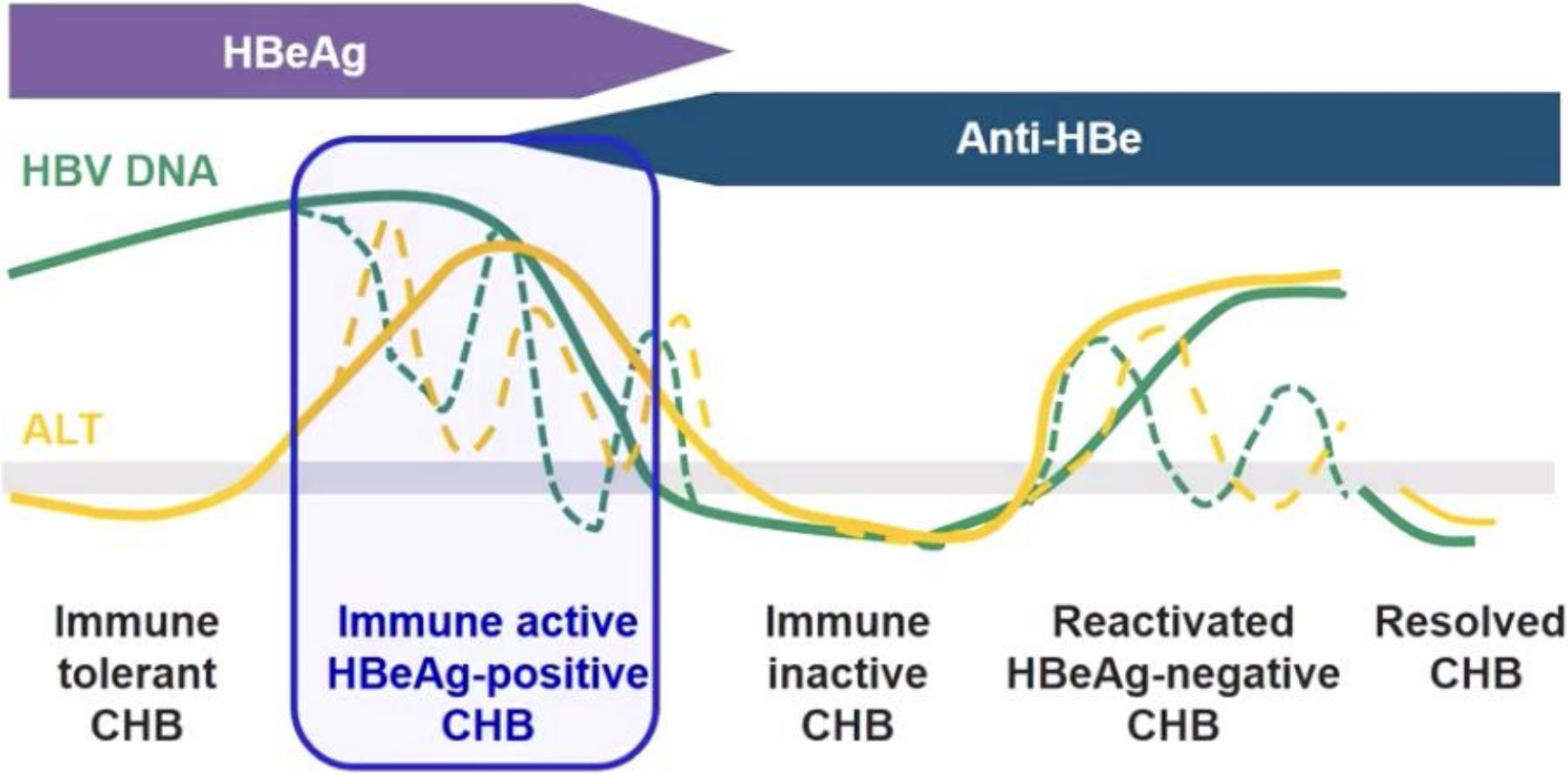
Lok AS, et al. *Arch Intern Med*. 2006;166:9.

Immune Tolerant Chronic Hepatitis B

- Defined by:
  - HBeAg positive
  - ALT levels normal (<30 IU/L males, <19 IU/L females)
  - HBV DNA levels high, usually $\geq 10^7$ IU/mL
- Typical of persons infected as infants/young children
- Median age of transition to immune active HBeAg-positive phase = 30 years
- **Treatment NOT indicated**

Keeffe EB, et al. *Clin Gastroenterol Hepatol*. 2006.
Lok AS and McMahon A, AASLD Guideline 2007.
Andreani T, *Clin Gastroenterol Hepatol*. 2007.

HBeAg-Positive "Active" Chronic Hepatitis B (CHB)



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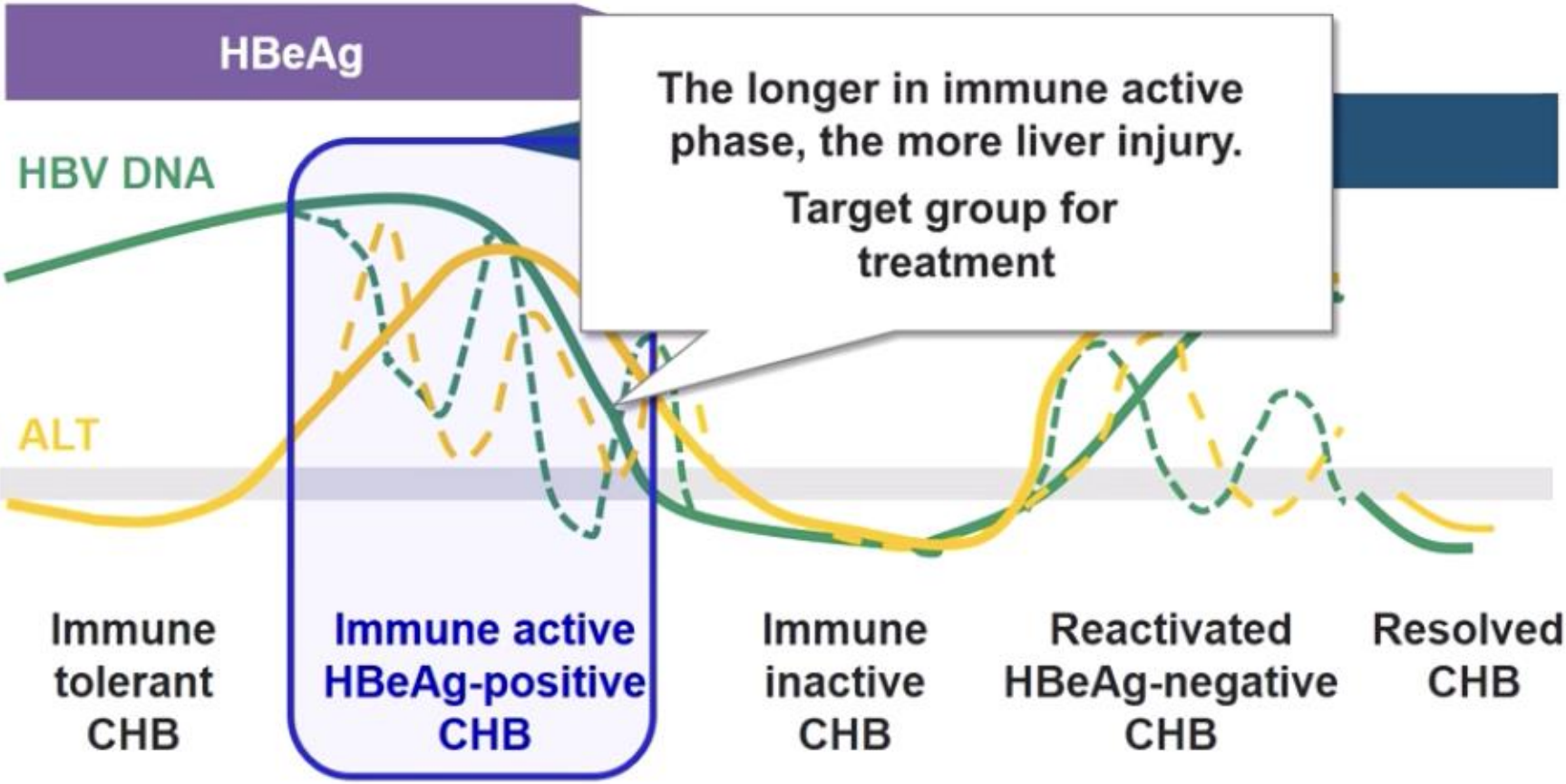
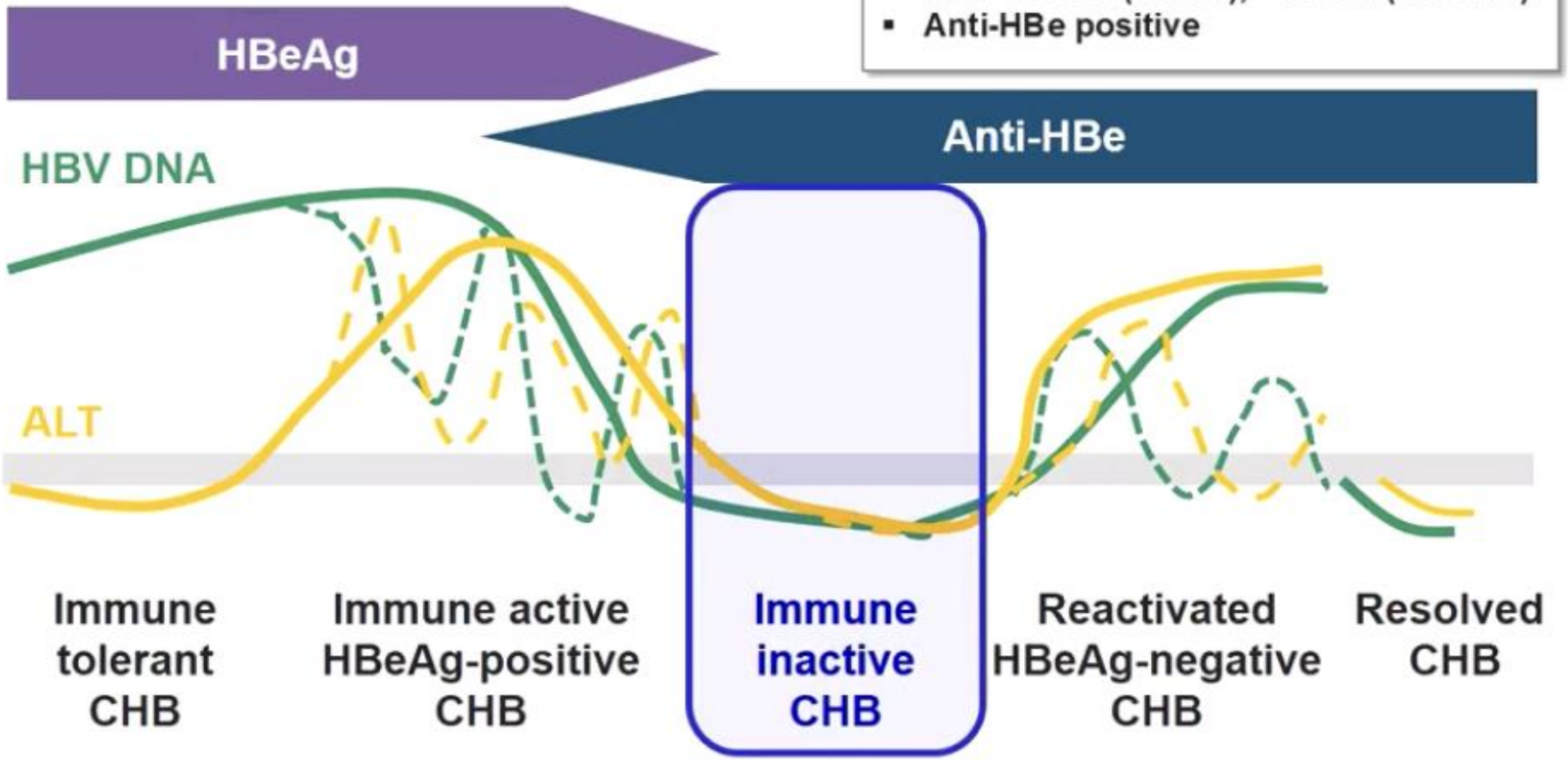


Lok AS, et al. *Arch Intern Med*. 2006;166:9.

