الجامعة السورية الخاصة
SYRIAN PRIVATE UNIVERSITY

VIRAL HEPATITIS

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2018

Prevalence in Syria

4% of the population

ندوة التهابات الكبد الفيروسية ـالمجلس الأعلى للعلوم

2003

CHRONIC HEPATITIS B
THE PERSISTENCE OF HBsAg FOR LONGER THAN 6 MONTHS.

Infectivity

Like AIDS but

Hep B 100 times more concentrated in blood

It is ability to remain stable outside and infective in dried blood at room temperature for more than a week

HCV

It is ability to remain stable outside and infective in dried blood at room temperature for **16 hours**

When the serum HBV DNA level is under 200,000 IU/ml vertical transmission can be prevented simply by administering HBIG and HBV vaccine to the newborn.

Hep.B &Pregnancy

- Babies born to Mothers with HBsAg+ve &HBV DNA have *20 to 95%* risk of becoming Infected
- infectivity depends on HBV DNA level

- Babies of HBsAg+ve M others and HBeAg -ve ***uncommon*** to be chronic hepatitis B BUT at risk of severe acute neonatal hepatitis &acute liver failure

Recommendations (2009)

Accordingly, all infants should receive the first dose of hepatitis B vaccine as soon as possible (<24 hours) after birth.

This should be followed by 2 or 3 doses to complete the series

- **The risk of HCV transmission after percutaneous exposure is low, approximately 1.8%**

The risk of HBV seroconversion after a percutanous injury ranges from 32% to 62% in unvaccinated person and is dependent on the hepatitis B e antigen status of the source ,DNA ---

Mode of Transmission of HBV

Infected blood transfusion or blood products

Needle stick injuries: HCW - injection drug users

Hemodialysis

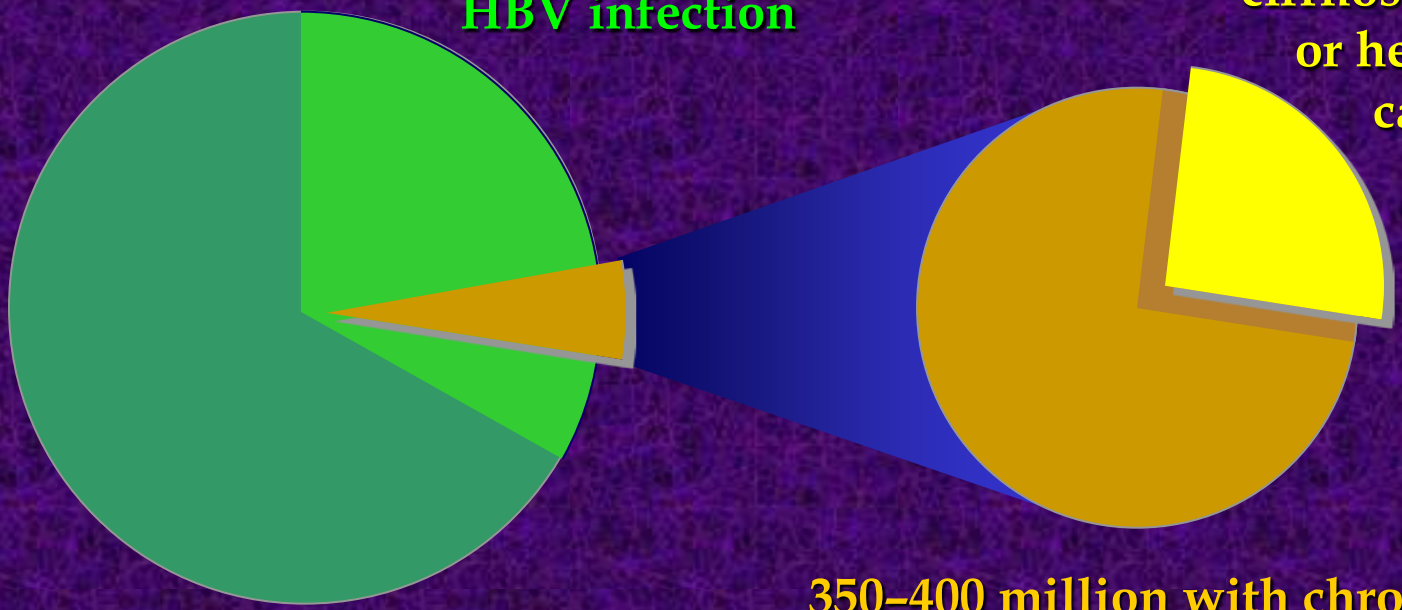
Sexual transmission: heterosexual - homosexual

