

# Hepatitis B

## The Basics



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28<sup>th</sup> July 2020



# Objectives

- Learn about the various tests used to assess hepatitis B infection
- Understand the natural history of hepatitis B
- Use what you learned to manage patients with hepatitis B

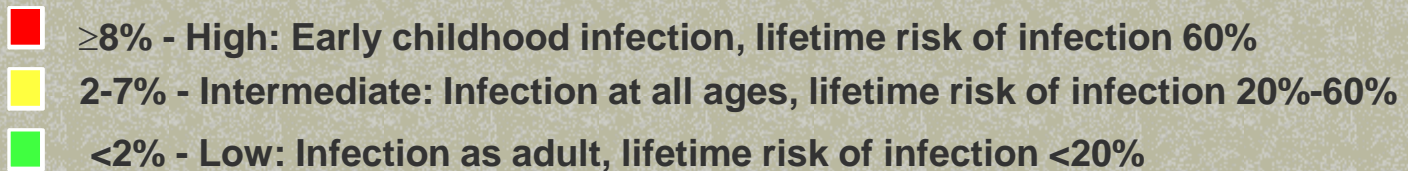




# What we know about HBV

- Viral infection that can cause chronic hepatitis, cirrhosis, cancer
  - Ranks as top 10 infectious killer in the world
- HBV can live in host for decades
  - Virus can adapt through mutations
  - Immune system can adapt to virus
- Vaccine can prevent infection
  - Cure of chronic infection unlikely







# epidemiology

- 257m world wide
- 887,000deaths in 2017
- 90% of infected individuals not a ware
- 80% of HCC patients at UCI positive for HBV





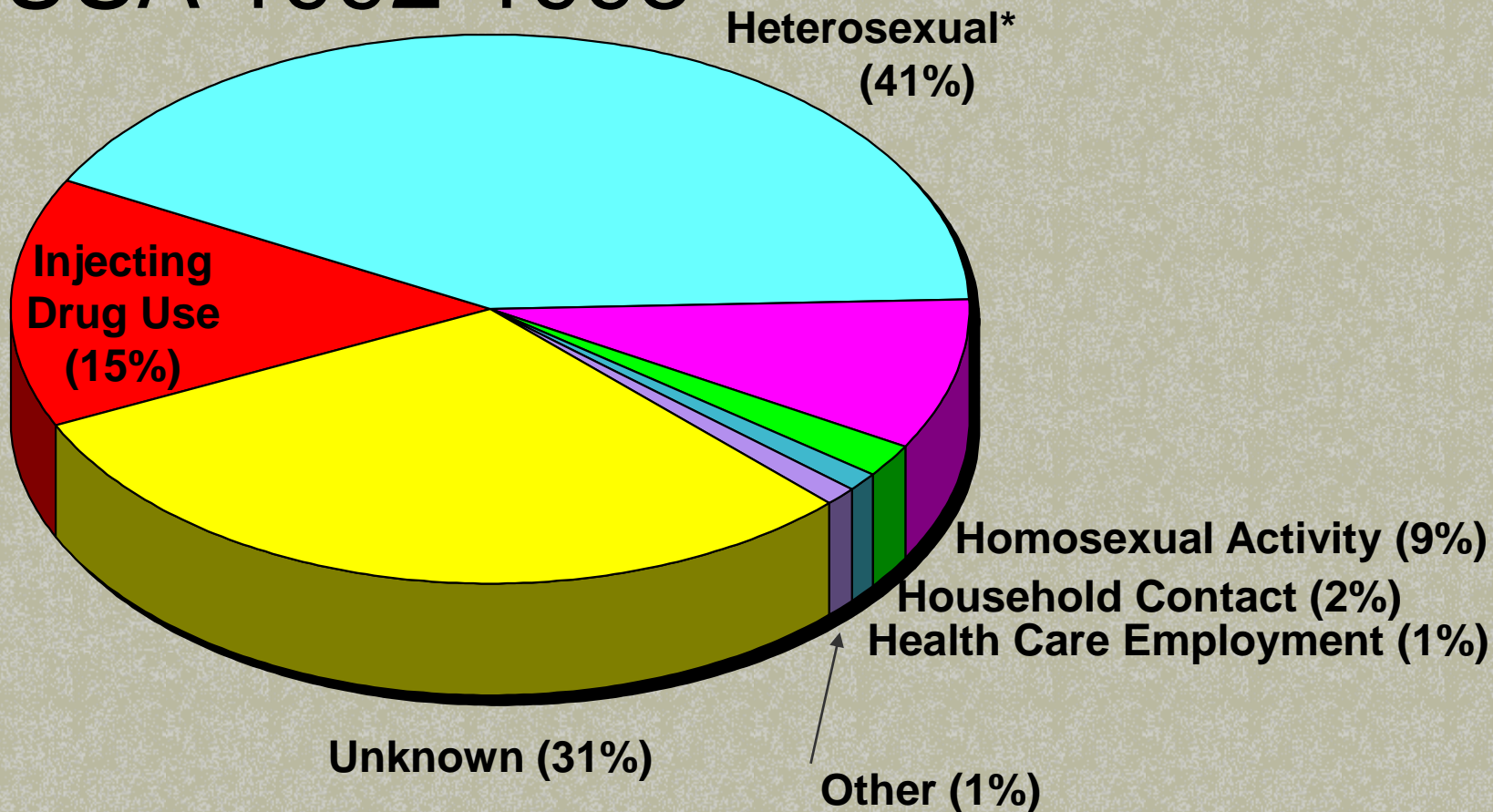


# HBV in body fluids

High	Moderate	Low/Not Detectable
blood	semen	urine
serum	vaginal fluid	feces
wound exudates	saliva	sweat
		tears
		breastmilk