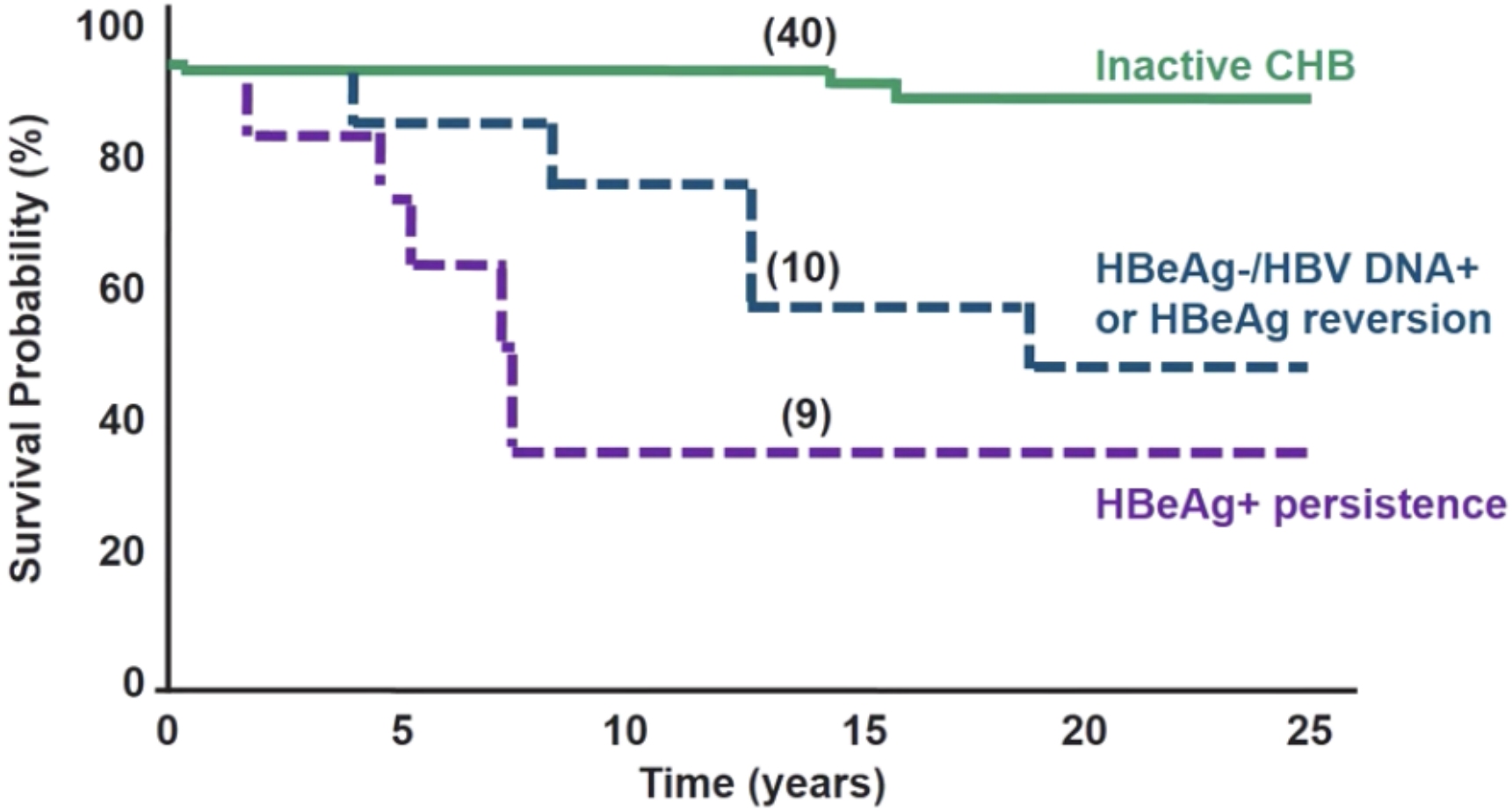
Immune Inactive Chronic Hepatitis B (CHB)

- HBV DNA <2000 IU/mL
- ALT <30 U/L (males), <19 U/L (females)
- Anti-HBe positive



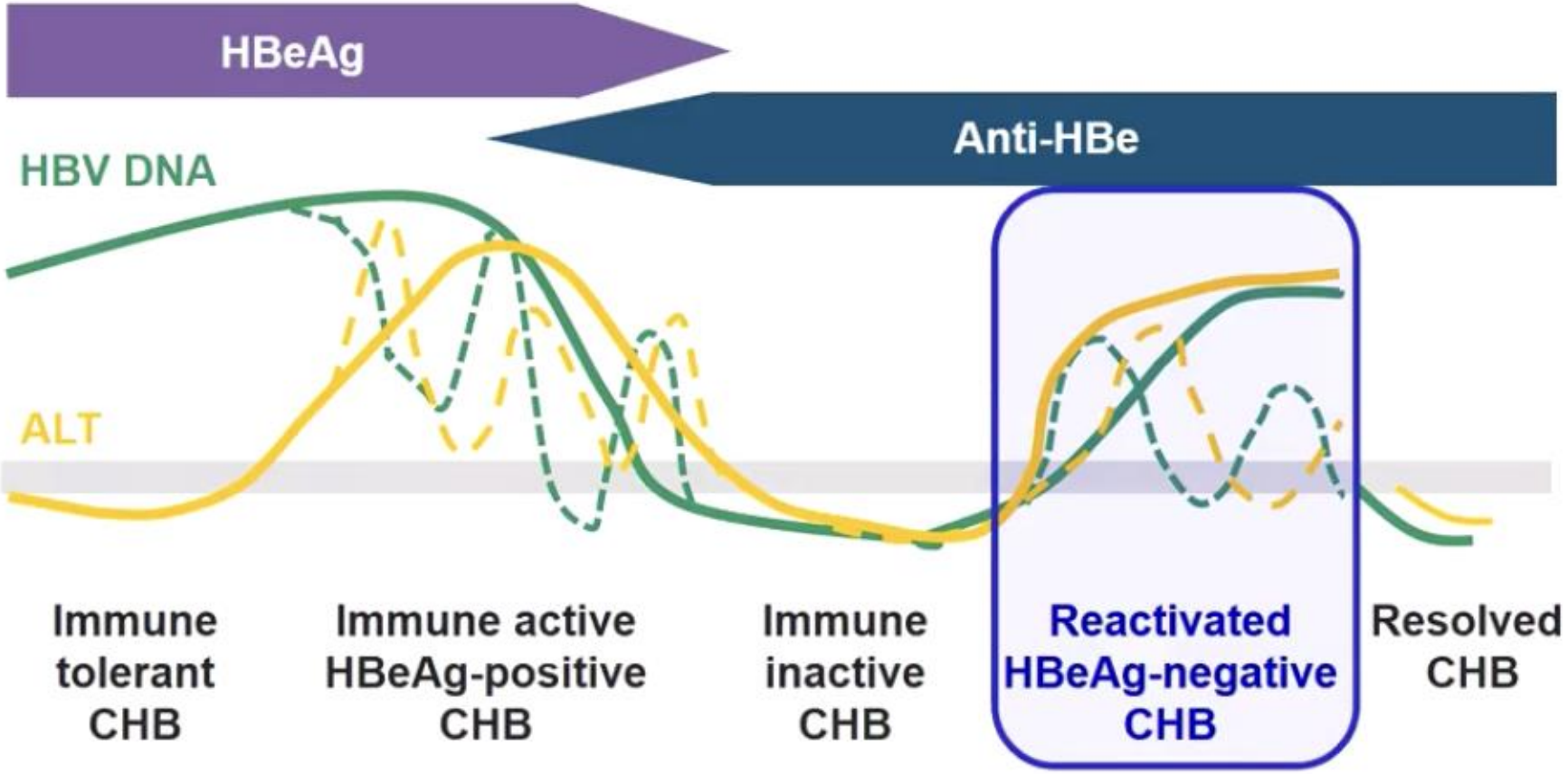
Lok AS, et al. *Arch Intern Med*. 2006;166:9.

Natural History of Untreated CHB: Survival Highest if Inactive CHB



Fattovich G, et al. *Gut*. 2008 Jan;57(1):84-90.

HBeAg Negative "Active" Chronic Hepatitis B (CHB)



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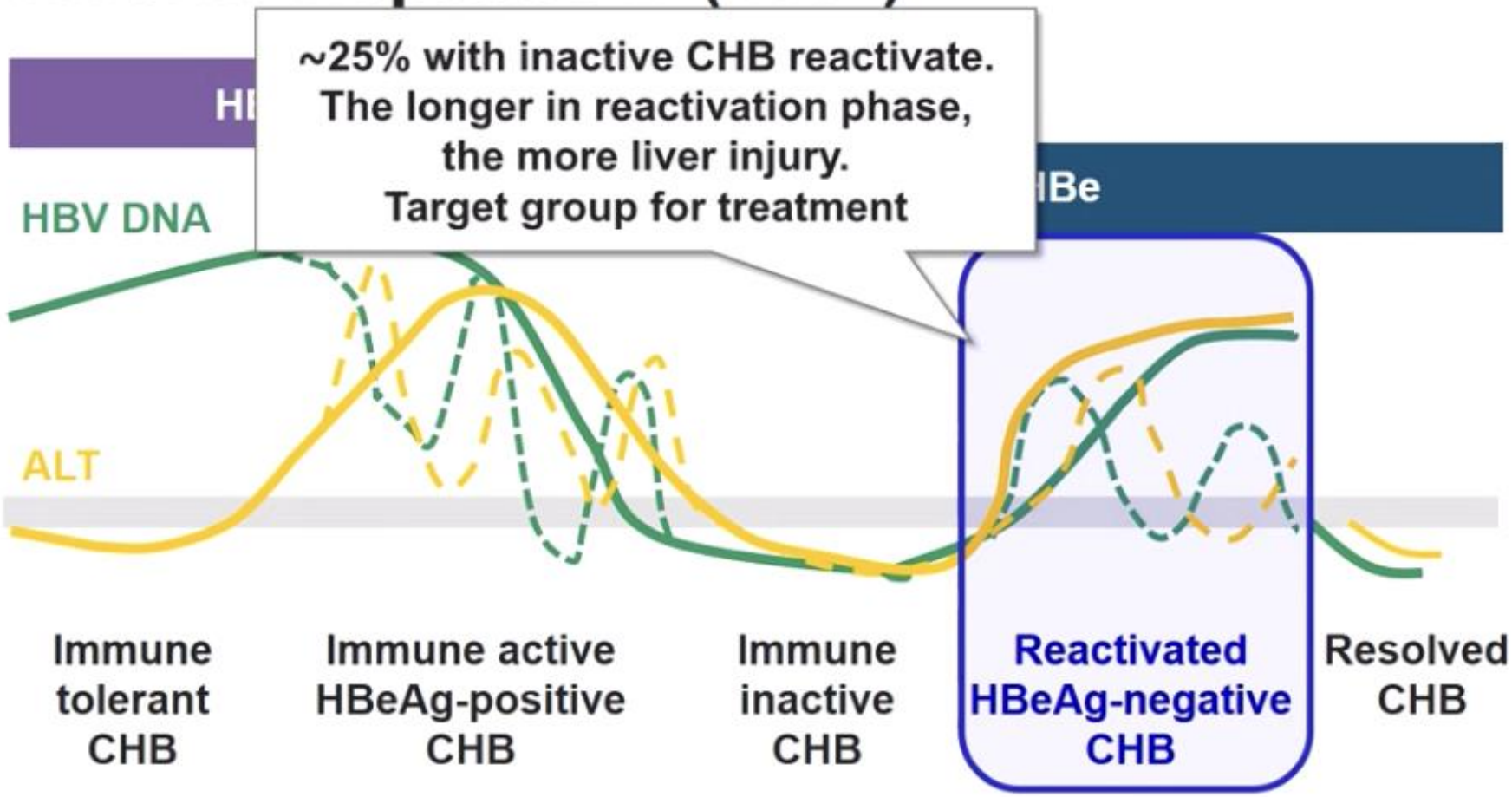
HBeAg Negative "Active" Chronic Hepatitis B (CHB)