Horizontal transmission: childhood - family member

Vertical Transmission (mother to newborn)

Unsafe Procedures: ear piercing - tattooing - barbering

Global Impact Of Hepatitis B Infection



Worldwide: ~1 million / year die from HBV-associated liver disease

نسبة المعدل الوطني للإصابات المكتشفة بالفحوص بالنسبة للحمى B و C ومقارنتها مع نسبة الإصابات المكتشفة بالدم لبقية الأمراض

السنة	1996	1997	1998	1999	2000	2001	2002
B	%7.01	%5	%4.46	%3.94	%3.85	% 3.69	%3.61
C	%2.53	%1.81	%1.77	%1.74	%1.19	%0.74	%0.46
HIV	%0.07	%0.10	%0.15	%0.13	%0.10	%0.10	%0.16
CMV IgM	%0.41	%0.32	%0.21	%0.42	%0.11	%0.65	%0.33

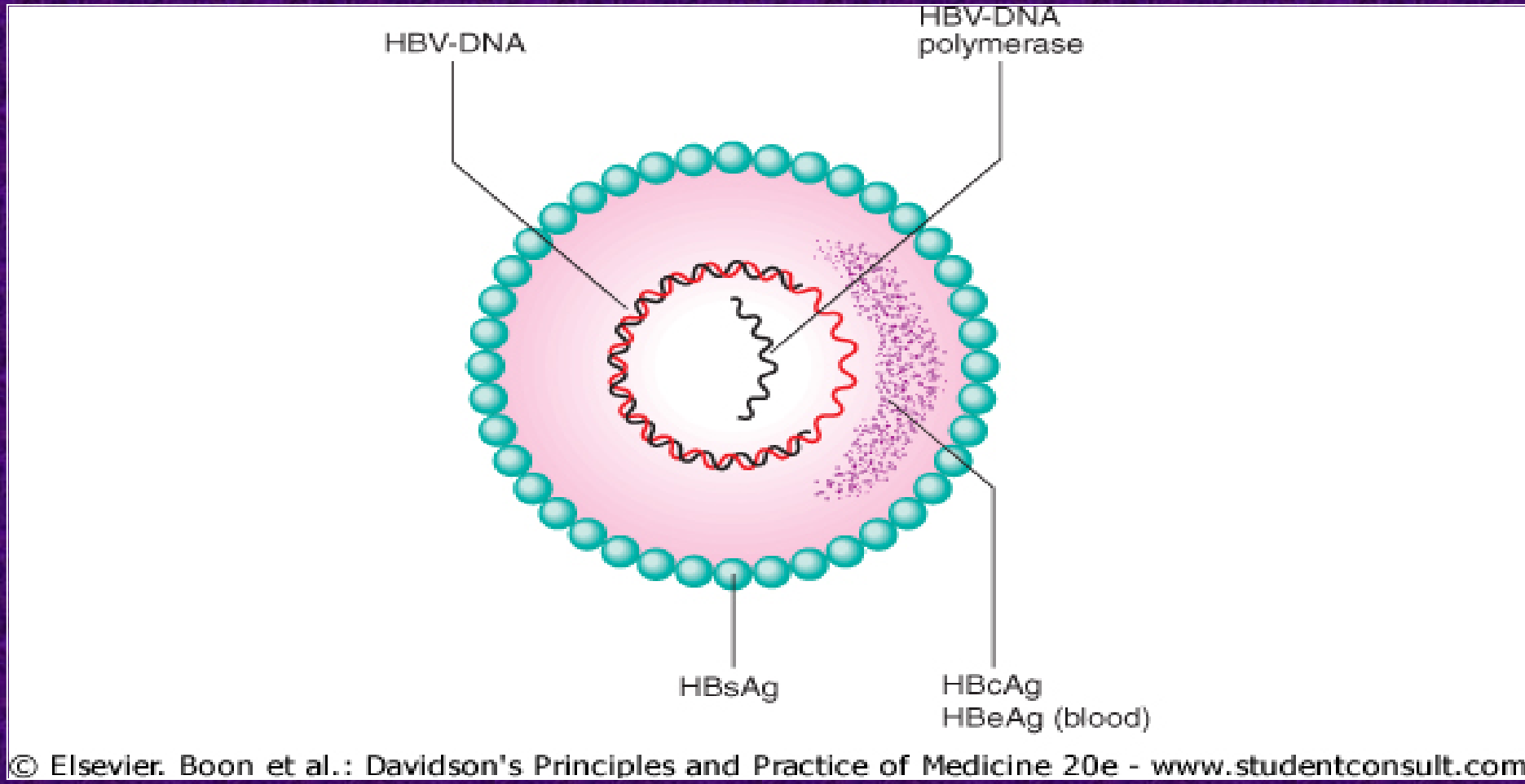
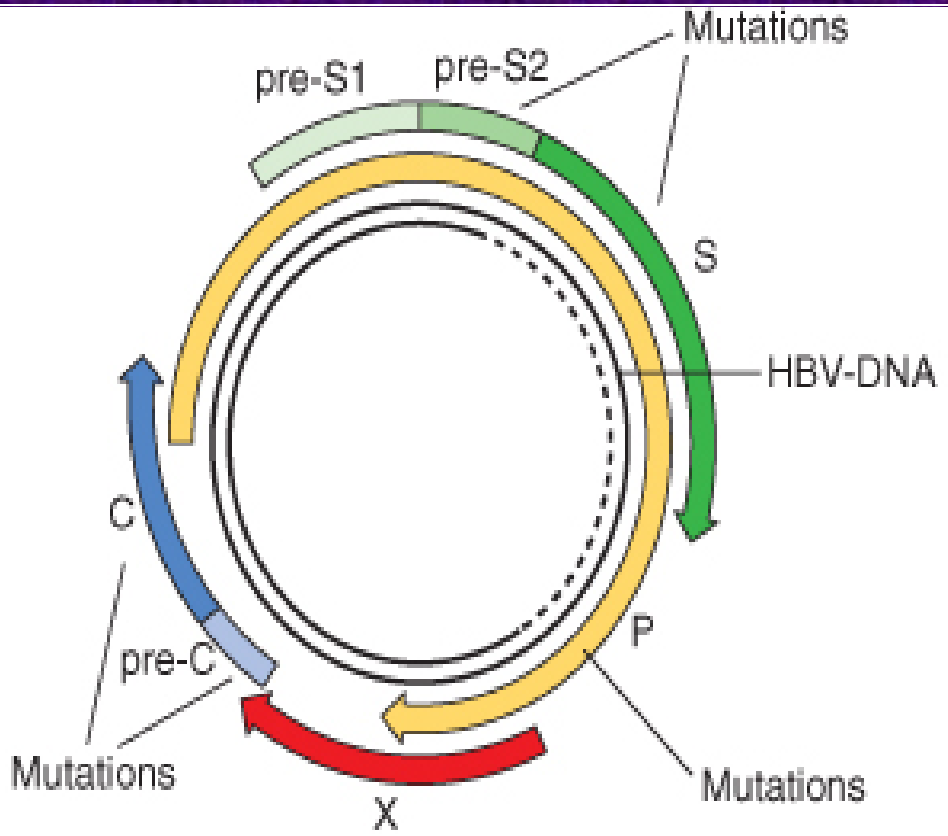