# Transmission risk factors USA 1992-1993



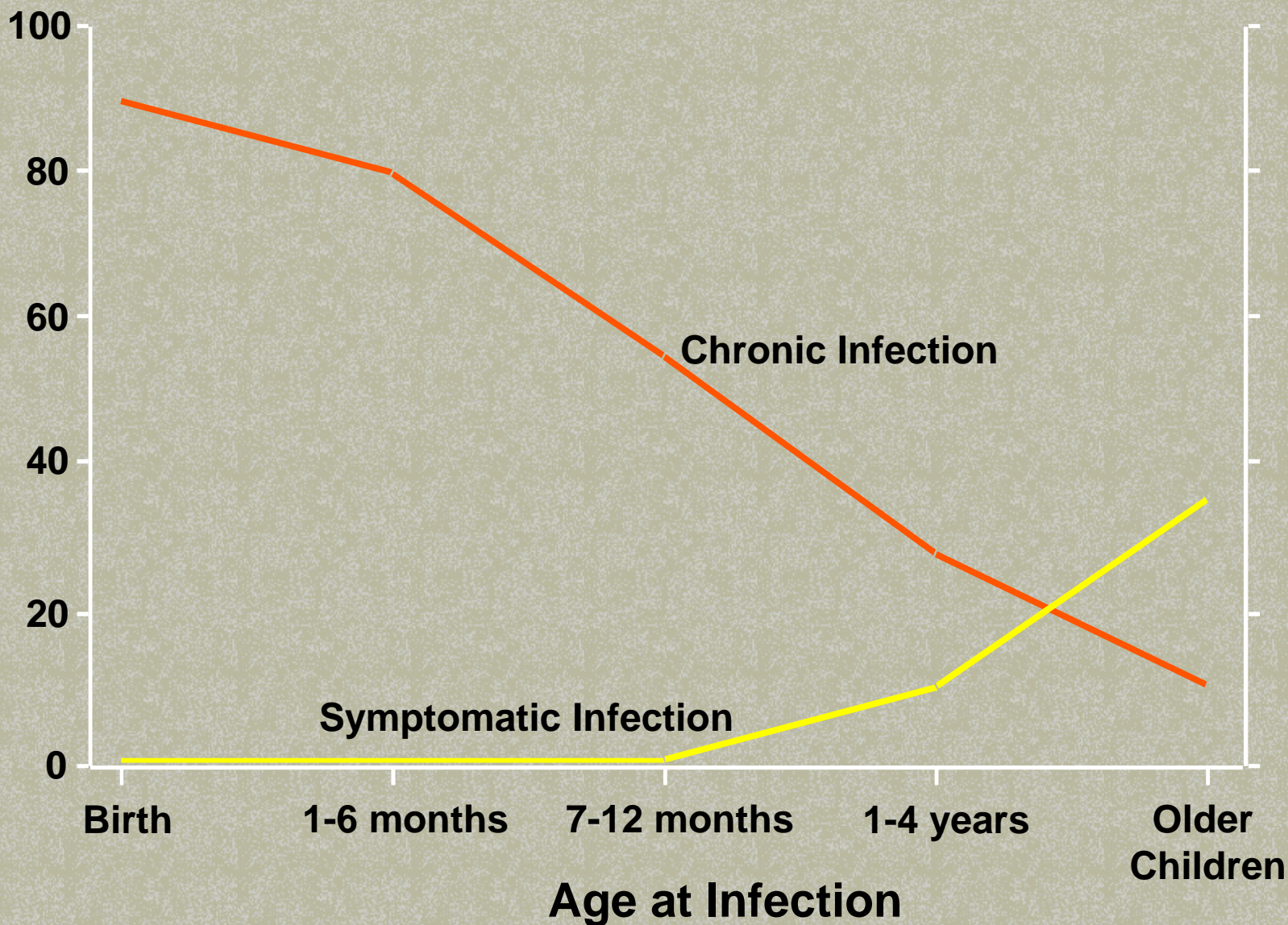
*\* Includes sexual contact with acute cases, carriers, and multiple partners.*

*Source: CDC Sentinel Counties Study of Viral Hepatitis*





# Outcome of HBV infection by age







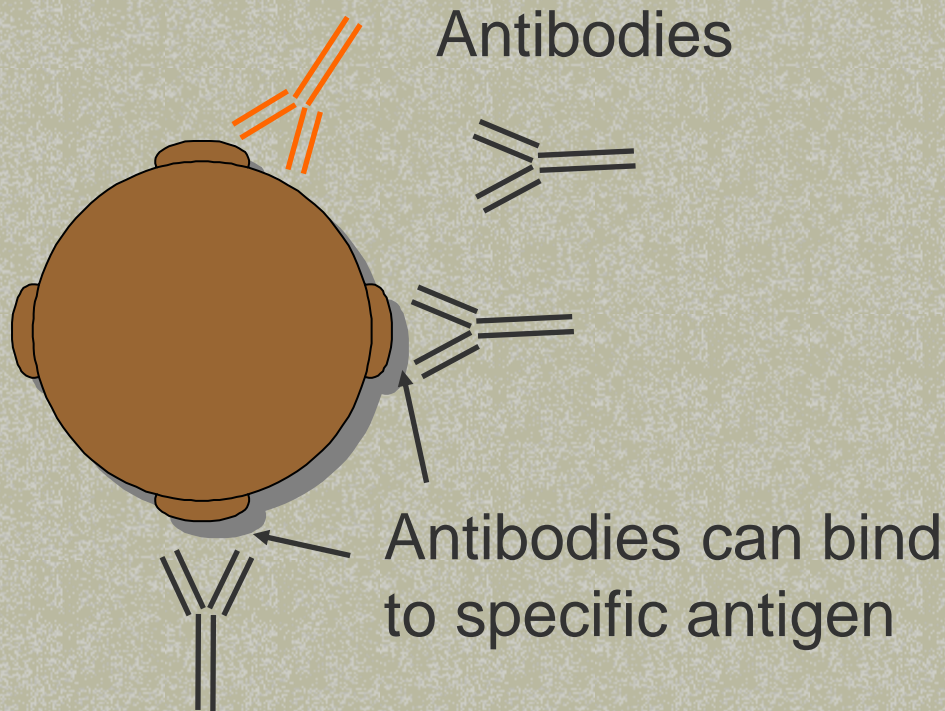
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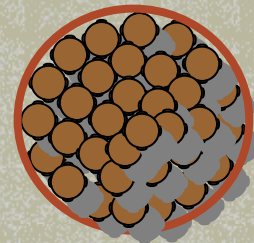