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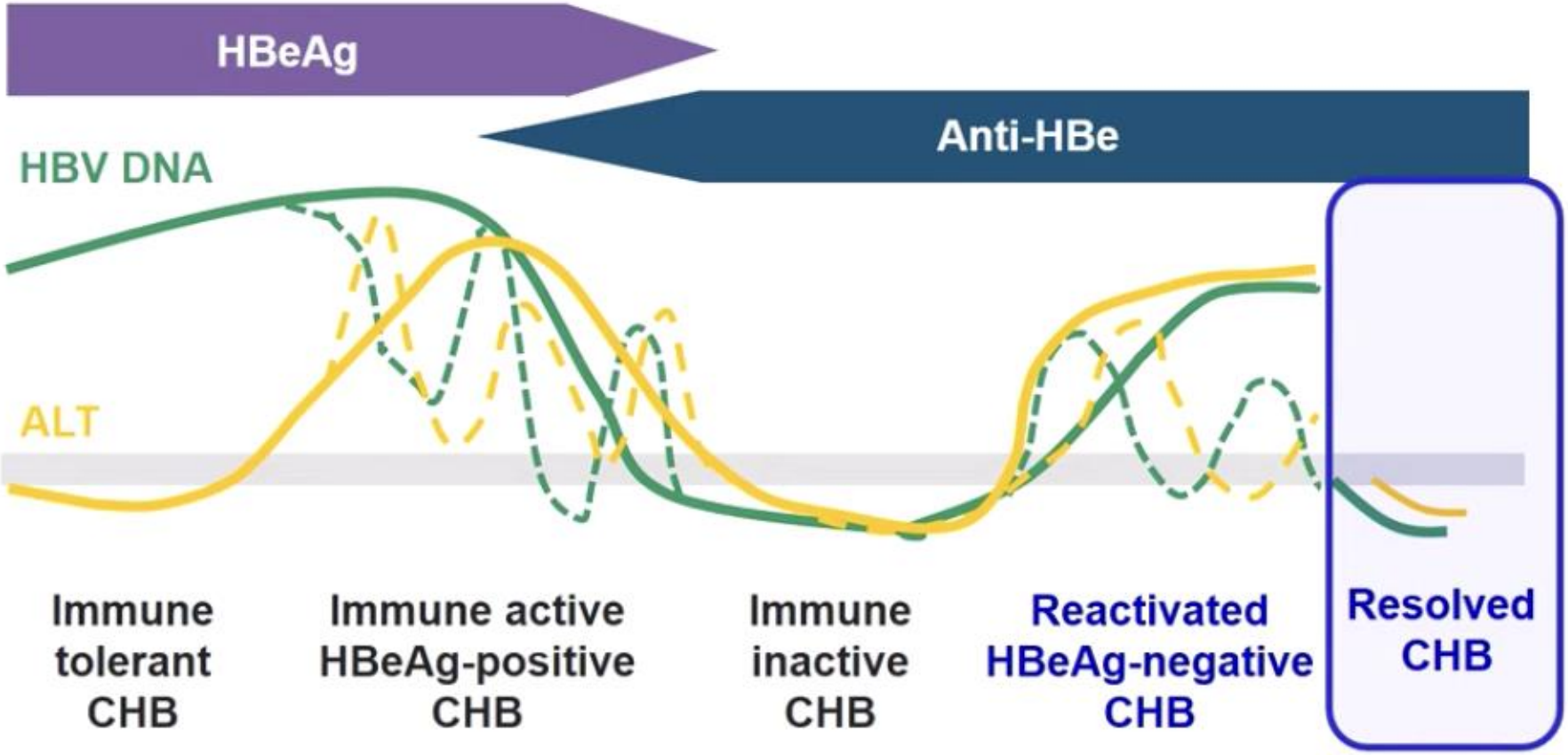
HBsAg Seroclearance
Resolved Chronic Hepatitis B (CHB)



Lok AS, et al. *Arch Intern Med*. 2006;166:9.

Summary (2)
Phases of Chronic HBV Infection

Phase	Management
Immune tolerant	Monitor ALT every 3-6 months
HBeAg positive immune active	Treat
Inactive chronic HBV	Monitor ALT every 6 months
HBeAg negative immune active (Reactivation)	Treat
Resolved HBV	Monitor ALT every 6 months

Identifying Treatment Candidates

Algorithm to Identify Treatment Candidates

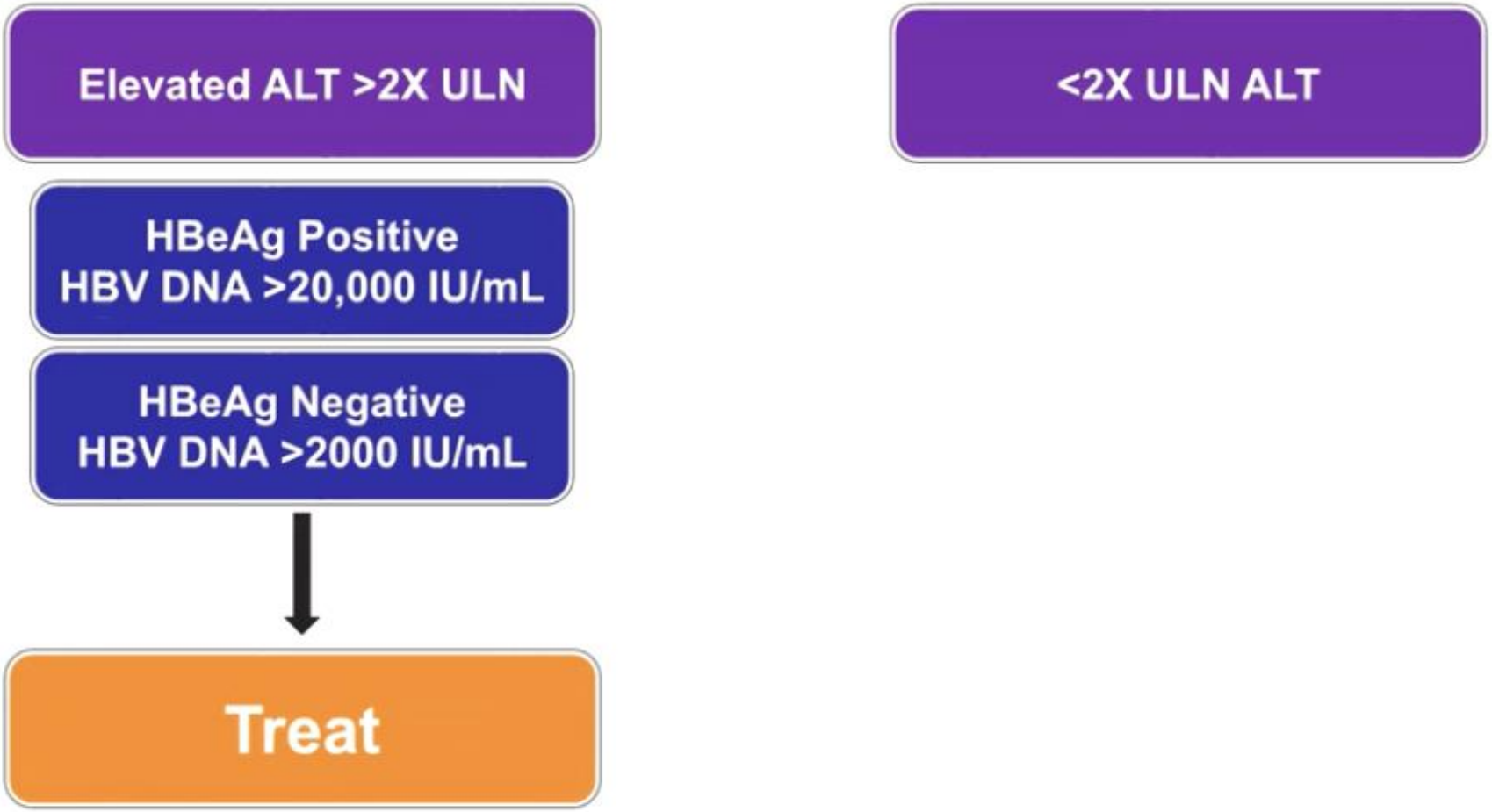
Elevated ALT >2X ULN

<2X ULN ALT

ULN = upper limit of normal

Adapted from AASLD Practice Guidelines.

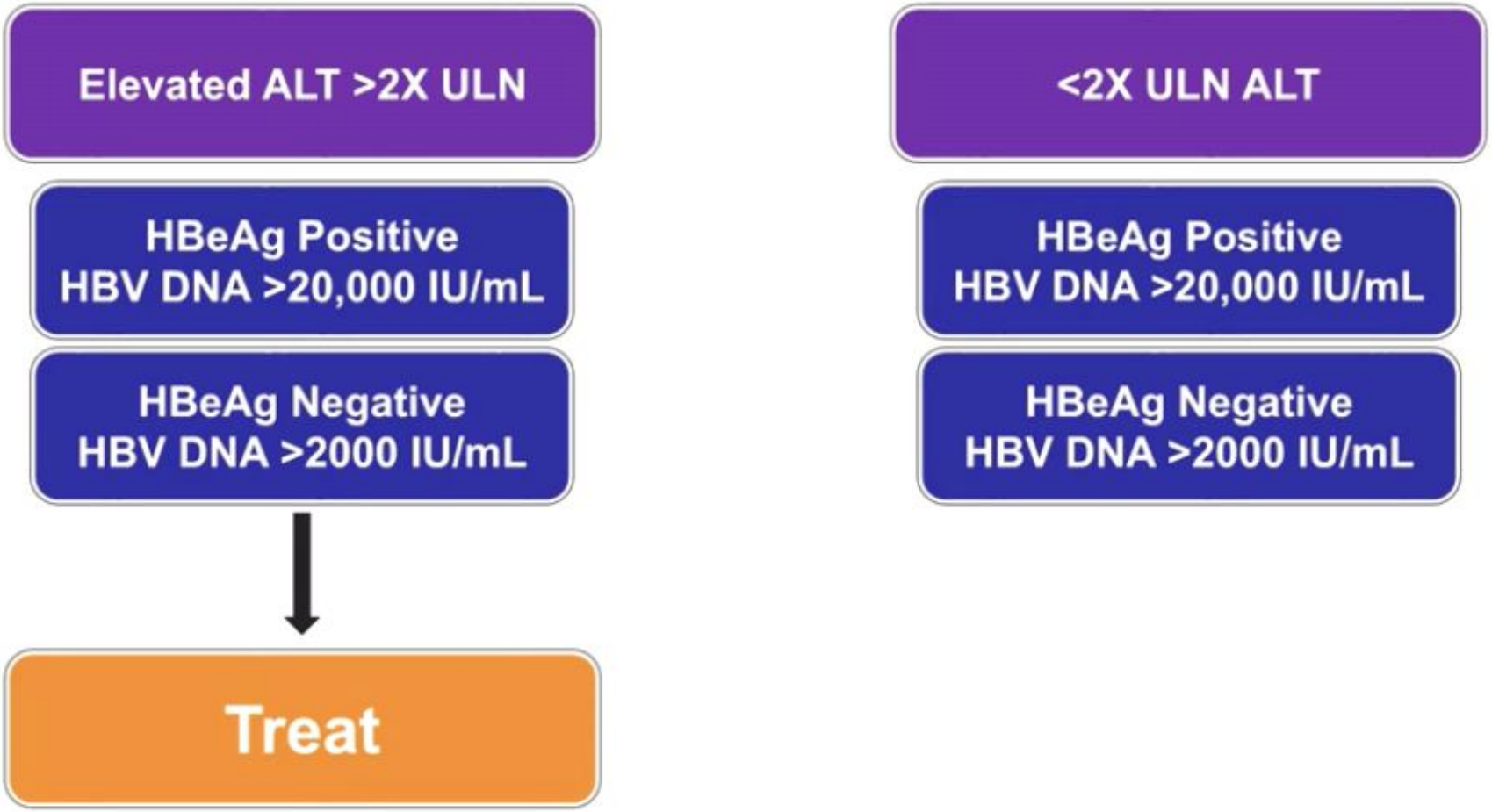
Algorithm to Identify Treatment Candidates



ULN = upper limit of normal

Adapted from AASLD Practice Guidelines.

