HEPATITIS B

BACKGROUND
AND
CASES

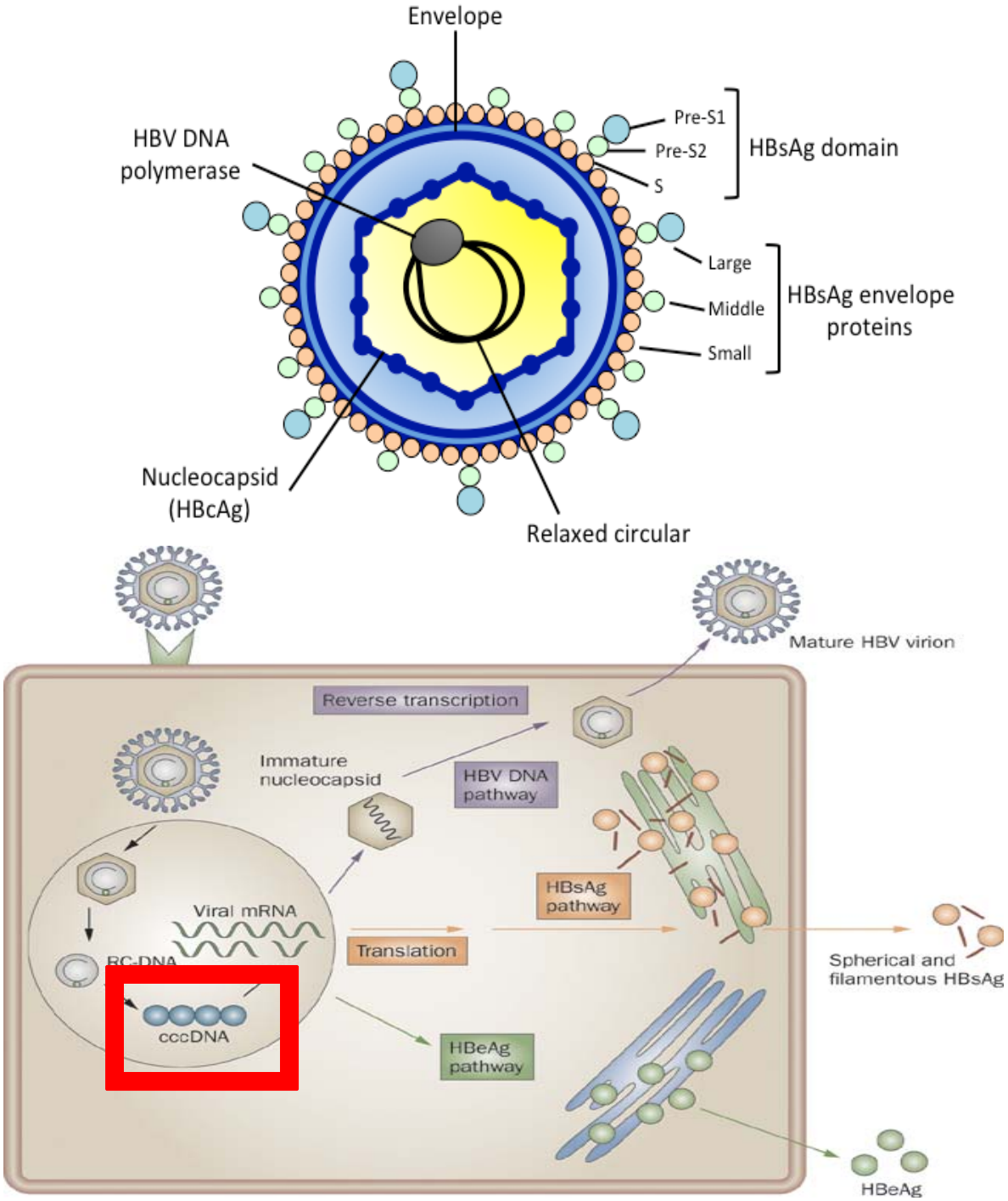
August 23rd, 2016

Hepatitis B

- Most common chronic liver disease worldwide
- ~ 2 billion exposed; >300 million carriers
- Varying prevalence around the world
  - High: China, Southeast Asia, Sub-Saharan Africa
    - Common mode: perinatal/vertical transmission
  - Low: North America and Western Europe
    - Common mode: sexual and IVDU

Hepatitis B

- DNA virus, hepadnavirus family
- Genotypes A-H
- A common cause of *chronic* liver disease however can be "spontaneously cleared" 80-90%
  - Vertical (young): progression to chronicity common
  - Acquired (older): often cleared
- Causes damage…but in the context of a host immune response/inflammation
- Oncogenic virus (regardless of cirrhosis)



Double stranded DNA Virus makes 4 Proteins:

Surface: attachment

Core: inner core included e

Polymerase: replication

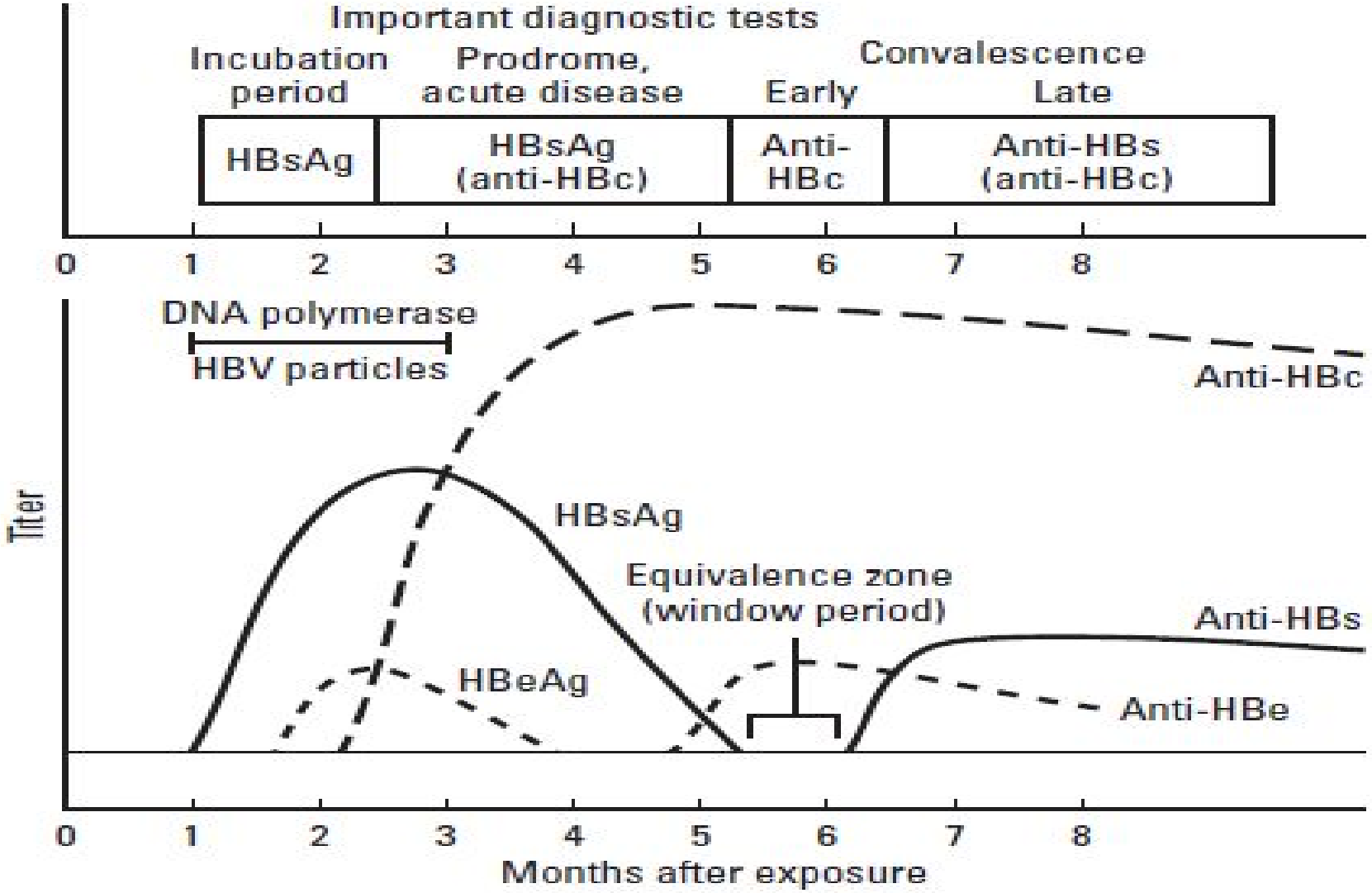
X: causes cancer

cccDNA: protected shell of HBV DNA in the hepatocyte nucleus THAT NEVER GOES AWAY!!!

What we can measure:

Surface Ag and Ab
Core Ab
E Ag and Antibody
HBV DNA

Acute Hepatitis B



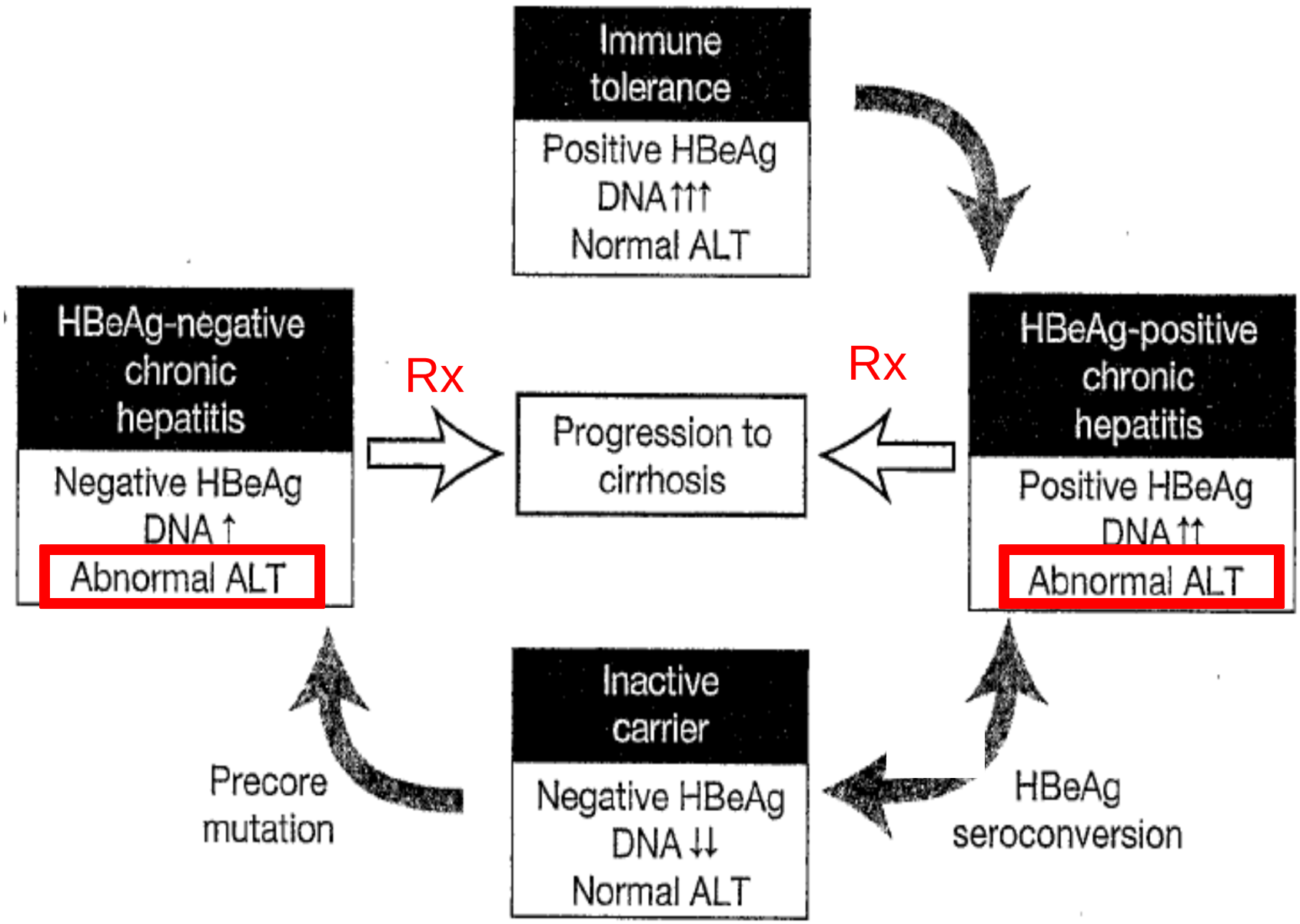
“Rules for Acute Hepatitis B”

- Start with surface Antigen: if reactive, assume they have hepatitis B (acute or chronic)
- Detailed history of exposure
- If not reactive….verify with core
  - Core IgM: reactive is acute HBV
  - Core Total (IgG): implies exposure
- eAg expression implies recent acquisition
- Track CMP and PT/INR
- Antiviral therapy is not indicated unless there is liver failure, spontaneous clearance about 80% of the time
- Reassessment in about 6 months in the outpatient setting to check for surface antibody…….