# Serology

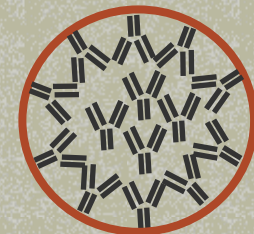
## Antigens and Antibodies



Test for antibody



Test for antigen



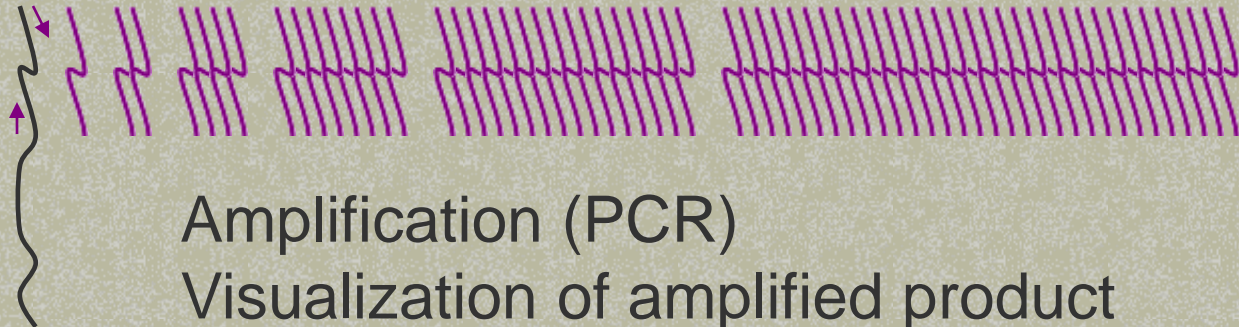


# Nucleic Acid Testing

## Hybridization vs Amplification

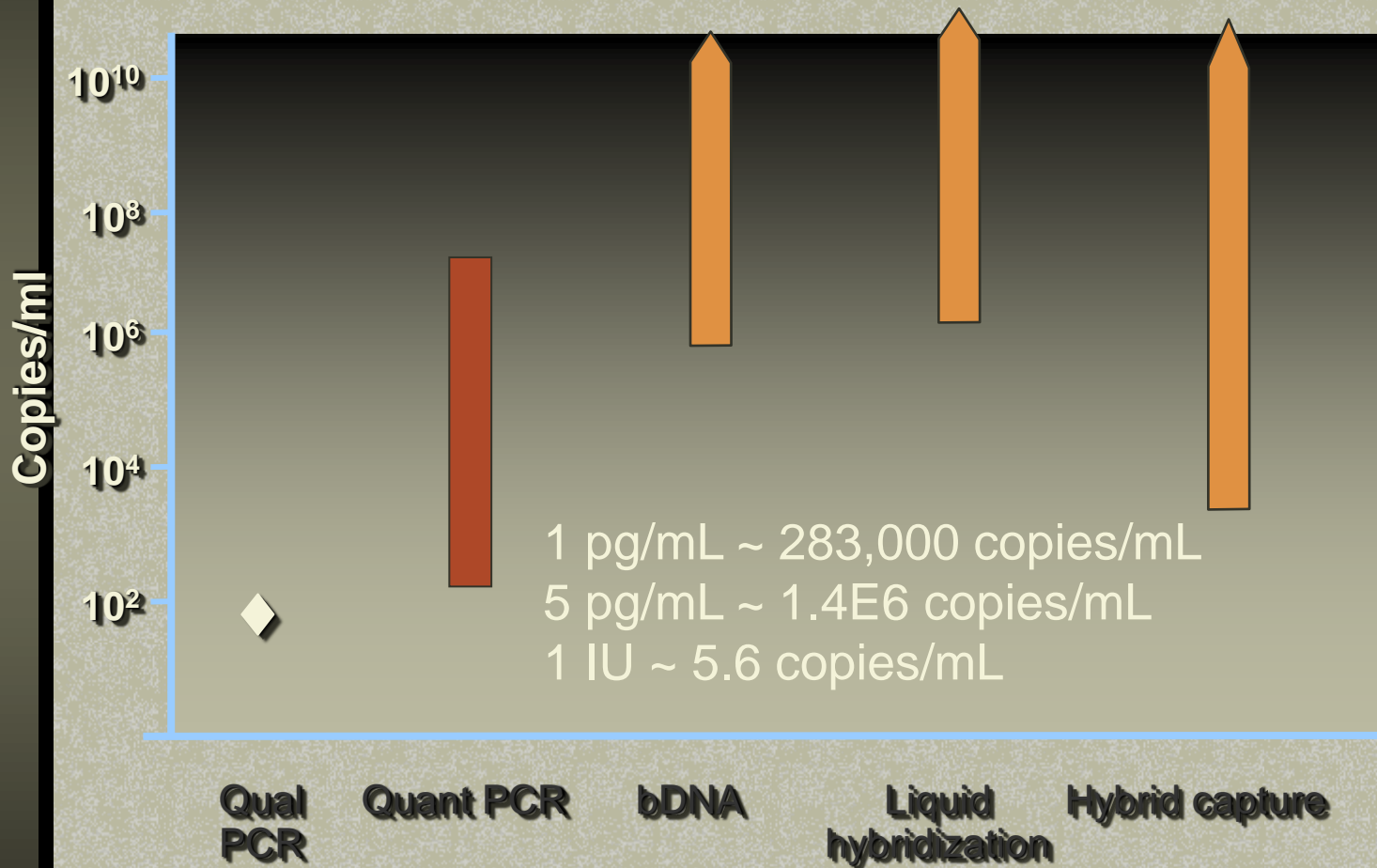


Hybridization:  
Visualization of unamplified probe



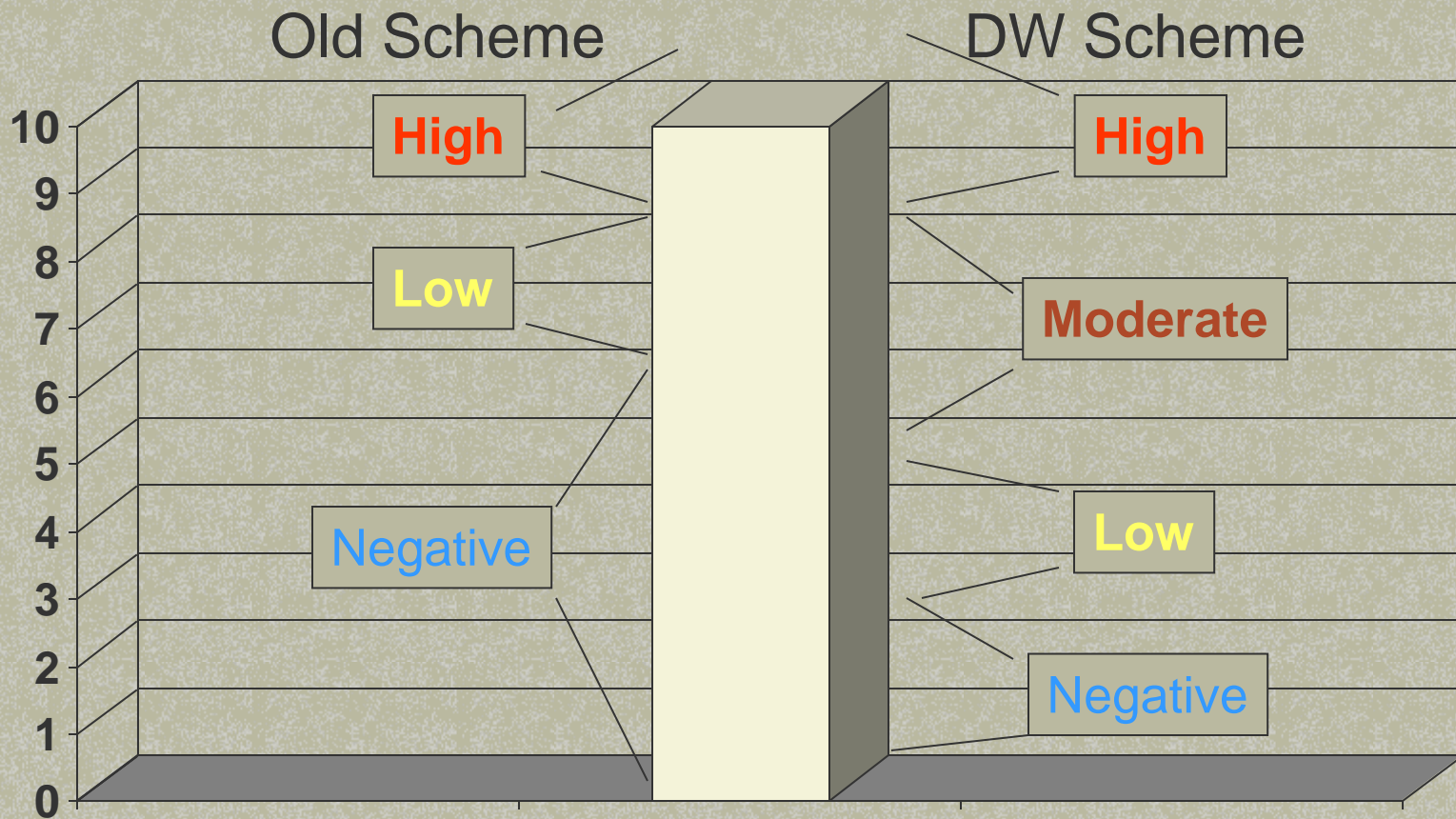
Amplification (PCR)  
Visualization of amplified product