Algorithm to Identify Treatment Candidates



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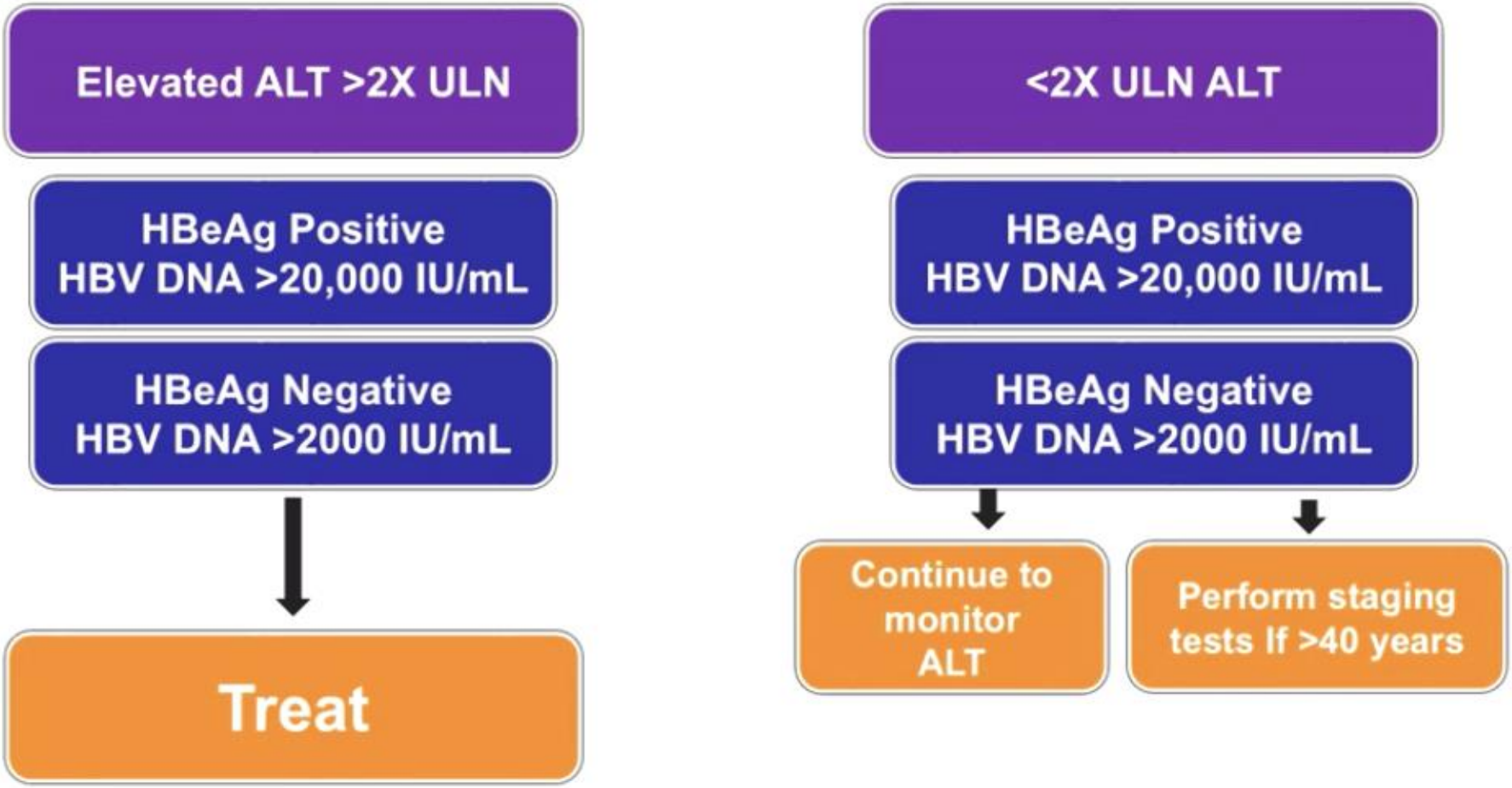

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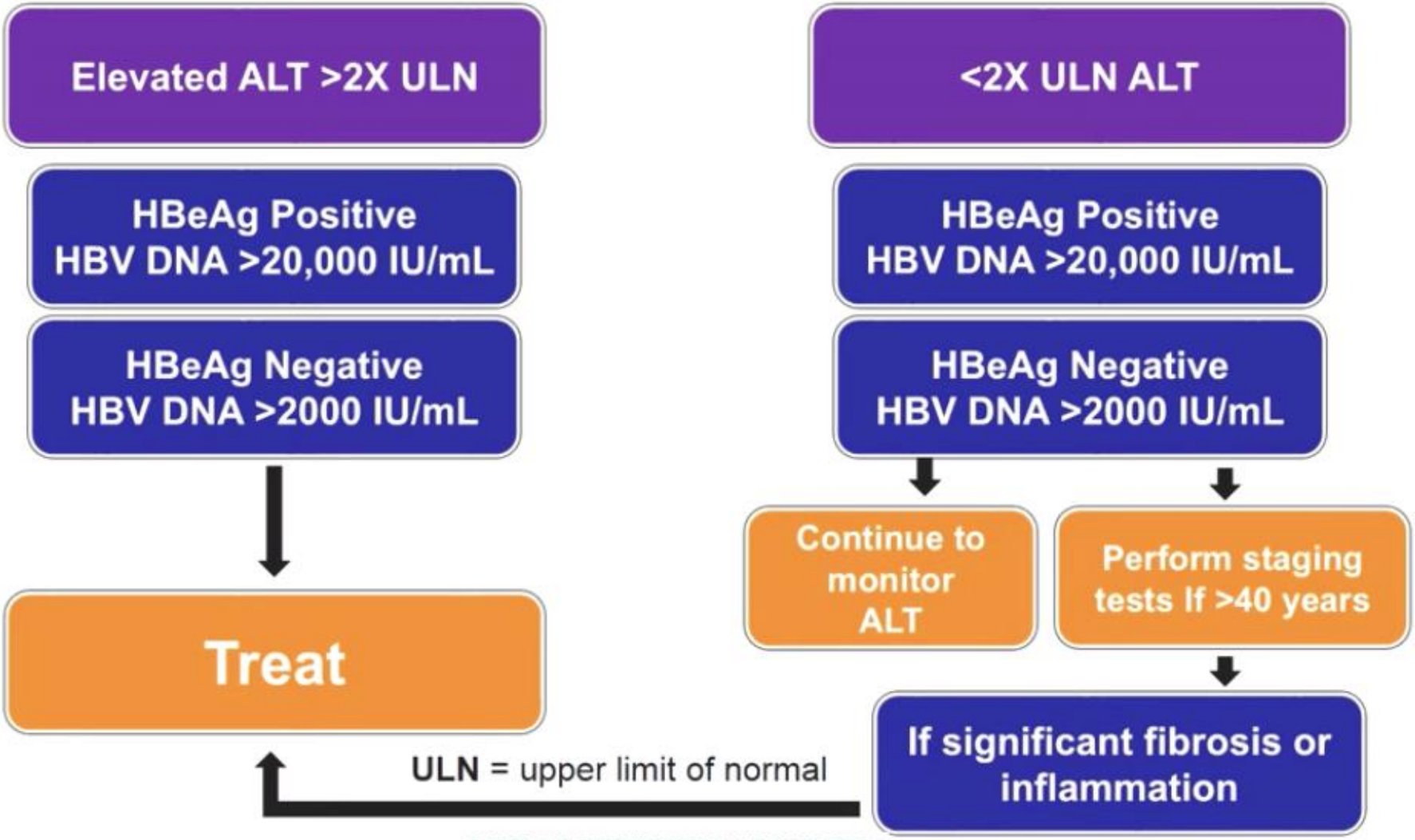
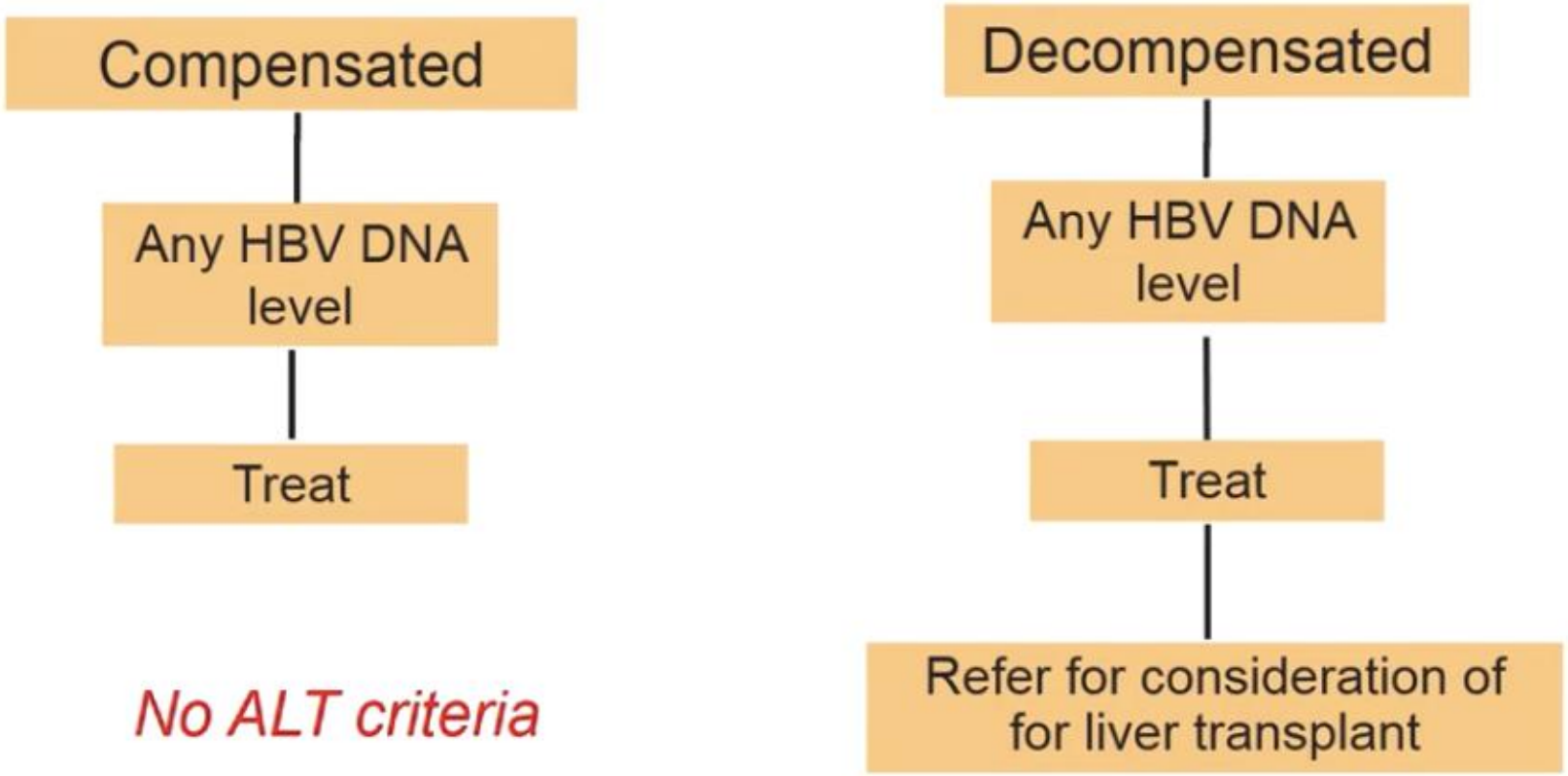


Adapted from AASLD Practice Guidelines.

Importance of Identifying Patients with HBV Cirrhosis

- Warrant surveillance for complications of cirrhosis
  - Varices
  - Hepatocellular carcinoma
- Treatment guidelines differ
  - Urgency of treatment
  - Duration of therapy
  - Use of peg-interferon versus nucleoside analogues

Algorithm for Management of Patients with Cirrhosis



Goals of HBV Treatment

- Suppress HBV replication
- Decrease liver necrosis and inflammation
- Reverse liver fibrosis
- Prevent progression to cirrhosis, liver failure, and hepatocellular carcinoma (HCC)

Lok AS, et al. *Hepatology*. 2007; 45: 507-539.
Lok AS, et al. *Hepatology*. 2009; 50: 661-662.
Terrault N, et al. *Hepatology*. 2016; 63: 261-283.