Figure 23.25 Schematic diagram of hepatitis B virus. Hepatitis B surface antigen (HBsAg) is a protein which makes up part of the viral envelope. Hepatitis B core antigen (HBcAg) is a protein which makes up the capsid or core part of the virus (found in the liver but not in blood). Hepatitis B e antigen (HBeAg) is part of the HBcAg which can be found in the blood and indicates infectivity.



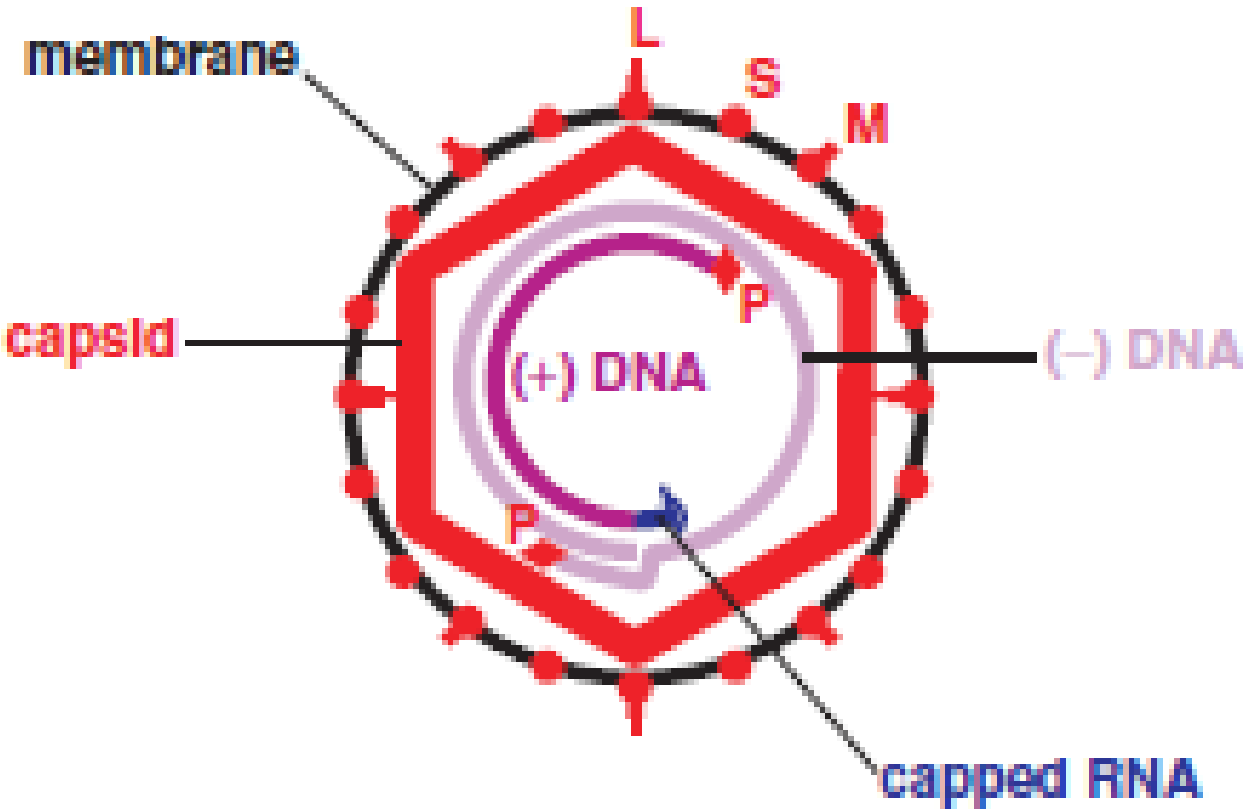
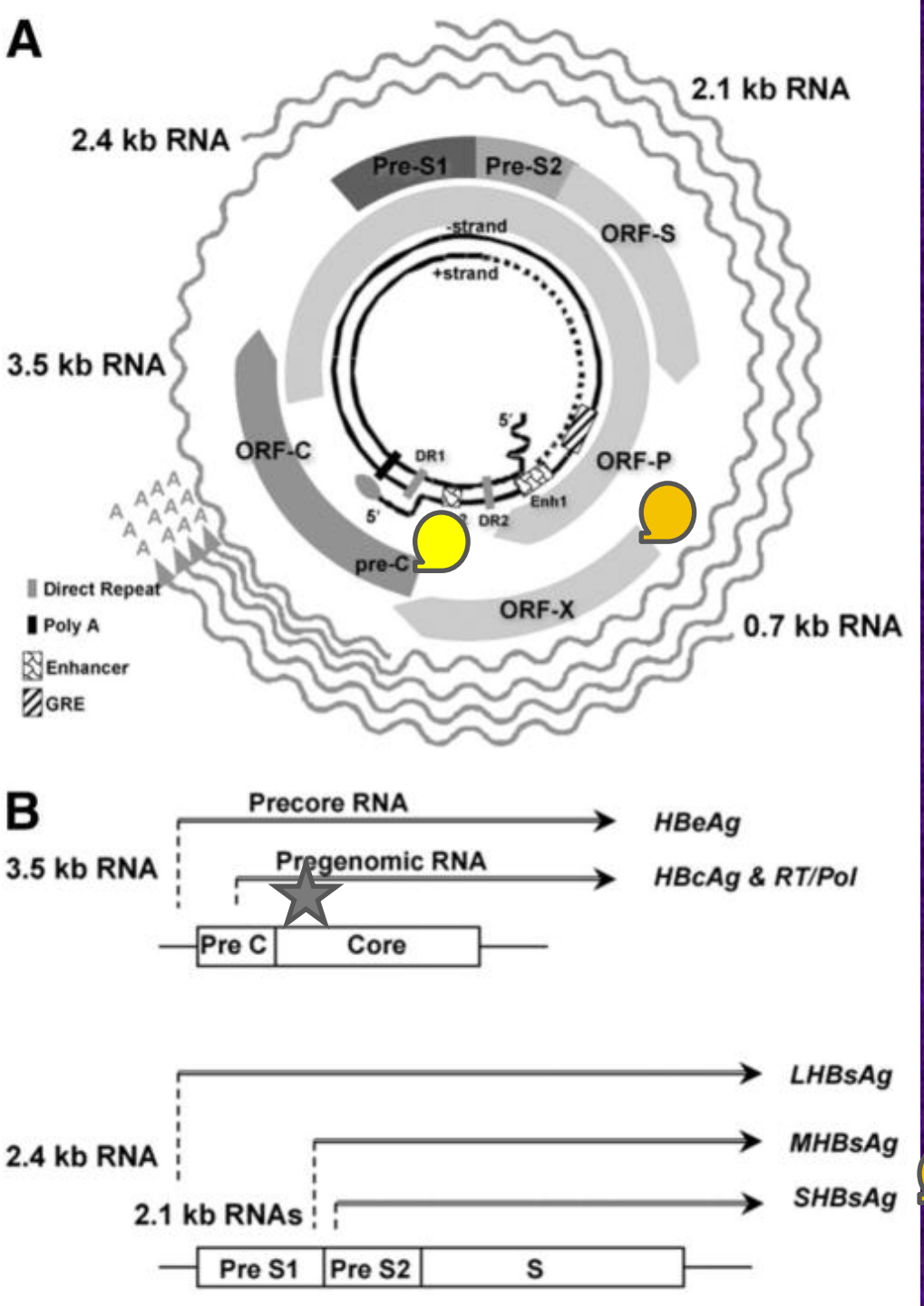
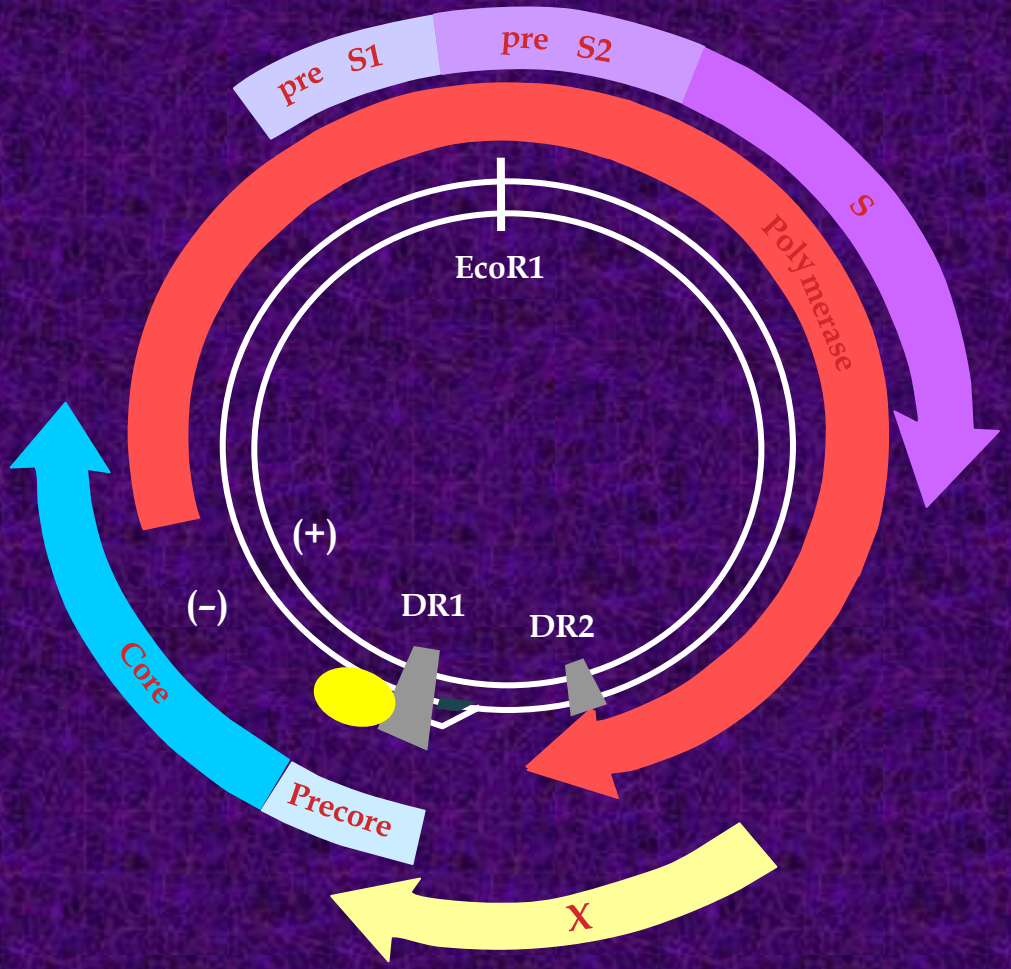