# Assays of HBV viral load



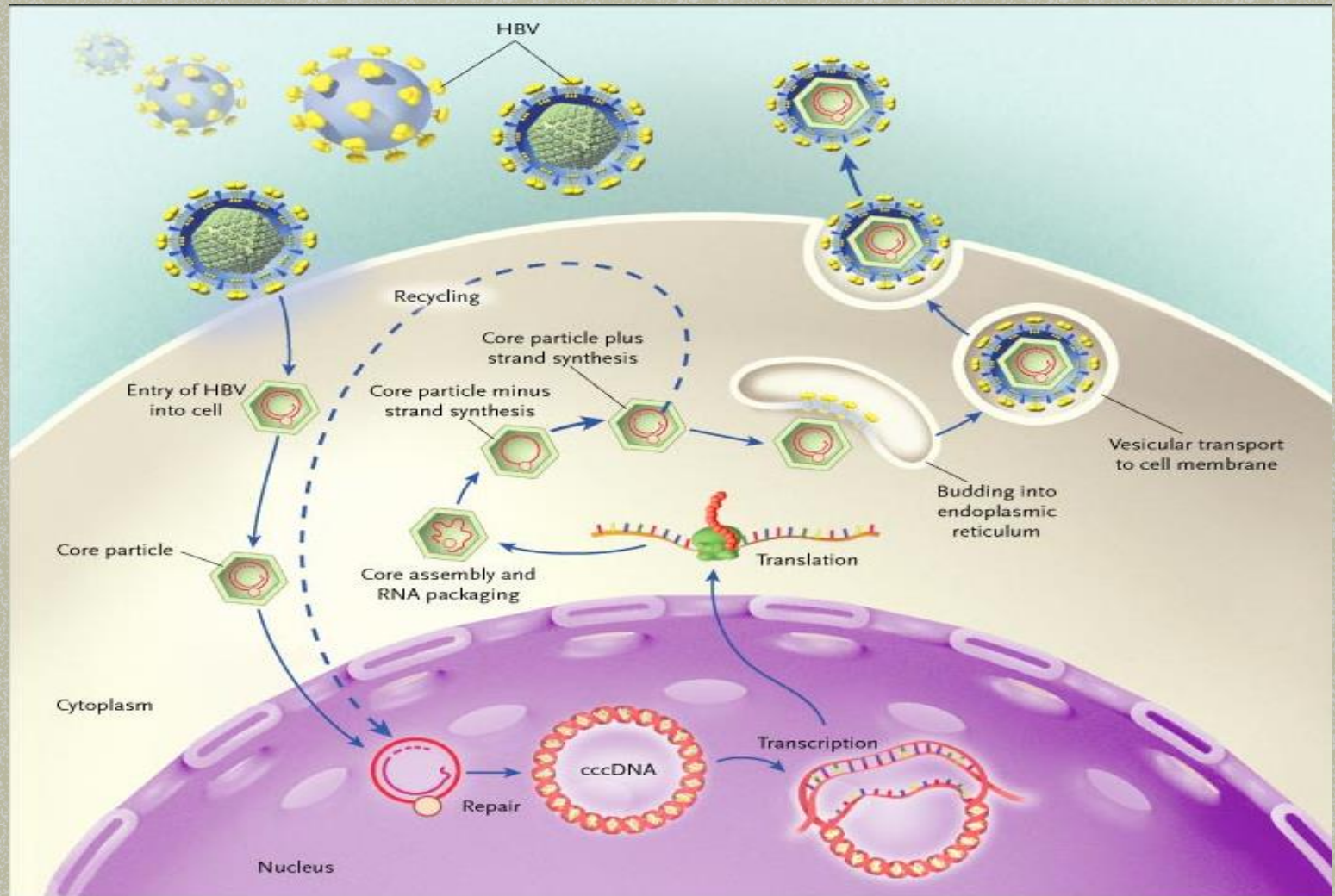


# Interpreting viral loads



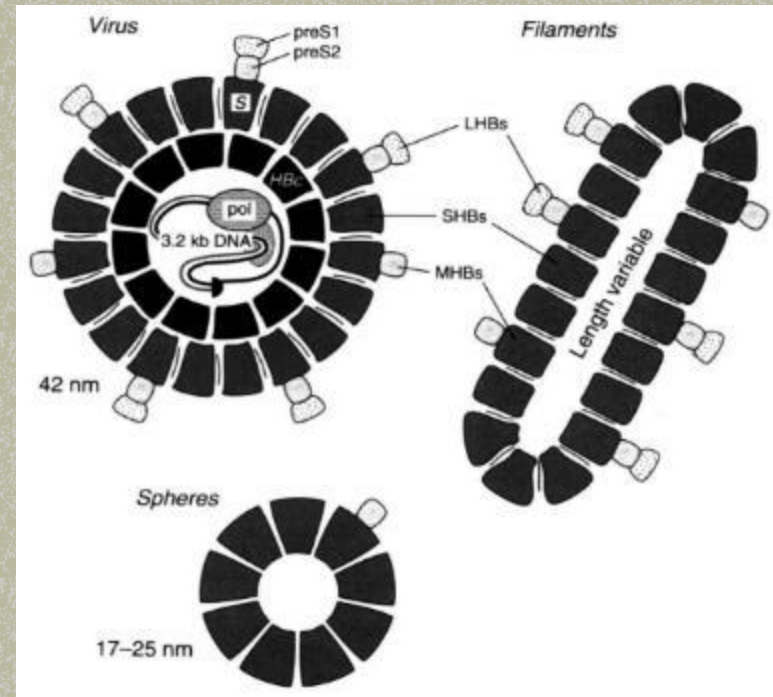
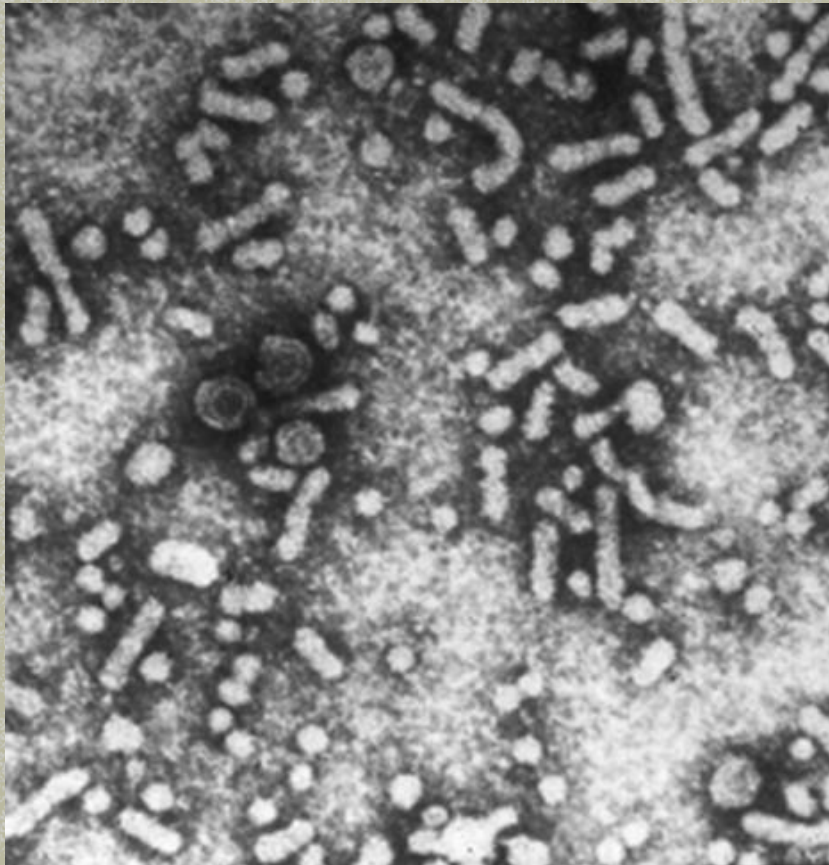