Approved HBV Treatments

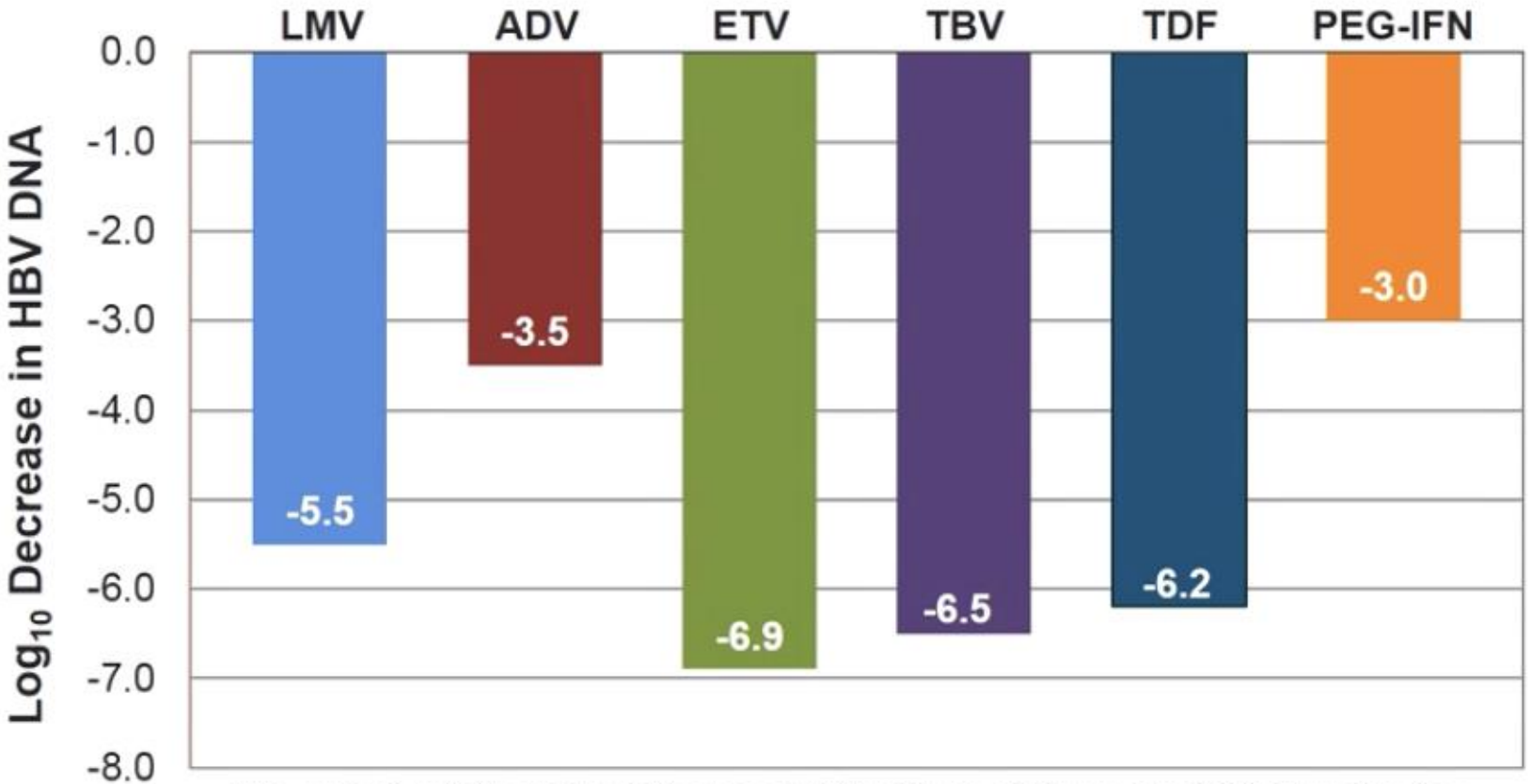
- **Interferons (IFN)**
  - Standard IFN alfa
  - Pegylated IFN alfa
- **Nucleos/tide Analogues**
  - Lamivudine (Epivir®, LMV)
  - Adefovir (Hepsera®, ADV)
  - Entecavir (Baraclude®, ETV)
  - Telbivudine (Tyzeka®, TBV)
  - Tenofovir disoproxil fumarate (Viread®, TDF)
  - Tenofovir alafenamide (Vemlidy®, TAF)

Responses to HBV Treatment

- **Virologic/Serologic Response**
  - Decrease in serum HBV DNA to undetectable levels
  - HBeAg loss and seroconversion to anti-HBe, applicable to HBeAg+ patients only
  - HBsAg loss: Ultimate goal
- **Biochemical Response**
  - Decrease in ALT levels to normal
- **Histological Response**
  - Decrease in inflammation and fibrosis (seldom assessed in clinical practice)

Lok ASF, McMahon BJ. *Hepatology*. 2007; 45: 507-539.
Lok ASF, McMahon BJ. *Hepatology*. 2009; 50: 661-662.
Terrault N, et al. *Hepatology*. 2016; 63: 261-283.

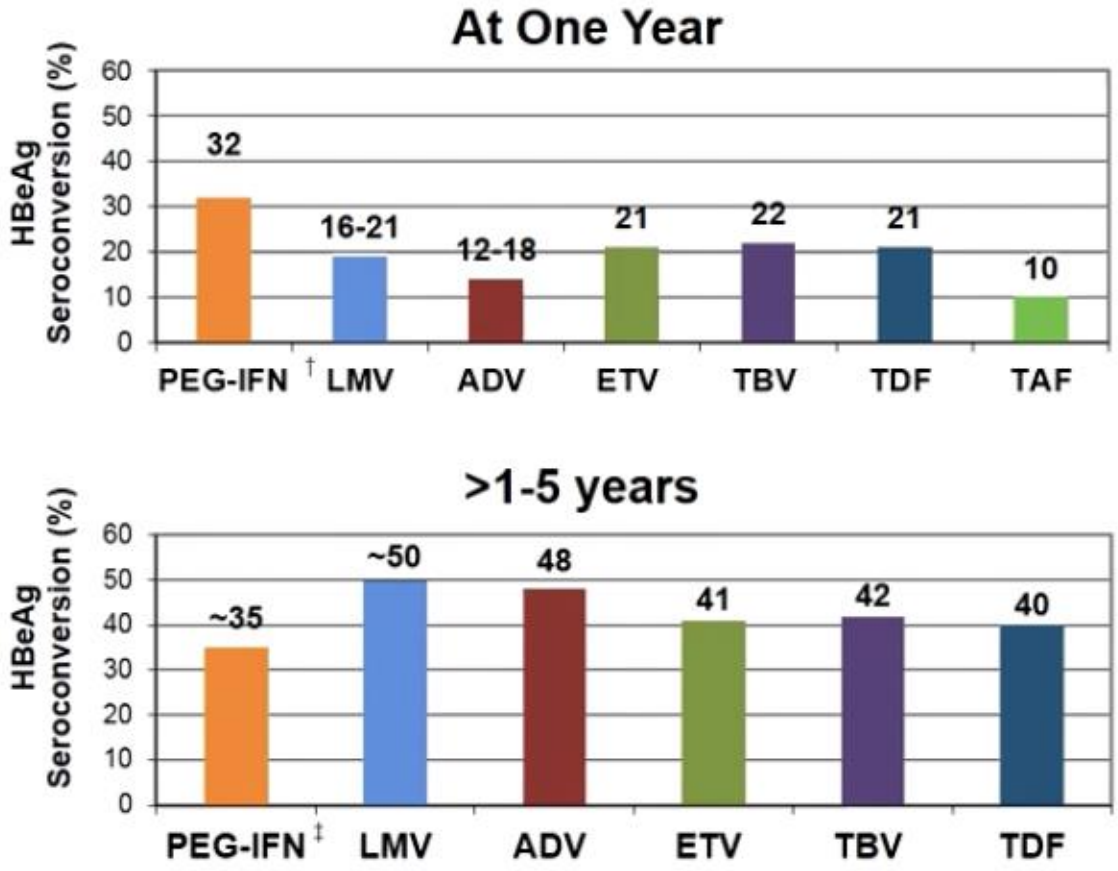
Decrease in Serum HBV DNA After 1 Year of Treatment in HBeAg+ or HBeAg- Patients with Chronic Hepatitis B



LMV, lamivudine; ADV, adefovir; ETV, entecavir; TBV, telbivudine; TDF, tenofovir; PEG-IFN, peginterferon.

Scaglione SJ, Lok AS. *Gastro*. 2012; 142: 1360-1368.

HBeAg Seroconversion After 1 to 5 Years of Treatment



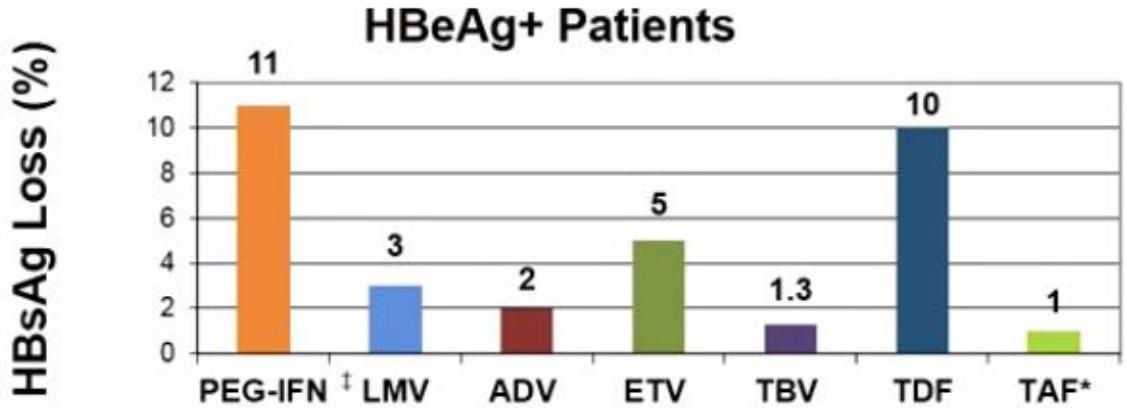
PEG-IFN, peginterferon
LMV, lamivudine
ADV, adefovir
ETV, entecavir
TBV, telbivudine
TDF, tenofovir

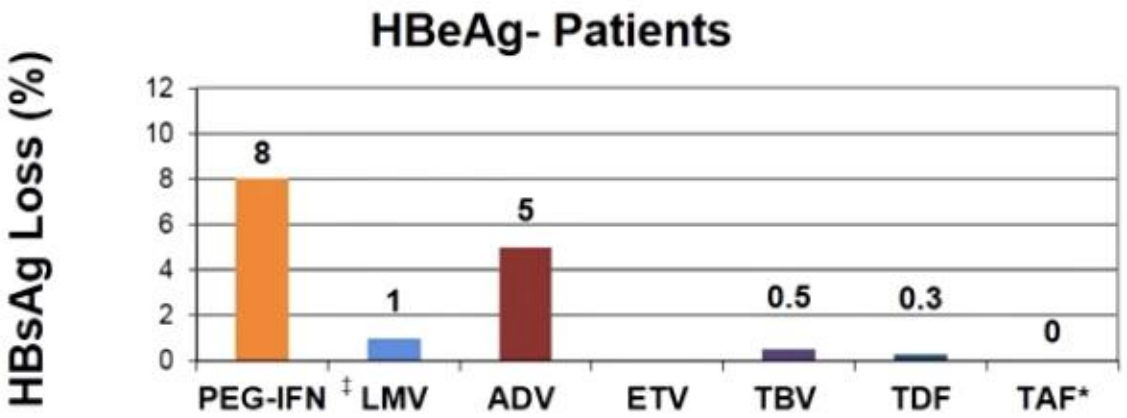
Response of Peg-IFN assessed after treatment
† = 6 months off Rx
‡ = 3 years off Rx

Response of nucleos/tide analogue assessed on treatment

Scaglione SJ, Lok AS. *Gastro*. 2012; 142: 1360-1368.
Chan H, Lancet Gastrohep 2016; 1: 185

HBsAg Loss After 1 to 5 Years of Treatment





PEG-IFN, peginterferon
LMV, lamivudine
ADV, adefovir
ETV, entecavir
TBV, telbivudine
TDF, tenofovir

Response of IFN assessed after treatment
‡ = 3 years off Rx

Response of nucleos/tide analogue assessed on treatment

Scaglione SJ, Lok AS. *Gastro.* 2012; 142: 1360-1368.
Chan H, Lancet Gastrohep 2016; 1: 185; Buti M, Lancet Gastrohep 2016; 1: 196