Figure 18.2 *The HBV virion.* S: small envelope protein. M: medium envelope protein. L: large envelope protein. P: polymerase (one molecule is covalently linked to the 5′ end of the (+) DNA; the virion may contain a second molecule of P, as indicated here

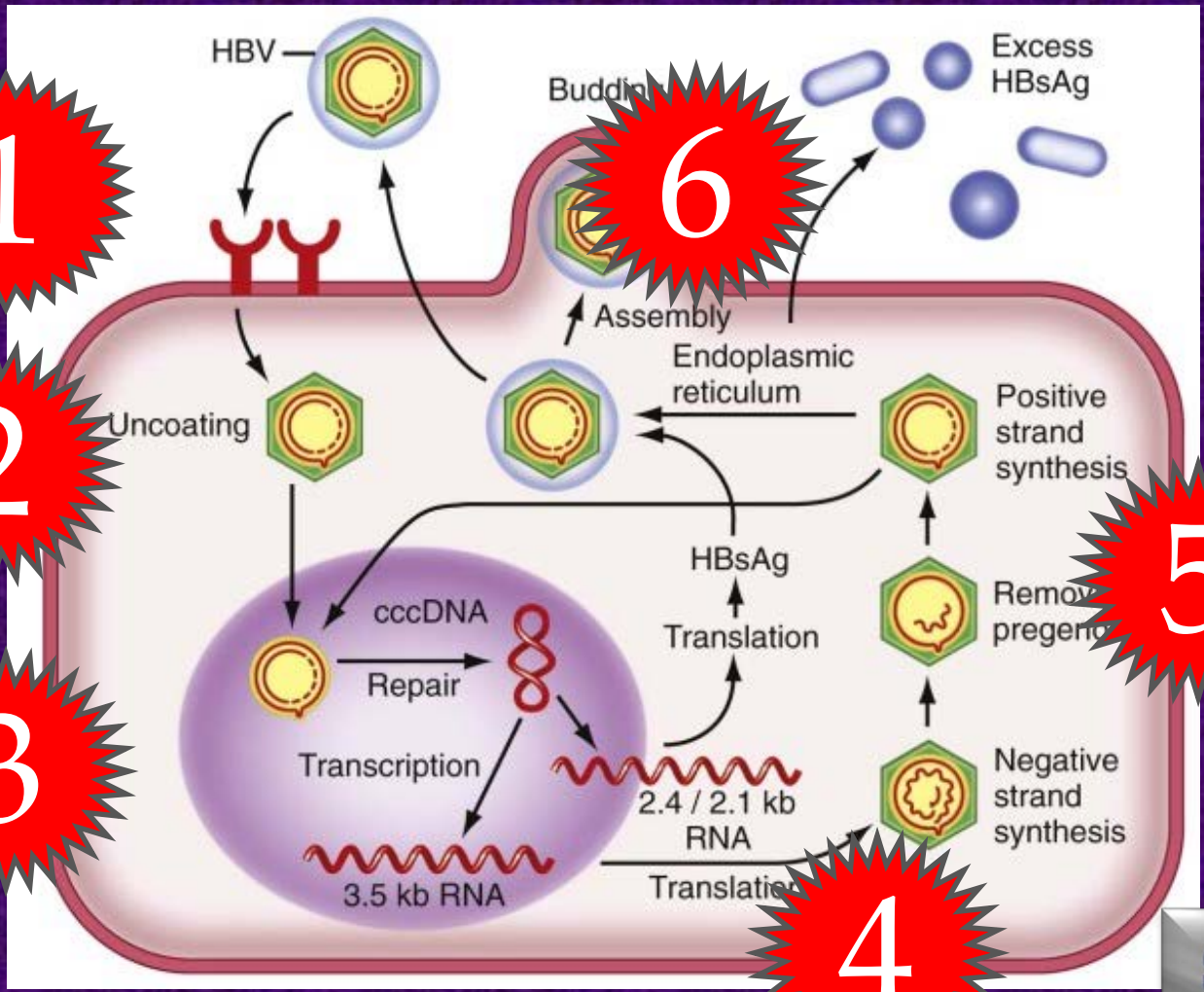
DNA PCR



Hepatitis B Virus Genome



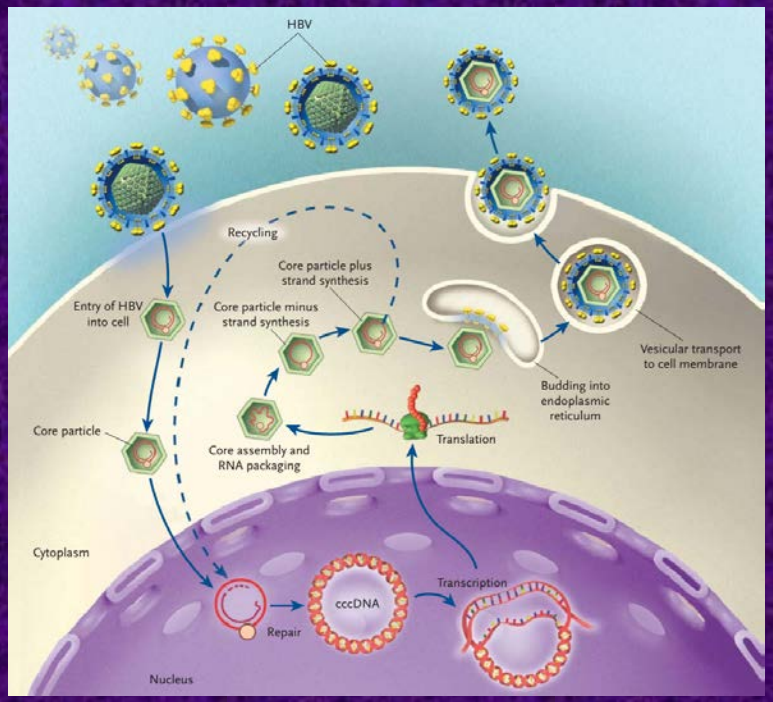
Life cycle of the hepatitis B virus (HBV)



Covalently Closed Circular DNA (cccDNA)

A

cccDNA



Covalently Closed Circular DNA (cccDNA)

- **Very stable within the hepatocyte**
- **Persist after antiviral therapy and even after clearance of HBsAg**