# HBV Life Cycle



# HBsAg – Envelope antigen

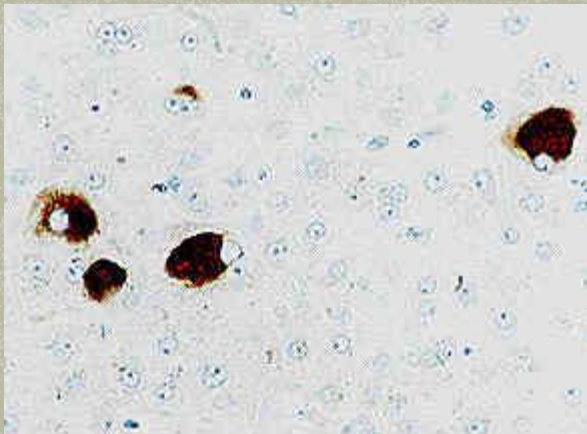
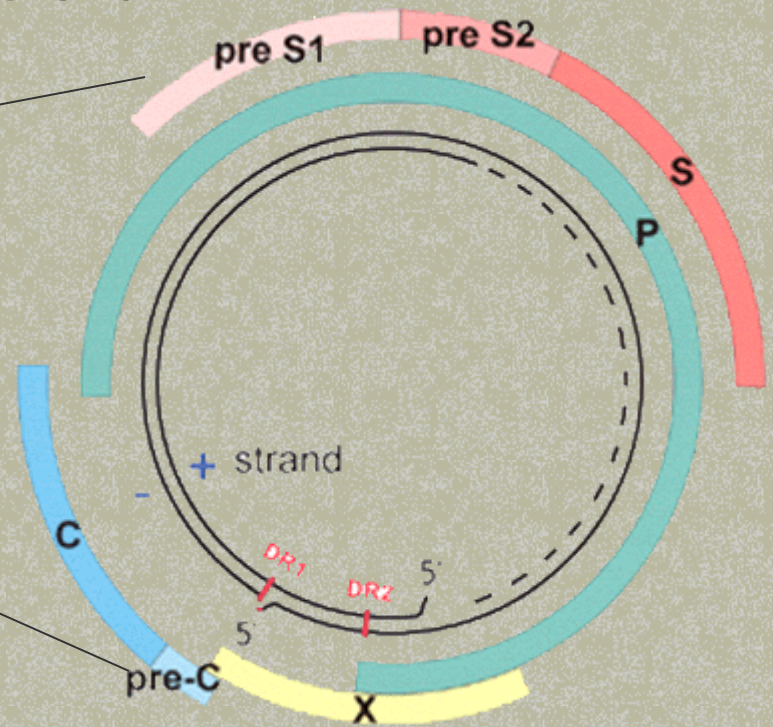
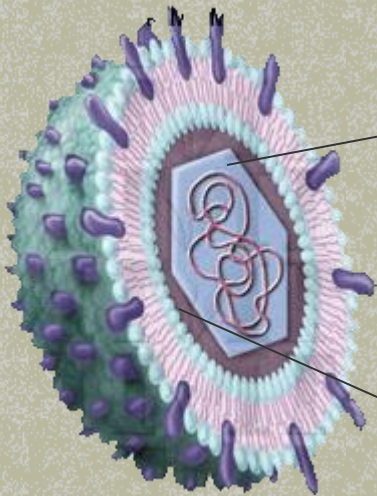
## Good test indicating infection





# HBeAg – nucleocapsid protein

## Old test for viral load





# Summary

## Tests for hepatitis B

- Infection
  - HBsAg: ongoing infection
  - Anti-HBs: infection resolved
- Viral load or infectivity
  - Indirect tests
    - HBeAg: high viral load
    - Anti-HBe: low viral load
  - Direct tests
    - Nucleic acid testing



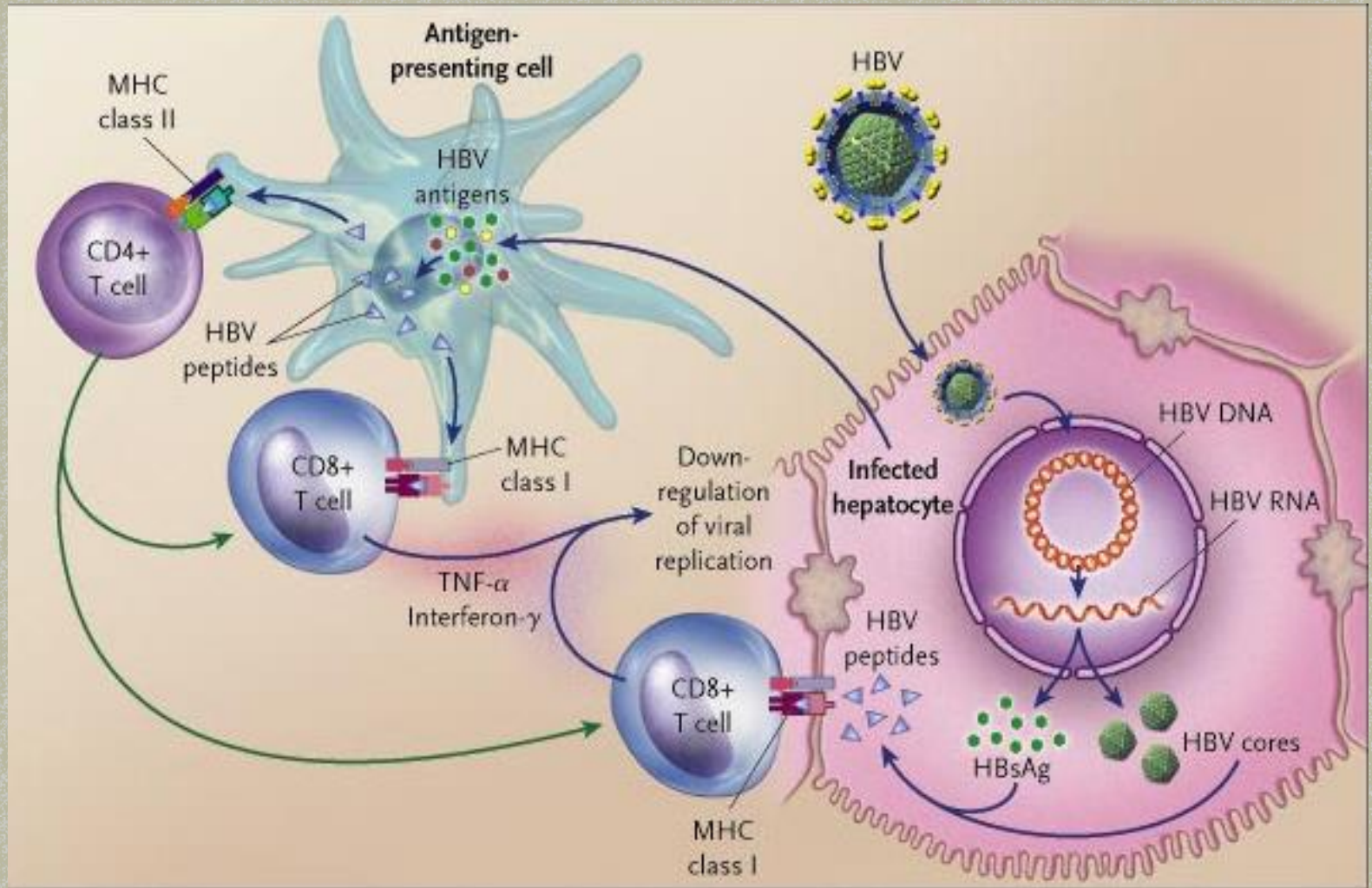
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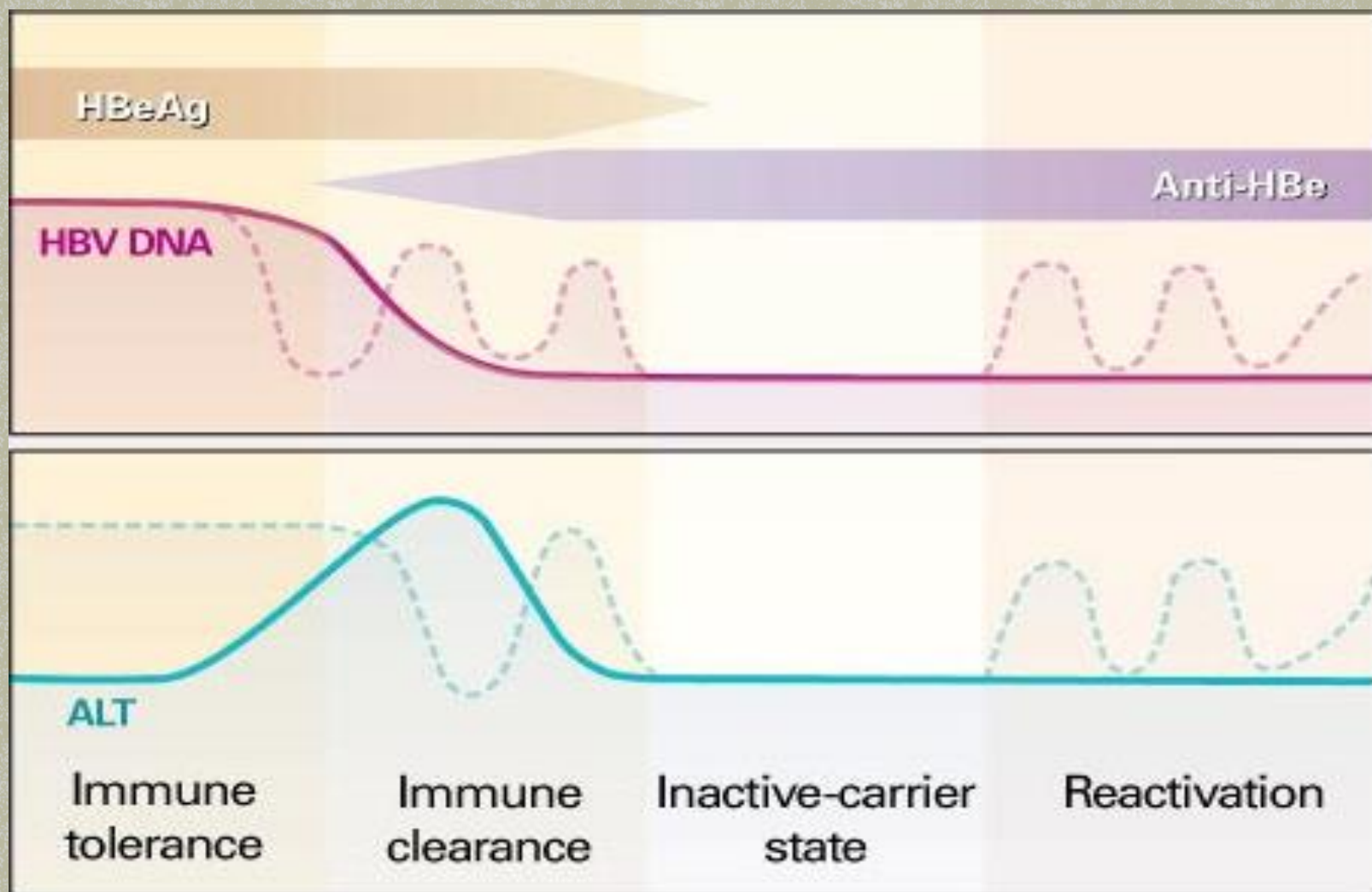