* Results for TAF, HBsAg loss at 1 year

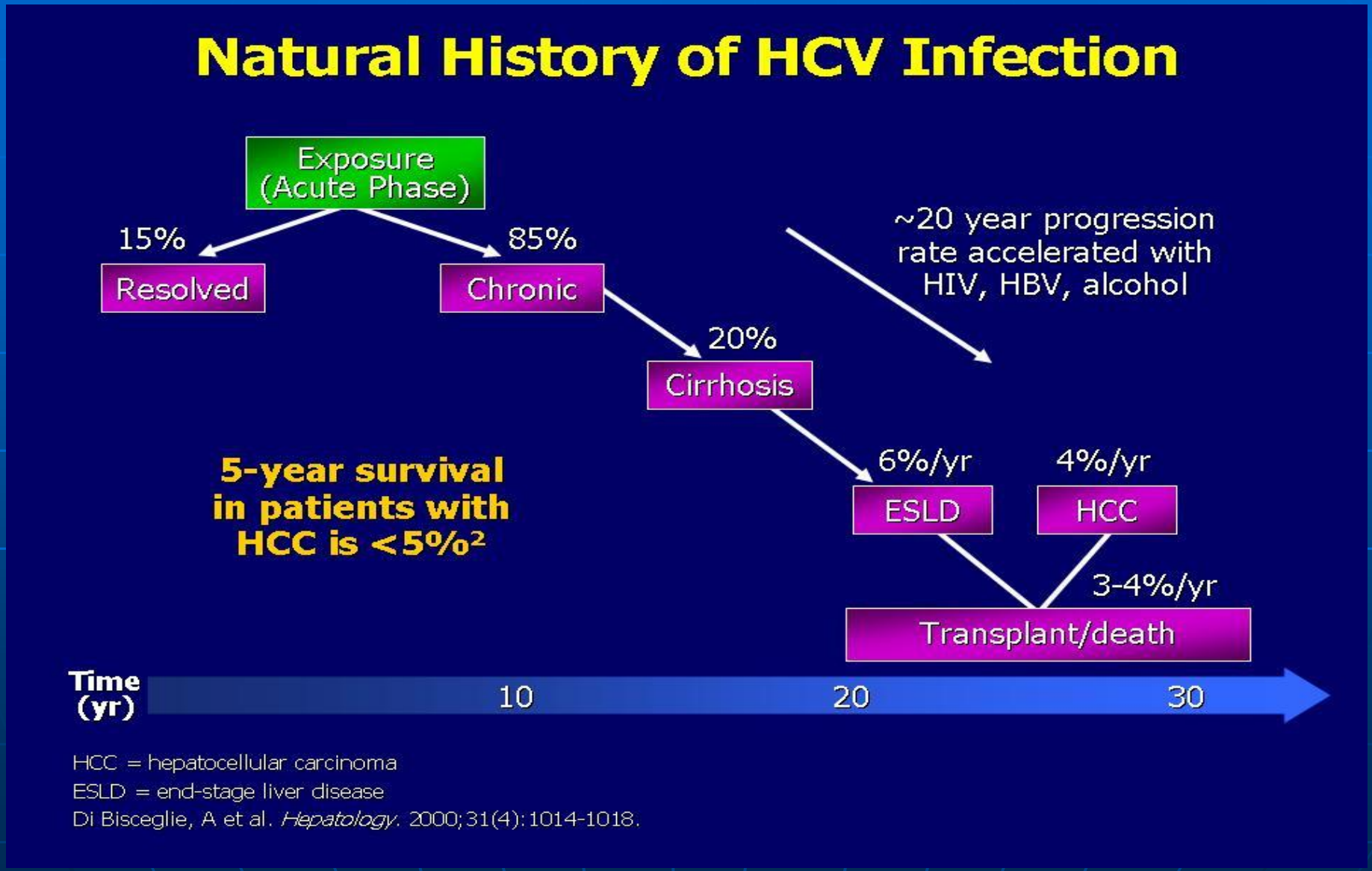
When to Stop Nucleos/tide Analogues?

- Non-cirrhotic
  - HBeAg+: After confirmed HBeAg seroconversion and an additional 12 months of consolidation therapy
  - HBeAg-: After HBsAg loss
- Compensated cirrhosis
  - Never or after HBsAg loss
- Decompensated cirrhosis
  - Never

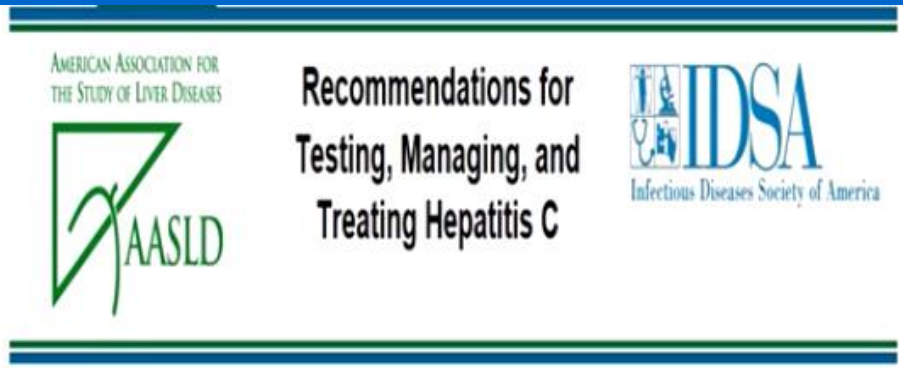
Lok ASF, McMahon BJ. *Hepatology*. 2007; 45: 507-539.
Lok ASF, McMahon BJ. *Hepatology*. 2009; 50: 661-662.
Terrault N, et al. *Hepatology*. 2016; 63: 261-283.

HCV infection

Natural History of Hepatitis C



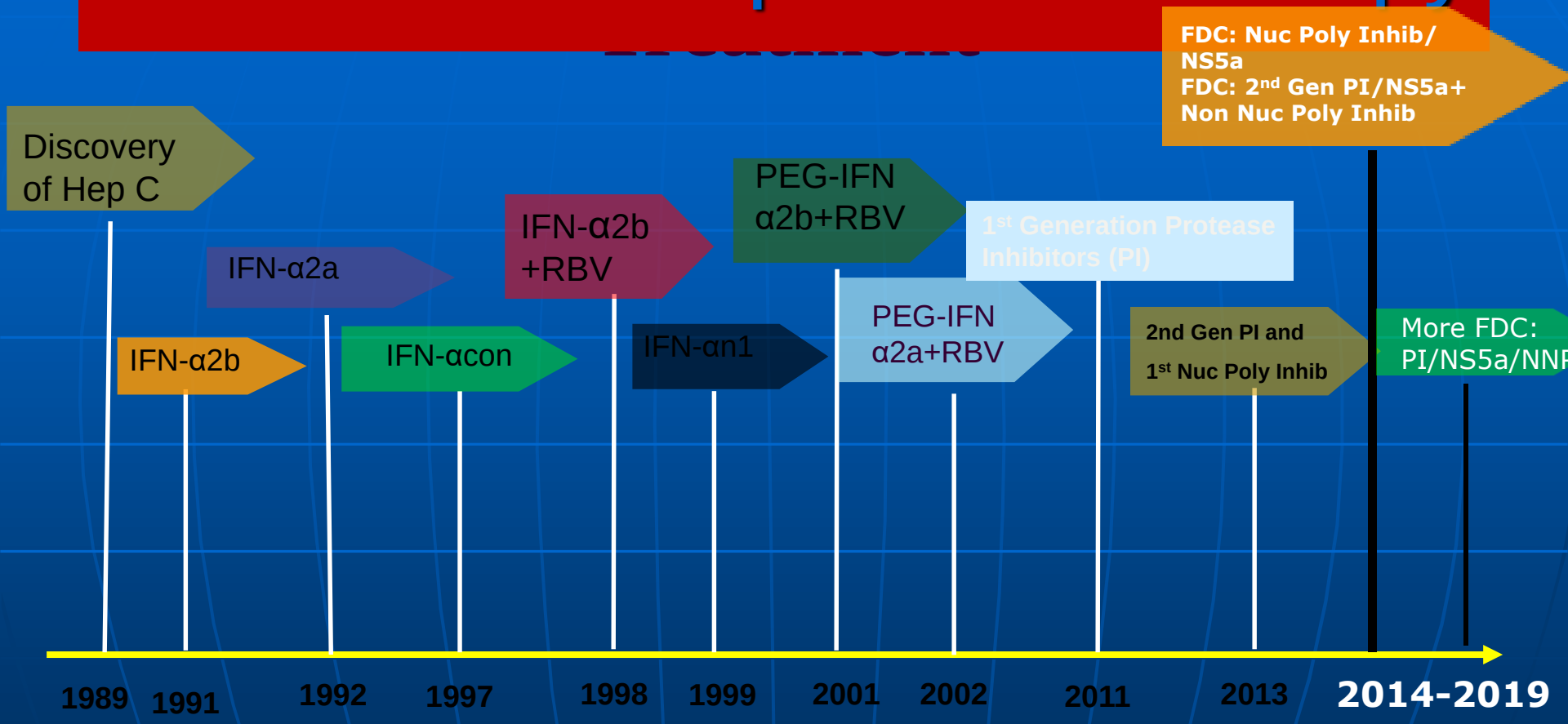
Who to treat



- Successful hepatitis C treatment results in sustained virologic response (SVR), which is tantamount to virologic cure, and, as such, is expected to benefit nearly all chronically infected persons.
- Antiviral treatment is recommended for all patients with chronic HCV infection, except those with limited life expectancy due to nonhepatic causes. (I-A)
- If resources limit the ability to treat all infected patients immediately as recommended, then it is most appropriate to treat those at greatest risk of disease complications before treating those with less advanced disease.
- Use of noninvasive testing or liver biopsy is recommended in order to assess the degree of hepatic fibrosis, and hence the urgency of immediate treatment. (I-A)

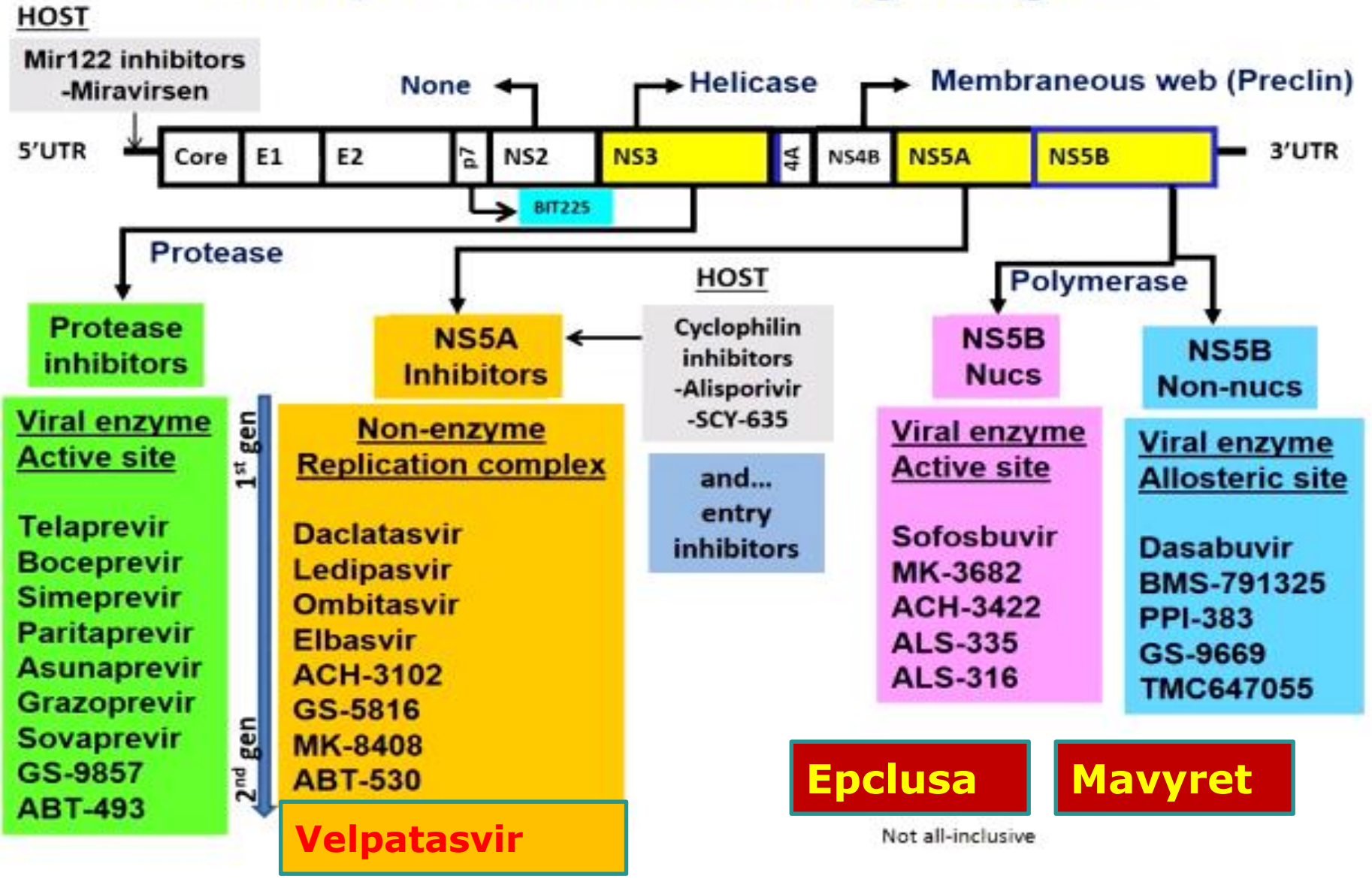
AASLD/IDSA HCV Guidelines; www.hcvguidelines.org