Chronic Hepatitis B: The Four Phases

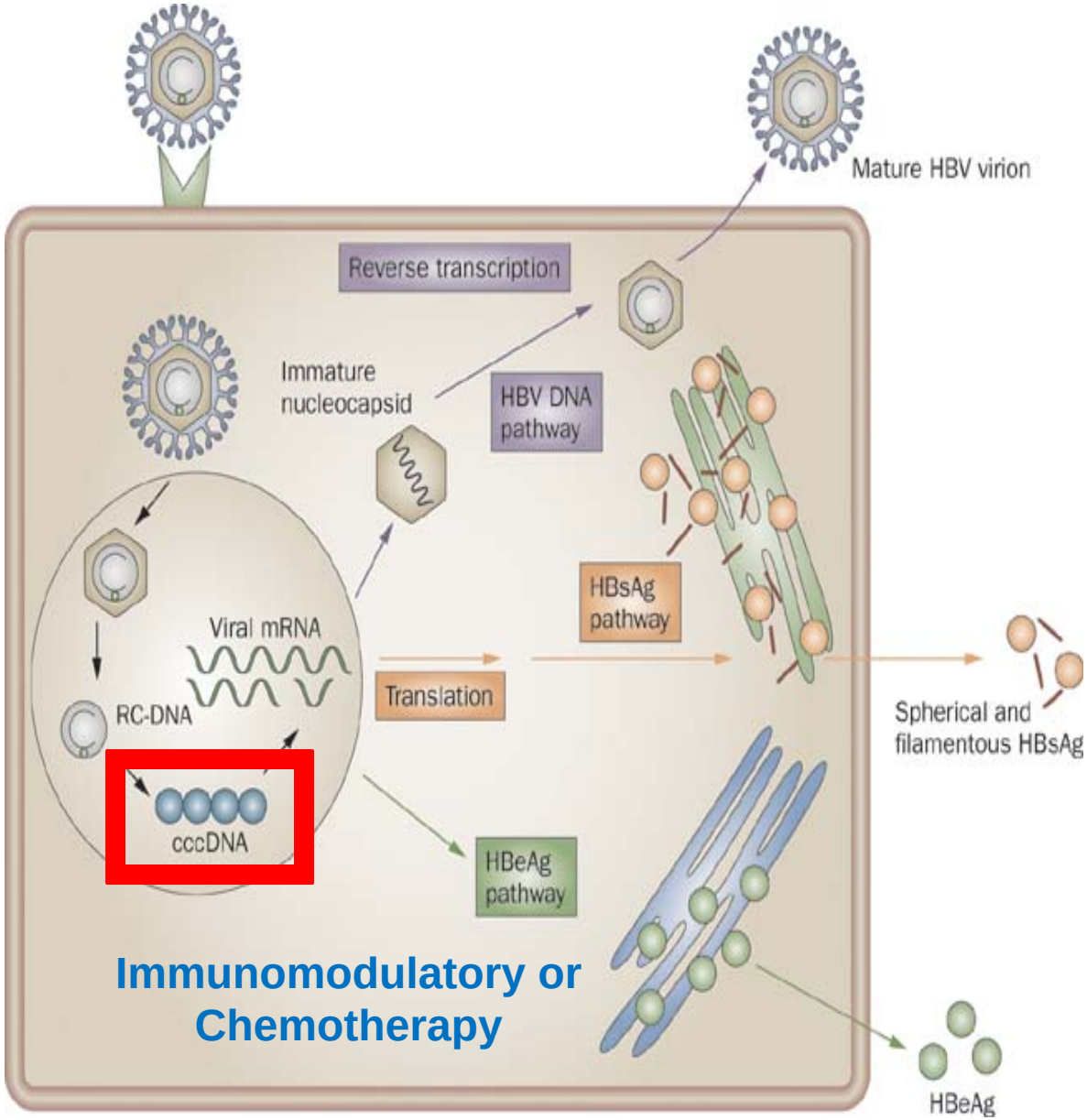
- For those who don't acquire sAb at 6 months or who obtain vertically…progression to chronicity
- Phase 1: Immune Tolerant
  - sAg: pos, eAg pos, HBV DNA High, LFTs normal
- Phase 2: "eAg positive" Chronic hepatitis B
  - sAg: pos, eAg pos, HBV DNA wherever, **LFTs abnormal**
- Phase 3: Chronic carrier
  - sAg: pos, eAg negative, eAb pos, HBV DNA Low, LFTs normal
- Phase 4: "eAg negative" Chronic hepatitis B
  - sAg: pos, eAg negative, eAb pos, HBV DNA wherever, **LFTs abnormal**

Chronic Hepatitis B: The Four Phases



Hep B SAg	Anti HBs	IgM Anti-HBc	IgG Anti-HBc	HepB eAg	HepB Anti HBe	ALT	
+	-	+	-	+	-	HIGH	Acute HBV
+	-	-	+	+	-	HIGH	eAg pos CHB
+	-	-	+	-	+	LOW	Chronic Carrier
+	-	-	+	-	+	HIGH	eAg neg CHB
-	+	-	-	-	-	LOW	Immunized
-	+	-	+	-	+	LOW	Exposed

HBV Reactivation



People with "resolved" infection

sAb: NonReactive
cAb: Reactive

sAb: Reactive
cAb: Reactive

Are at risk for reactivation

Prior to starting biologic or chemotherapy: Assess for sAb AND core total antibody

If core total is present….consider antiviral

Hepatitis D Virus

- Hepatitis D virus: defective RNA virus, requires HBV to help with replication
- Can cause pathogenesis in 2 forms
  - Co-infection
  - Superinfection
- Treatment or immunization against HBV should treat/prevent HDV
- Uncontrolled co-infection increases risk for liver failure
- Viruses travel in groups….document HCV and HIV status

Hepatocellular Cancer

- Hepatitis B Virus is a carcinogen
- Risk of hepatocellular cancer increases with
  - Increased duration of infection
  - Higher levels of HBV DNA
- Risk for HCC exists irrespective of cirrhosis
- Guidelines are age based for those from areas of endemicity

Treatment of HBV

- Immunization
  - Series: birth, 2, 6 mos
  - If mother infected: HBIG at birth/immunizations

- Treatment
  - Nucleos(t)ide analogs
    - Tenofovir (Viread)
    - Entecavir (Barraclude)

Case 1:

A 42 year old WM with history of polysubstance abuse presents to the ER with one week history of fatigue, malaise, and worsening jaundice. He reports ongoing use of methamphetamine and heroin up until a few weeks ago. Contrast CT of the abdomen is notable for hepatomegaly. Tylenol level is unremarkable. He reports he has never had a liver problem in the past.