# Immune responses to HBV





# Natural History of HBV



# Immune Tolerance



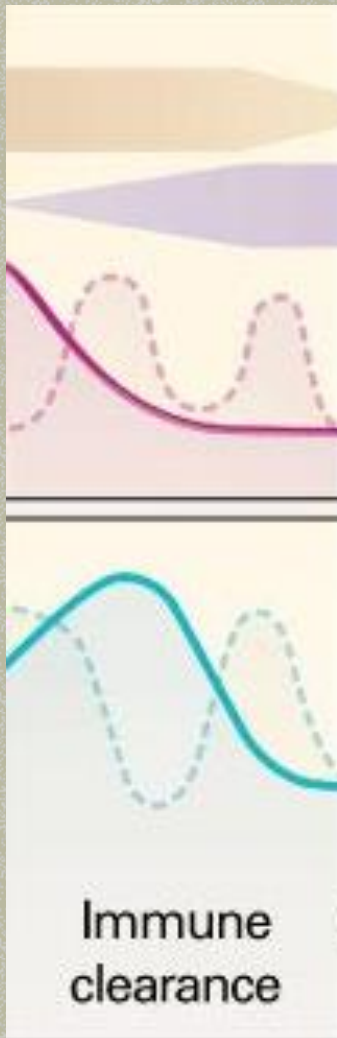
- No immune attack on virus
- Viral load very high
  - HBV DNA >  $10^{10}$  copies/mL
  - HBeAg-positive
- ALT levels normal
- Liver biopsy
  - No inflammation
  - No fibrosis
  - Lots of HBV in liver
- Treatment - NO

# Immune Clearance

HBeAg

HBV DNA

ALT



- Immune attack on virus
- Viral load getting lower
  - HBV DNA  $10^{(4)5-10}$  copies/mL
  - HBeAg-positive to negative
- ALT levels high
- Liver biopsy
  - Inflammation
  - Fibrosis increasing
  - Moderate levels HBV in liver
- Treatment - YES





# Inactive carrier

HBeAg

HBV DNA

ALT

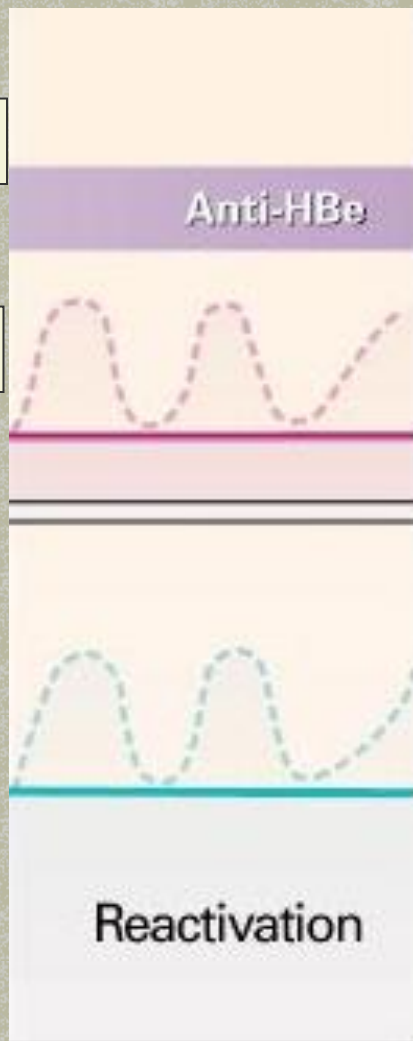
Inactive-carrier  
state

- Immune control
- Viral load low
  - HBV DNA  $<10^{(4)5}$  copies/mL
  - HBeAg negative
- ALT levels normal
- Liver biopsy
  - No Inflammation
  - Fibrosis established
  - Low levels HBV in liver
- Treatment - NO