Evolution of Hepatitis C Therapy



IFN=interferon, RBV=ribavirin, PEG=pegylated, FDC=fixed dose combination

Multiple Validated Drug Targets

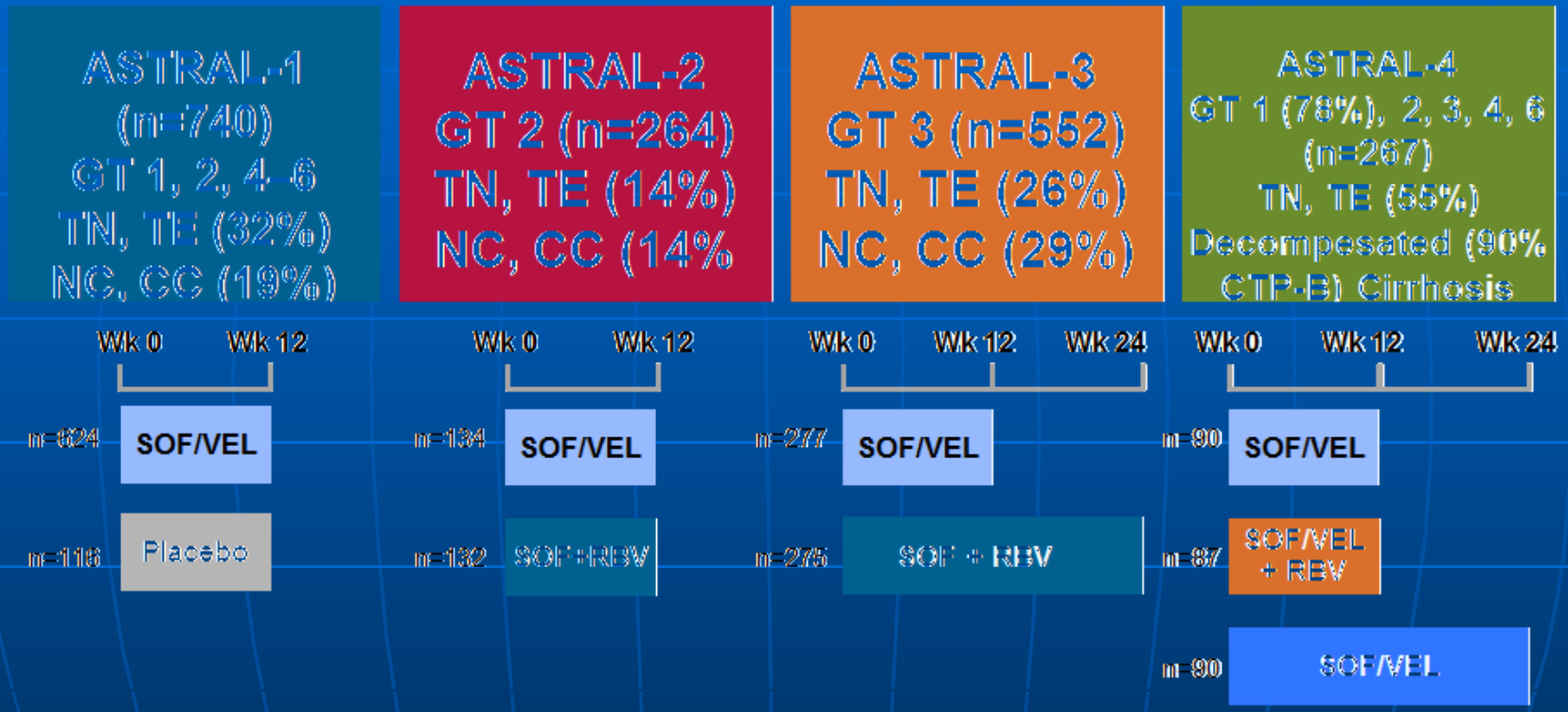


Critical clinical data to guide HCV therapy decision making

- Genotype/ subtype
- HCV RNA levels
- Liver disease stage- cirrhosis or no cirrhosis
- Prior treatment experience
- Kidney disease—Zepatier
- organ transplant
- Issues with ribavirin use

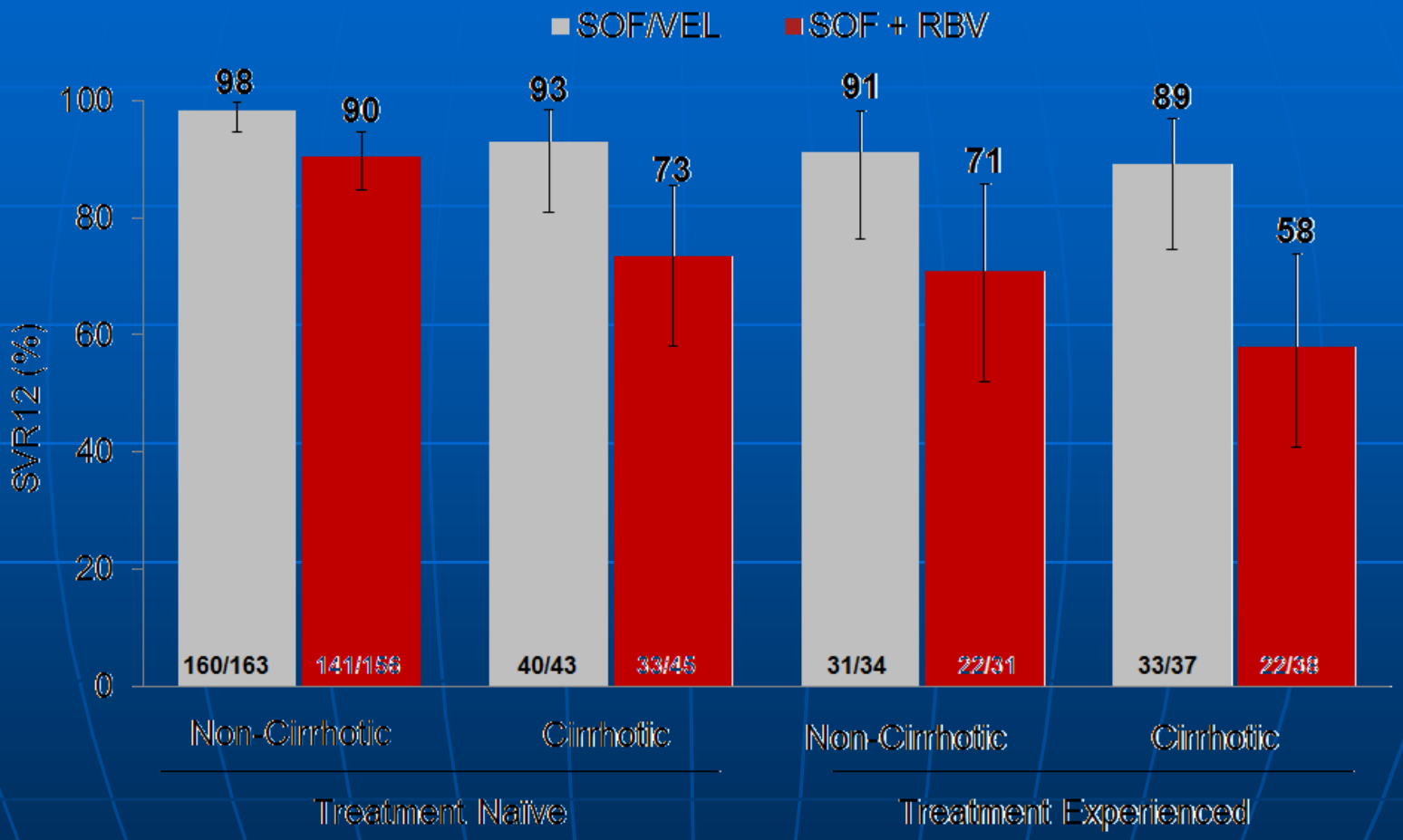
Pangenotypic DAAs

SOFOSBUVIR/VELPATASVIR (EPCLUSA): The ASTRAL Phase 3 Randomized Trials (N=1302)



- **Primary endpoints**
  - SVR12
  - Discontinuations due to AEs

ASTRAL-3 SVR12 by Cirrhosis Status and Treatment History



More Serious AEs (6% vs 2%) and D/C (3% vs 0%) due to AEs in SOF/RBV ARM.

Mangia, AASLD, 2015, 249. Foster GR, et al. *New Engl J Med*. 2015. DOI: 10.1056/NEJMoa1512612

Sustained Virologic Response

>90%

Sustained Virologic Response

- Hepatitis C PCR negative 3 months after stopping antiviral therapy
- Durable
  - 99% stay HCV negative for > 10 years
- Associated with Improved Outcomes
  - Leads to improved histology
  - Leads to clinical benefits
    - Decreased decompensation
    - Prevents *de novo* esophageal varices
    - Decreased hepatocellular carcinoma
    - Decreased mortality

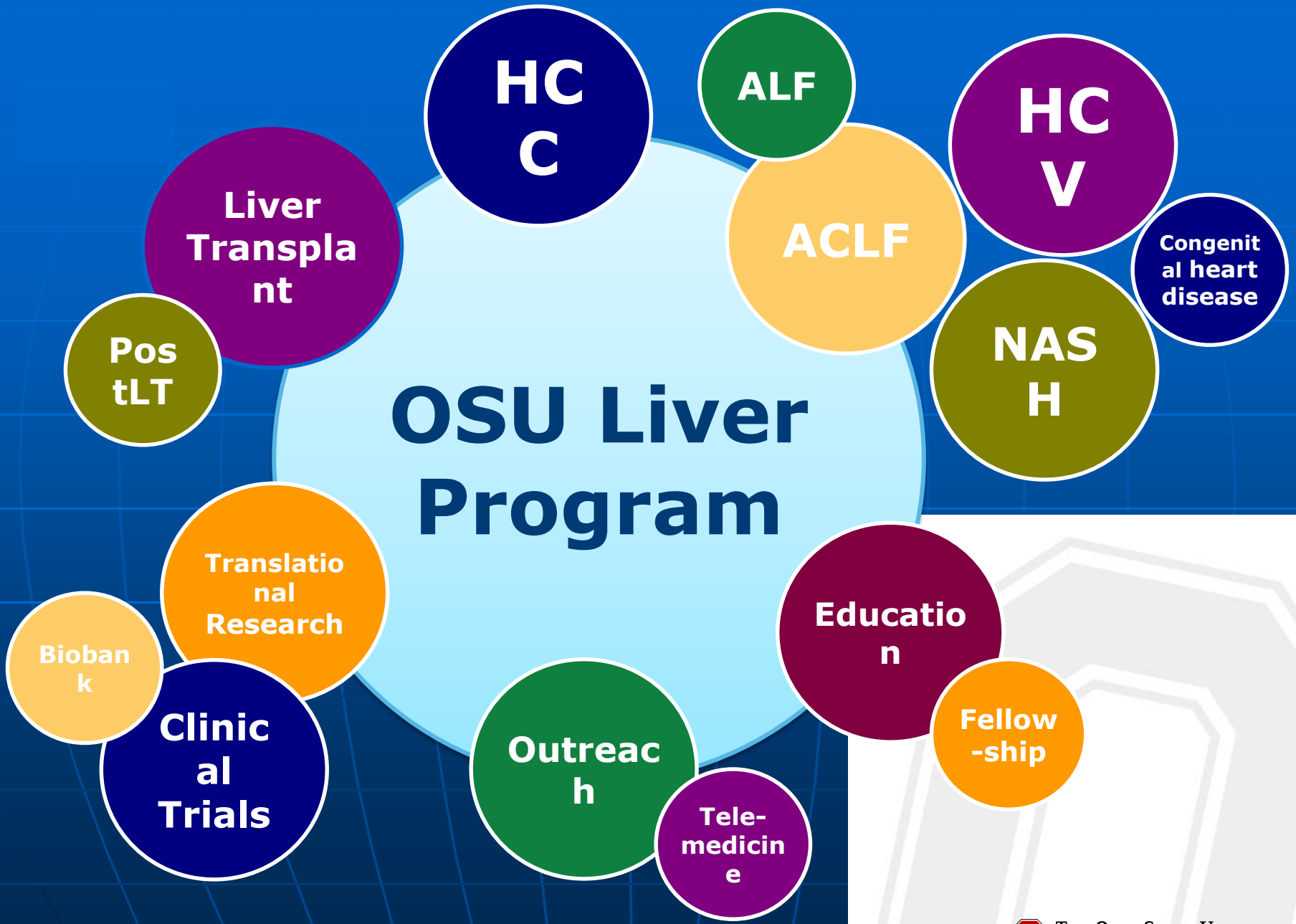
Bruno S, et al Hepatology 2010;51:2069-2076.
Veldt BJ, et al. Ann Intern Med 2007;147:677-684.
Maylin S, et al. Gastroenterology 2008; 135:821-9.