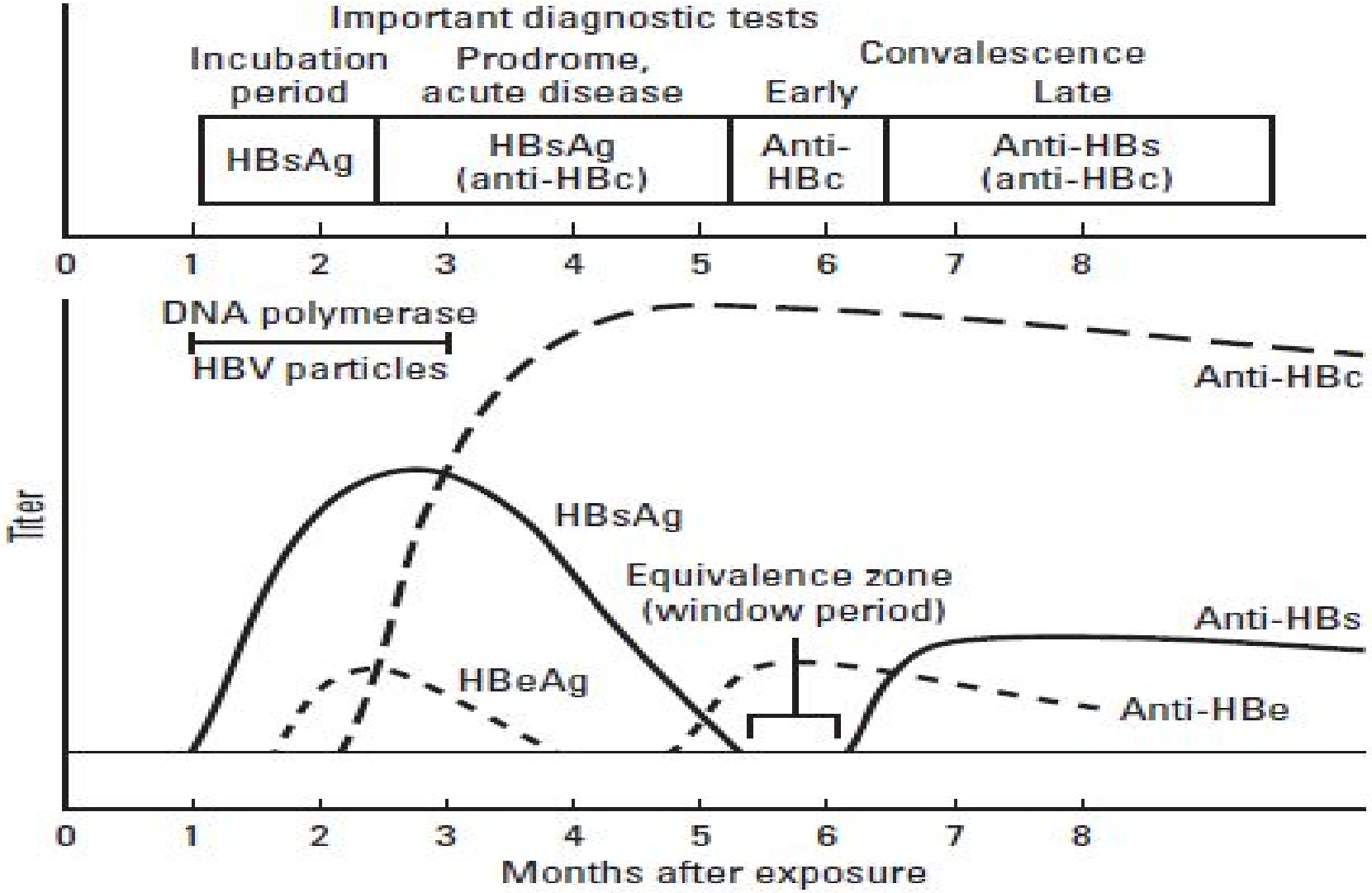
Physical Exam: Afebrile, HR: 80, BP:120/80, Resp: 12, and PO2: 100% on Room Air
ATOx4, jaundiced, mild TTP in RUQ, "track marks" on arms,
nonfocal neuro exam without asterixis

Laboratory assessment: AST: 2235 ALT: 2500 Tbil: 18.0 Alb: 4.0
INR: 1.0 Cr: 0.85
HAV Total Ab: non reactive
HepB sAg: reactive, Hep B Core IgM: reactive

Which of the following is **CORRECT** regarding **management of acute HBV:**

A. Tenofovir is indicated for 6 months with reassessment for surface Antibody
B. N-Acetylcysteine infusion is indicated for 48 hours
C. No immediate action is necessary apart from supportive measures
D. Antiviral is indicated when the Tbil is >20g/dL

Acute Hepatitis B



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Case 2:

A 56 year old Vietnamese lady presents to establish primary care. She emigrated at the age of 24 to pursue her masters degree in business. She reports history of hypertension; well controlled on lisinopril. She feels well. She recently learned her brother who lives in Vietnam was diagnosed with liver cancer and wonders if she is at risk. She brings in a recent laboratory report from her previous PCP done a few months prior:

Alb: 4.0 AST: 8 ALT: 10 Tbil: 0.3 Cr: 0.50 INR: 1.0 Plts: 450
Hep BsAg: reactive Hep BsAb: non reactive Hep B eAg: non reactive
Hep BeAb: reactive HepB core total: reactive HBV DNA: 20 copies

Which of the following statements is **CORRECT** regarding risk of liver cancer in this patient:

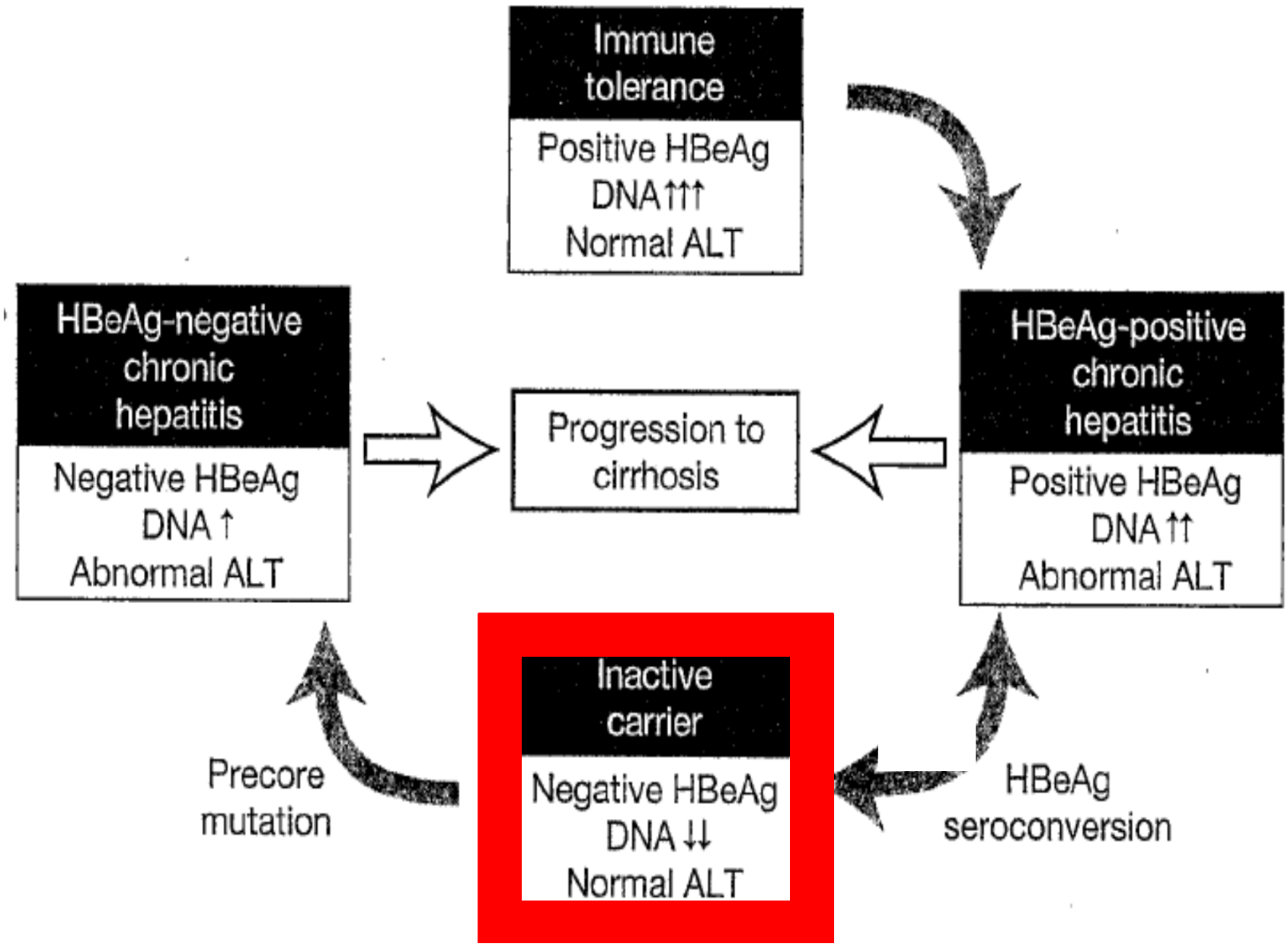
A. This patient is not at risk because she is a chronic carrier with low viral load

B. Risk of liver cancer is directly proportional to the Alpha fetoprotein (AFP)

C. Not at risk because there is no clear evidence of cirrhosis

D. Risk is tied to duration of infection and she should be enrolled in HCC screening with imaging

Chronic Hepatitis B: The Four Phases



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Case 3:

A 35 year old man comes to see you because of fatigue and lethargy. He has no past medical history apart from IVDU in his early 20s. He has been free of all illicit substances for over 10 years. Given his history, you elect to perform risk based testing for viruses. Workup results are below:

Alb: 4.0 AST: 74 ALT: 93 Tbil: 0.8 INR: 1.0 PLT: 200
HIV: Non reactive Hep A Total: Non reactive
HCV Ab: Non reactive
Hep B sAg: Reactive Hep B sAb: Non Reactive
Hep B core total: Reactive
Hep B eAg: Reactive Hep B eAb: Non Reactive HBV DNA: 25,000 copies/mL