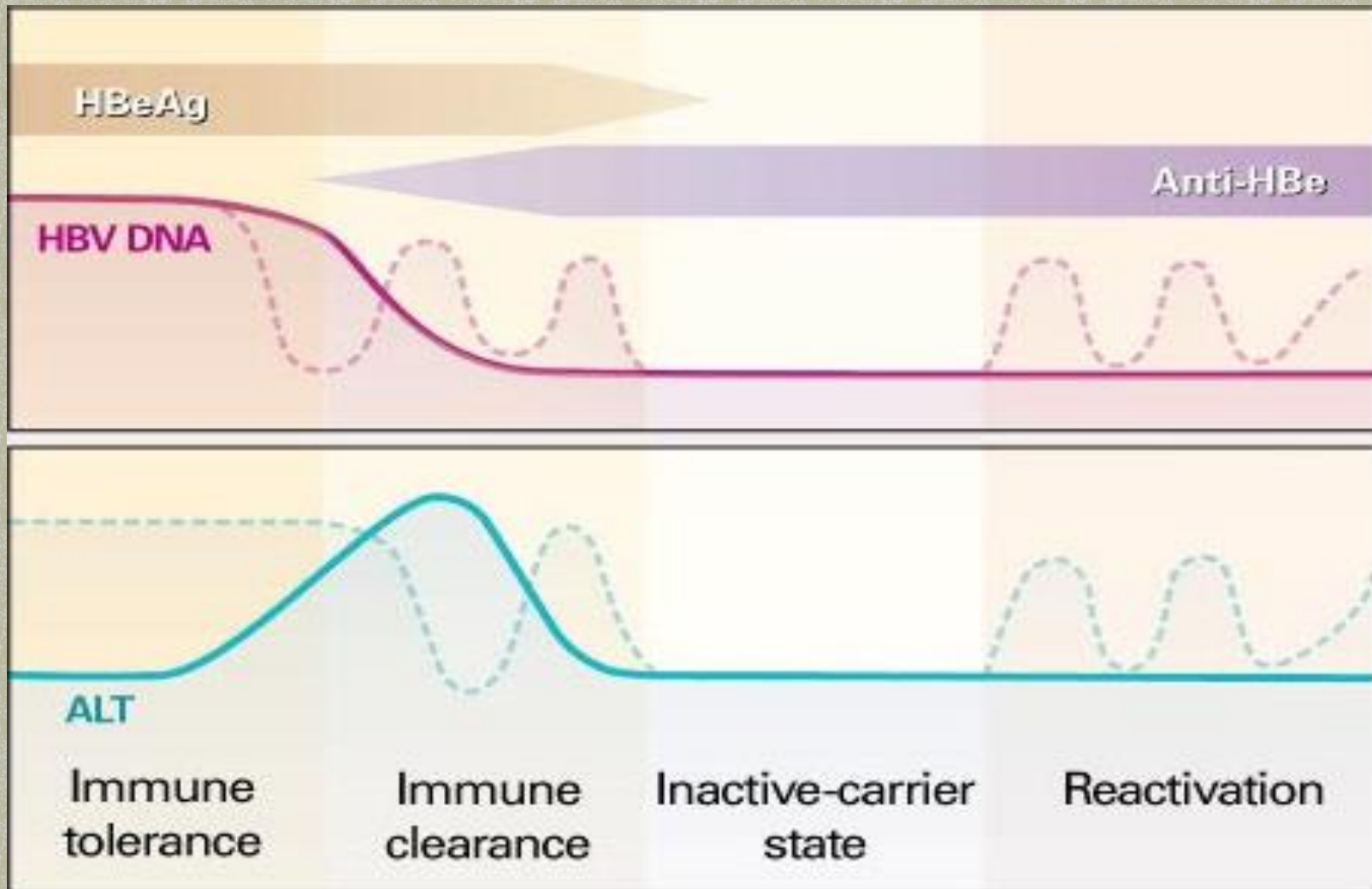
# Reactivation



- Loss of immune control
- Viral load fluctuating or high
  - HBV DNA  $<10^{(4)5}$  to  $>10^{(4)5-10}$
  - HBeAg negative
- ALT levels fluctuate
- Liver biopsy
  - Inflammation
  - Fibrosis increasing
  - Fluctuating levels HBV in liver
- Treatment - YES



# Review: History of HBV



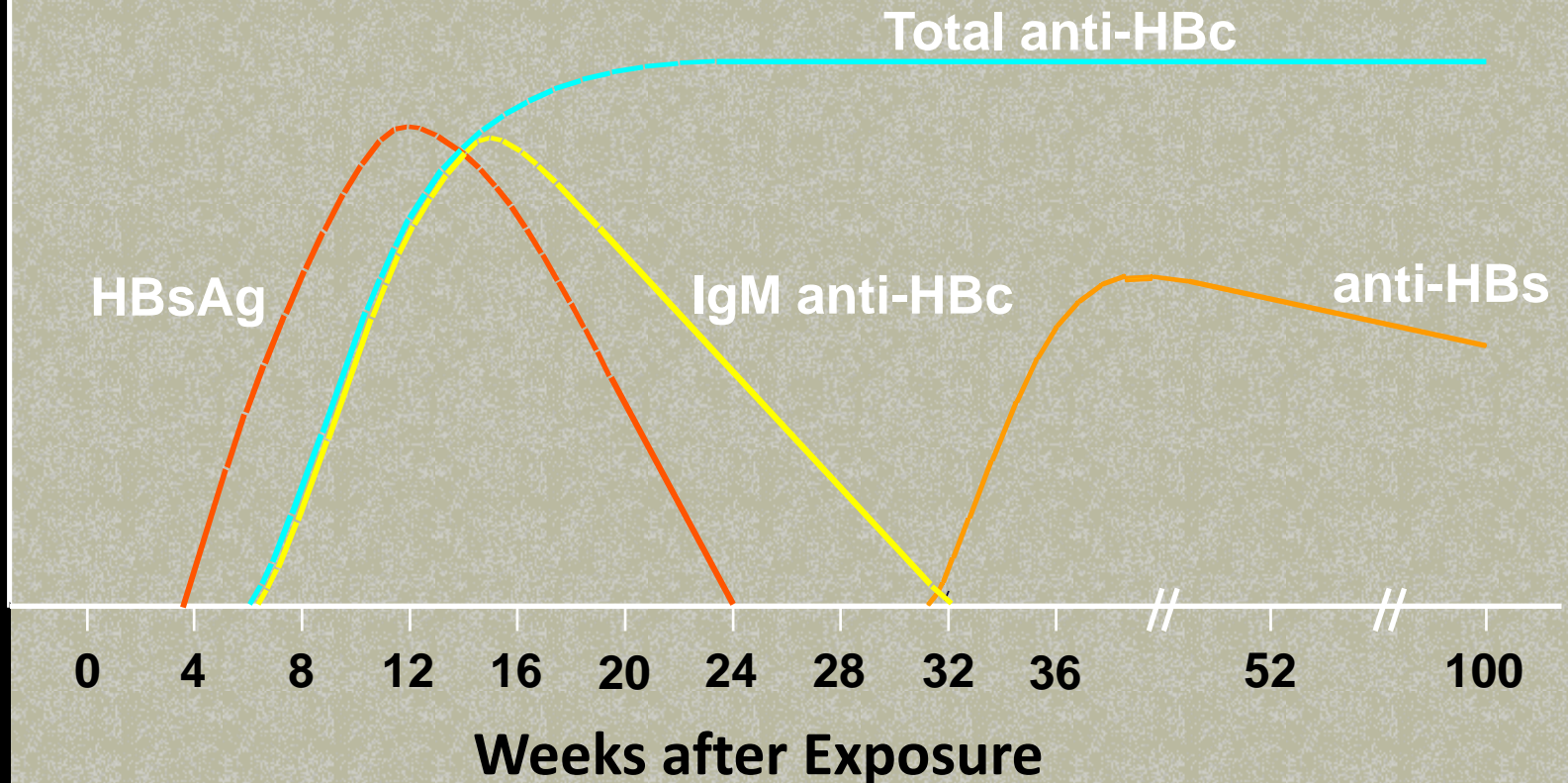
# Acute infection with recovery

Symptoms

HBeAg

anti-HBe

Titer



# HBV evolving to chronicity

Acute  
(6 months)

Chronic  
(Years)

HBeAg

anti-HBe

HBsAg

Total anti-HBc

IgM anti-HBc

Titer

0 4 8 12 16 20 24 28 32 36 52 Years

Weeks after Exposure





# Objectives

- Learn about the various tests used to assess hepatitis B infection
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# True, \*False or Don't know?