Conclusions

- **Acute hepatitis is a morbid and sometimes fatal condition**
- **Early diagnosis of severe form is important-NAC, anti-viral.**
- **There is an outbreak of HAV in Ohio; vaccination is warranted.**
- **HBV is self limiting in majority but can lead to ALF.**

Conclusions

- **Multiple Anti-virals are available for controlling chronic HBV infection.**
- **Acute HCV can progress to chronic phase in 60-70% of cases.**
- **Pangenotypic AVT for HCV is very effective >90% SVR has been reported.**
- **Cost of treatment and getting medication approval is the most challenging part.**


HCC
ALF
HCV
Liver Transplant
ACLF
Congenital heart disease
PostLT
NASH
OSU Liver Program
Translational Research
Biobank
Clinical Trials
Outreach
Education
Fellow-ship
Tele-medicine

Hepatology MDs

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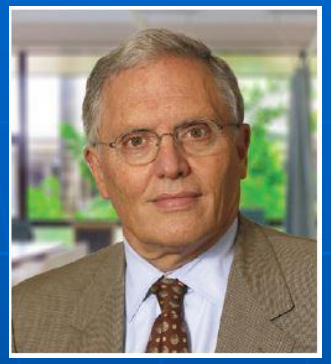
Director of Hepatology
Program Director, Transplant Hepatology Fellowship

Anthony Michaels, MD
Medical Director of Liver Transplantation

Robert Kirkpatrick, MD
Associate Director of GI Fellowship



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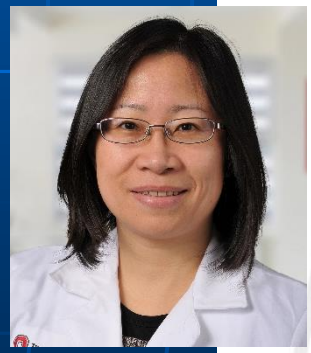


Sherry Ma,

Collaborative Clinical Efforts

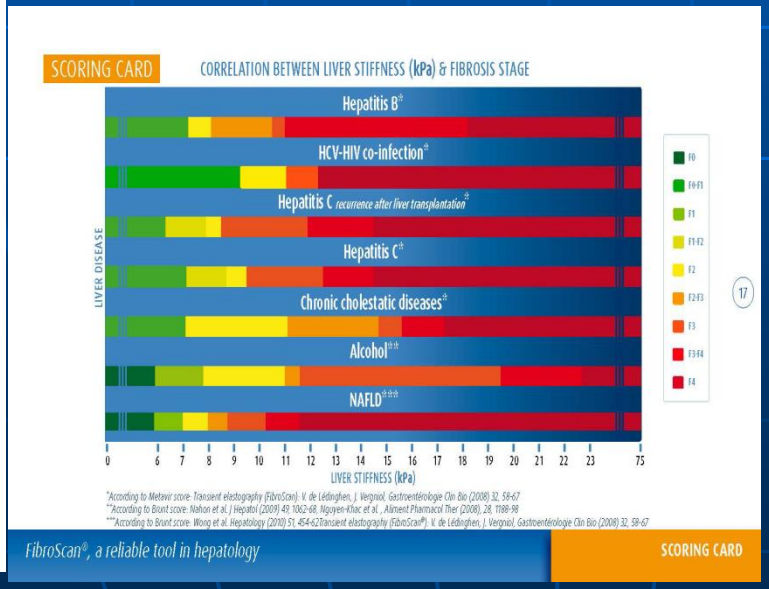
- Multi-disciplinary and sub-specialized clinics
  - Liver tumor clinic
  - HCV treatment
  - NASH and metabolic liver disease
  - Post-transplant care
  - Live Donor LT

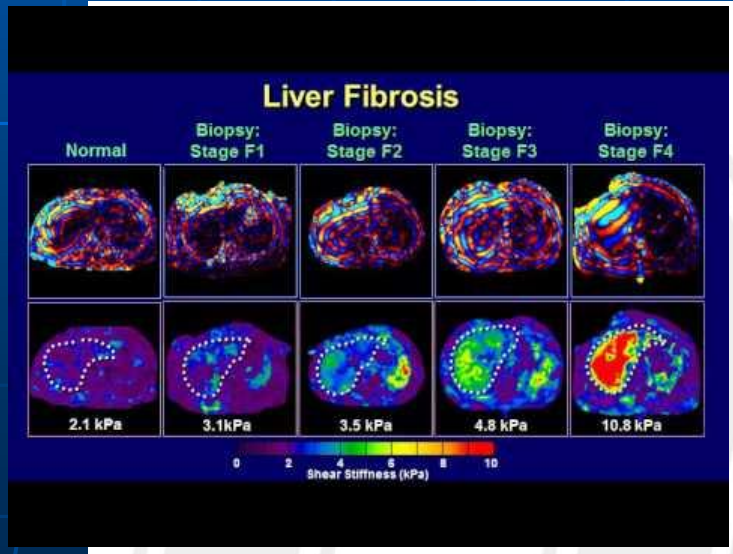
New Tools and Treatment Options

- Hepatocellular Carcinoma (HCC):
  - TACE
  - RFA
  - Y-90
  - SBRT
- Portal hypertensive bleeding:
  - Cyanoacrylate injection of gastric varices
  - Balloon-Occluded Retrograde Transvenous Obliteration (BRTO)

Transient Liver Elastography (Fibroscan)

- The most efficient approach to fibrosis assessment is to combine direct biomarkers and vibration-controlled transient liver elastography
  - A biopsy should be considered for any patient who has discordant results between the 2 modalities that would affect clinical decision making.





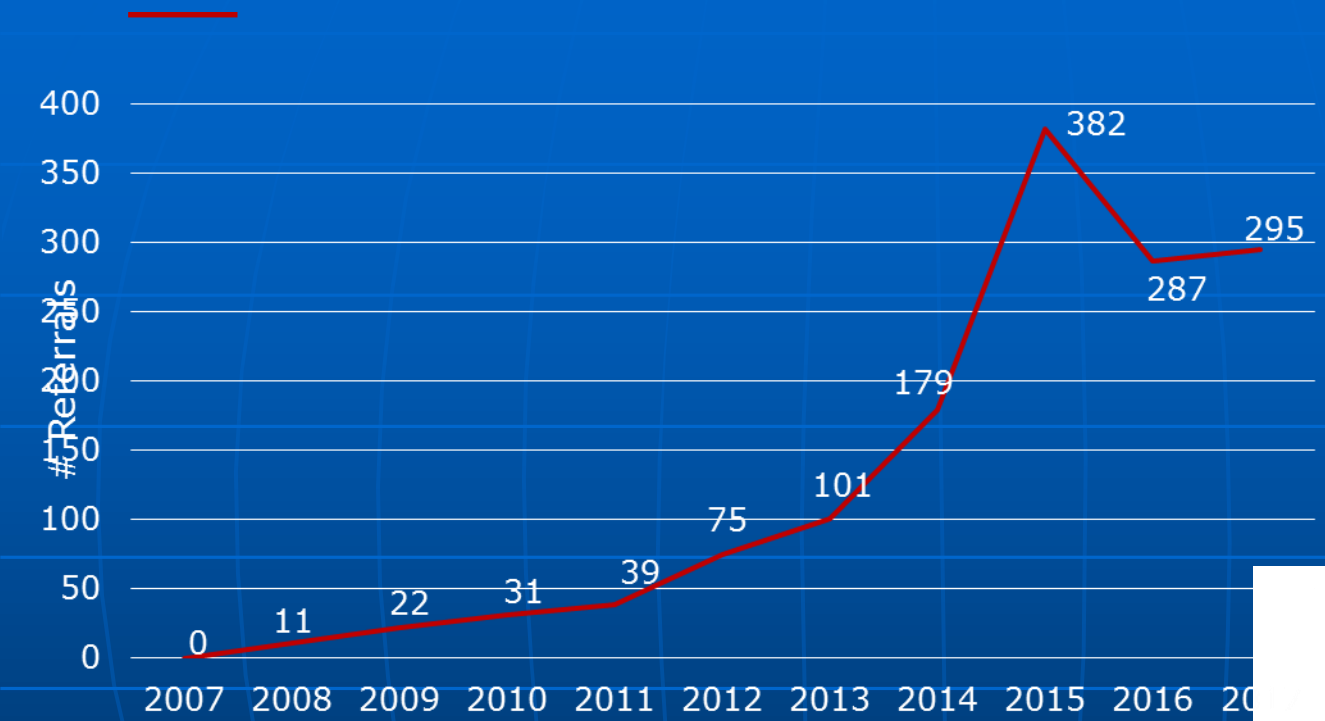
AASLD-IDSA. www.hcvguidelines.org/full-report-view.

NIH Research Trials

Clinical Research Trials

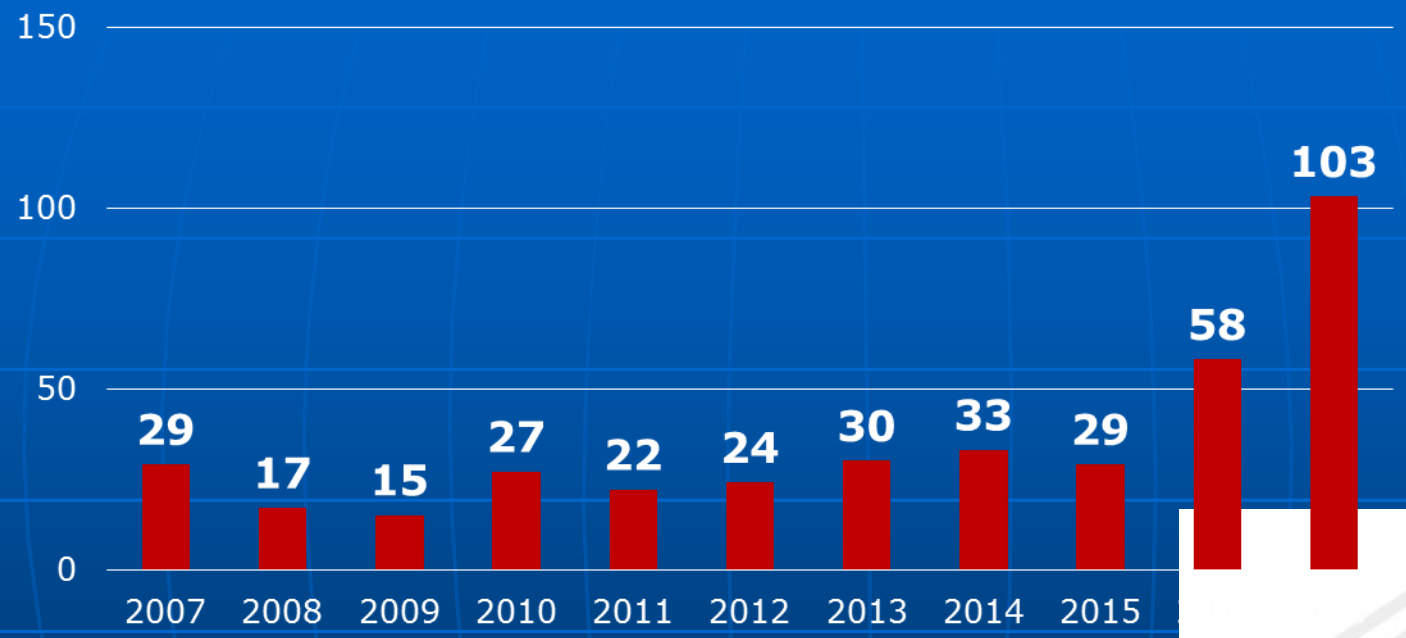
- NASH cirrhosis
  - Tocotrienol
  - Cenicriviroc (AURORA)
  - Obetacholic acid (REVERSE)
- Hepatorenal Syndrome (CONFIRM)
  - Terlipressin
- Acute on chronic liver disease
  - Albumin infusion (PRECIOSA)
- PBC with decompensated cirrhosis
  - Obetacholic acid
- HCV
  - NS5A Inhibitor + Sofosbuvir failure
  - New PCR assay

Hepatology Referrals



THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Ohio State Liver Transplant Volume



Living Donor Liver Transplantation

Thanks