Which of the following is **INCORRECT** regarding the management of this patient:

A. Antiviral therapy is indicated for treatment of eAg positive CHB

B. Immunization against HAV should occur

C. Antiviral therapy is indicated for treatment of eAg positive CHB is indicated and patient should be instructed that this will likely be lifelong

D. A liver biopsy could be performed but is not mandatory prior to treatment

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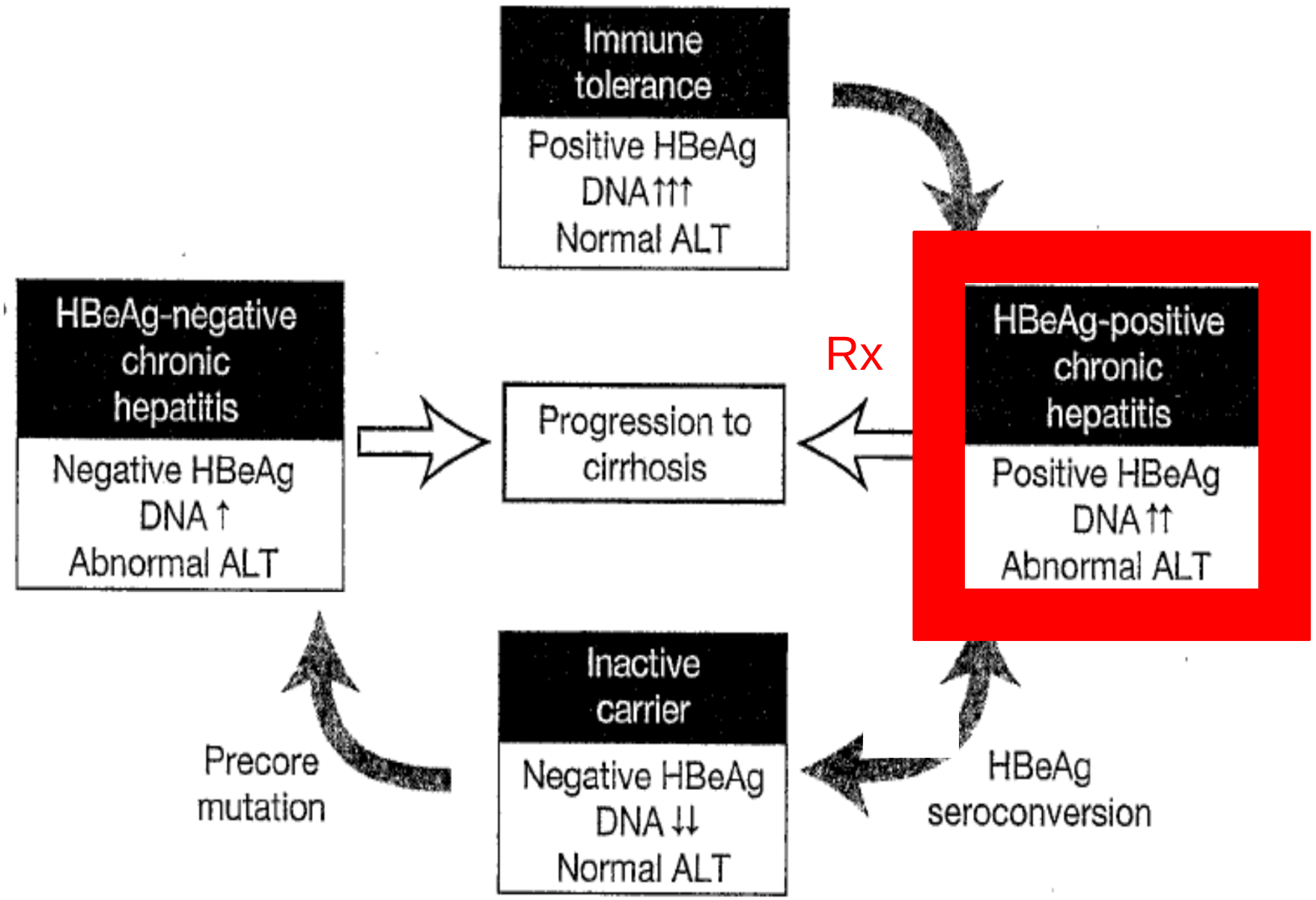

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Case 4:
A 56 year old you follow has recently developed fevers, night sweats, and unintentional weight loss. LDH is 8000. CT C/A/P confirms and biopsy confirms B-Cell lymphoma. Her oncologist plans to initiate Rituximab (Anti-CD20) based chemotherapy. Prior to initiation, you recall that chemotherapy may "reactivate" latent viruses in the body. You elect to perform additional testing which reveals:

Alb: 4.2 AST: 20 ALT: 18 INR: 0.9 Tbil: 0.4

HIV: Non reactive HAV Total: Reactive HCV: Non Reactive

Hep B sAg: negative Hep B sAb: reactive

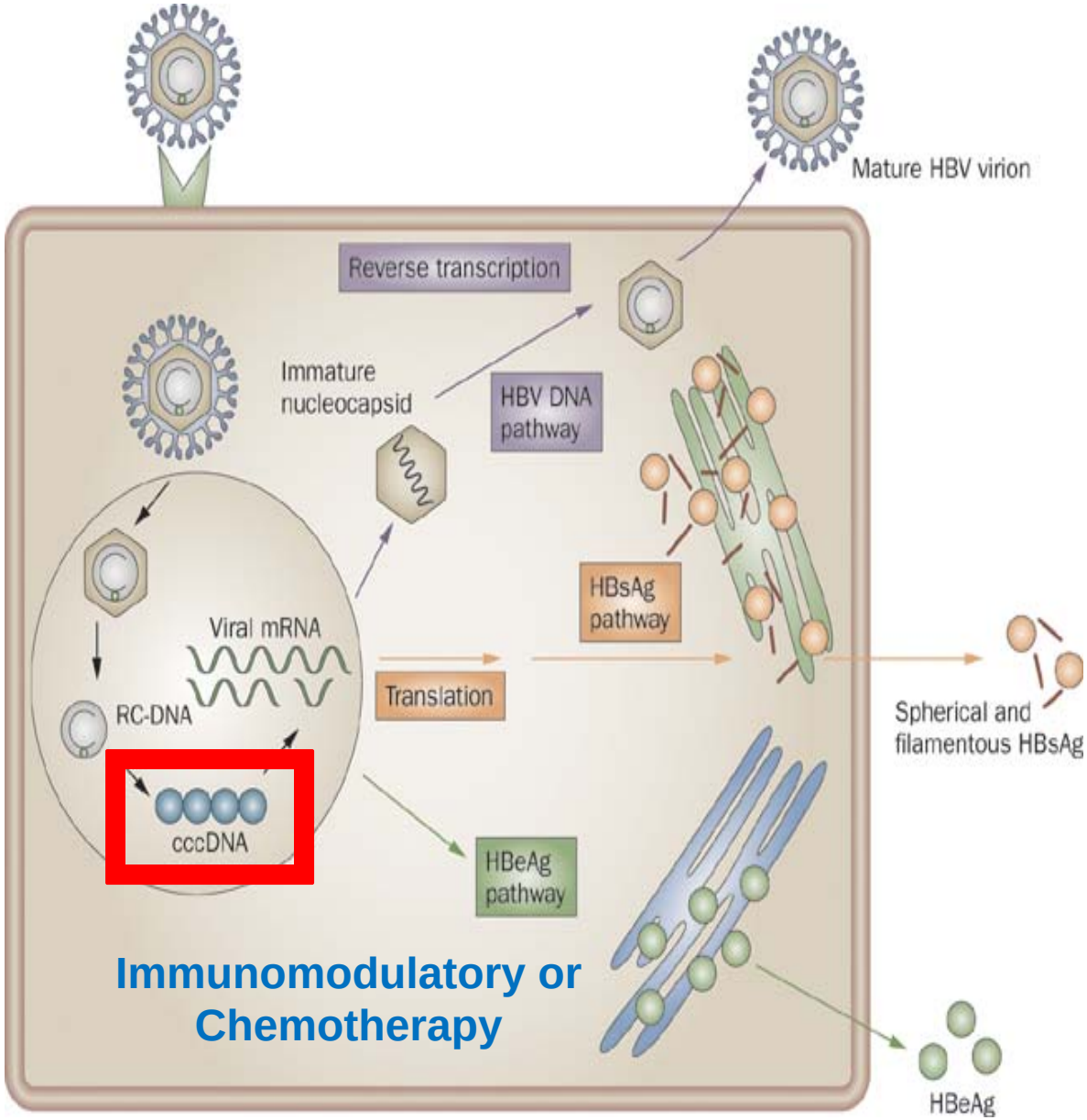
Hep B core total: positive Hep B eAg: negative Hep B eAb: positive

HBV DNA: Undetectable

Which of the following is correct regarding risk of HBV activation:

A. No risk, patient does not have HBV
B. No risk, patient has reactive HepBsAb
C. Risky, chemoprophylaxis should be considered
D. Risky, HBIG treatment should be considered during rituximab

HBV Reactivation



- **Reactivation can occur in ANYONE who has been exposed**
- **Need to evaluate core Ab status**
- **Risk is small but does occur**
- **Recommendation is to treat with antiviral during immunomodulatory therapy and continue for 6 months**
- **Not all immunomodulatory agents are equal**
- **If missed….options are very limited**

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Case 5:

A 35 year old nurse is referred to you for management of hepatitis B. She has no past medical history. You review outpatient laboratory studies which reveal:

Hep BsAb: reactive

You decide to complete the picture and obtain the following serologies:

Hep BsAg non reactive
Hep B core total: Non reactive IgM: non reactive IgG: non reactive
Hep B eAg: non reactive Hep B eAb: non reactive
HBV DNA: Undetectable

Which of the following is the **correct** next step in management:

A. Liver biopsy to stain for core antigen

B. Reassurance, the patient is immunized

C. Recheck in 6 months