- Patient A has been told he probably needs treatment of his HBV
  - ALT 125, HBeAg-positive
  - HBV DNA  **$5 \times 10^7$**  copies/mL
- Patient A is reluctant to start therapy and wants another test done in 2-3 months
  - ALT 85
  - HBV DNA tripled  **$1.5 \times 10^8$**  copies/mL
- This patient must start therapy right away as his hepatitis B has gotten worse





# Patient A – Answer: FALSE

## ■ Active disease

- ALT 125, HBeAg-positive
  - HBV DNA  $5 \times 10^7$  copies/mL
  - Increase viral load to  $1.5 \times 10^8$  copies/mL
    - 7.70 log copies to 8.18 log copies
    - Increase viral load by 0.48 log copies
- STABLE VIRAL LOAD

## ■ Treatment?

- Yes or wait





# Patient B

- 45 year old man
  - ALT 25, HBeAg-POS, HBV DNA  $5.8 \times 10^{10}$  copies/mL (10.8 log copies)
- This patient's status is:
  - \*A. Immune Tolerant – treat
  - B. Immune Tolerant – don't treat
  - C. Inactive Carrier – treat
  - D. Inactive Carrier – don't treat





# Patient C

- 45 year old man, hepatitis B for a long time, not being followed, asymptomatic
  - ALT 22, HBeAg-negative, HBV DNA  $8.2 \times 10^4$  copies/mL (4.91 log copies)
- Patient management is:
  - A. Inactive carrier, follow-up family physician
  - \*B. Status unknown
  - C. Immune Tolerance: yearly follow-up

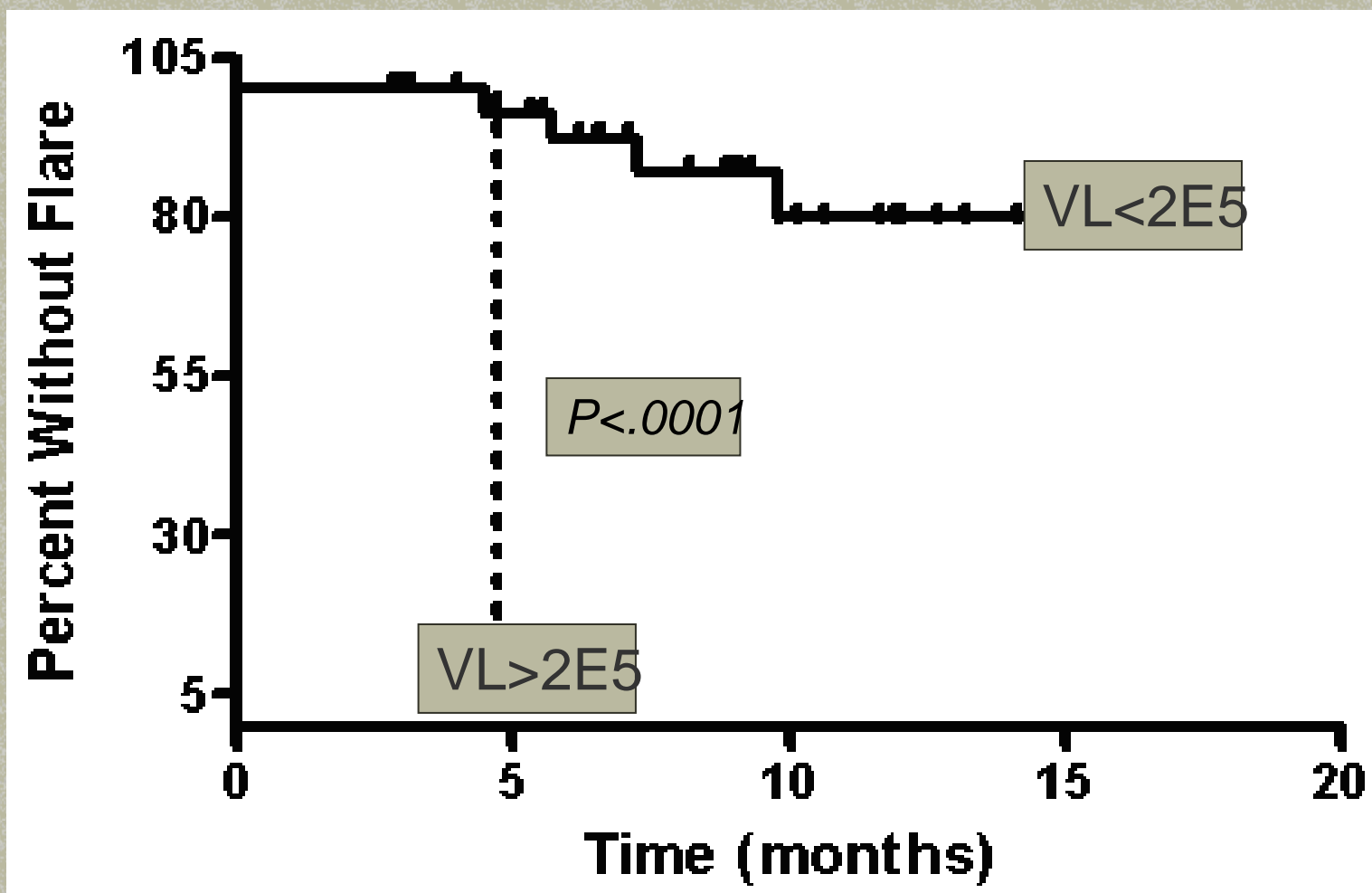






# Risk of ALT flare

HBV Viral Load  $2 \times 10^5$  cp/mL



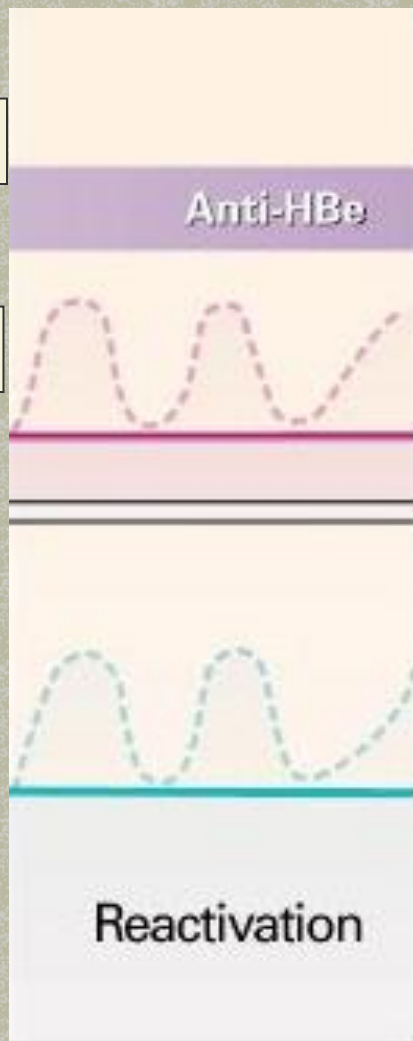


# True or \*False?

- Patient D with HBeAg-negative CHB
  - 0-48 wks: Rx PegIFN treatment
  - 72 wks: HBV DNA is negative (<400 copies/mL)
- This is an SVR and his hepatitis B is either cured or will remain inactive



# Reactivation



- Loss of immune control
- Viral load fluctuating or high
  - HBV DNA  $<10^{(4)5}$  to  $>10^{(4)5-10}$
  - HBeAg negative
- ALT levels fluctuate
- Liver biopsy
  - Inflammation
  - Fibrosis increasing
  - Fluctuating levels HBV in liver
- Treatment - YES



# True, \*False or Don't know?

- Patient A with HBeAg-positive CHB
  - 0-48 wks: Rx PegIFN treatment
  - 72 wks: HBV DNA is negative (<400 copies/mL)
    - Also HBeAg→anti-HBe, HBsAg→anti-HBs
- This is a cure of hepatitis B infection