- **Plays a significant role in reactivation of disease**

Werle-Lapostolle et al (2004) Gastroenterology 126:1750

N Engl J Med 2004;350:1118-29

Figure 18.4 *HBV capsid.* Derived from cryo-electron microscopy images of capsids assembled in *E. coli* cells expressing HBV C protein. The bar represents 5 nm. From Watts *et al.* (2002) *The EMBO Journal*, **21**, 876. Reproduced by permission of Nature Publishing Group and the authors.

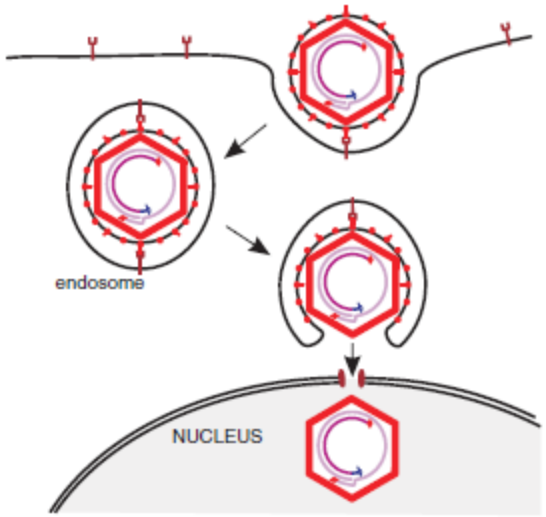


Figure 18.10 *Endocytosis of attached HBV virion followed by release of nucleocapsid and entry into the nucleus.*

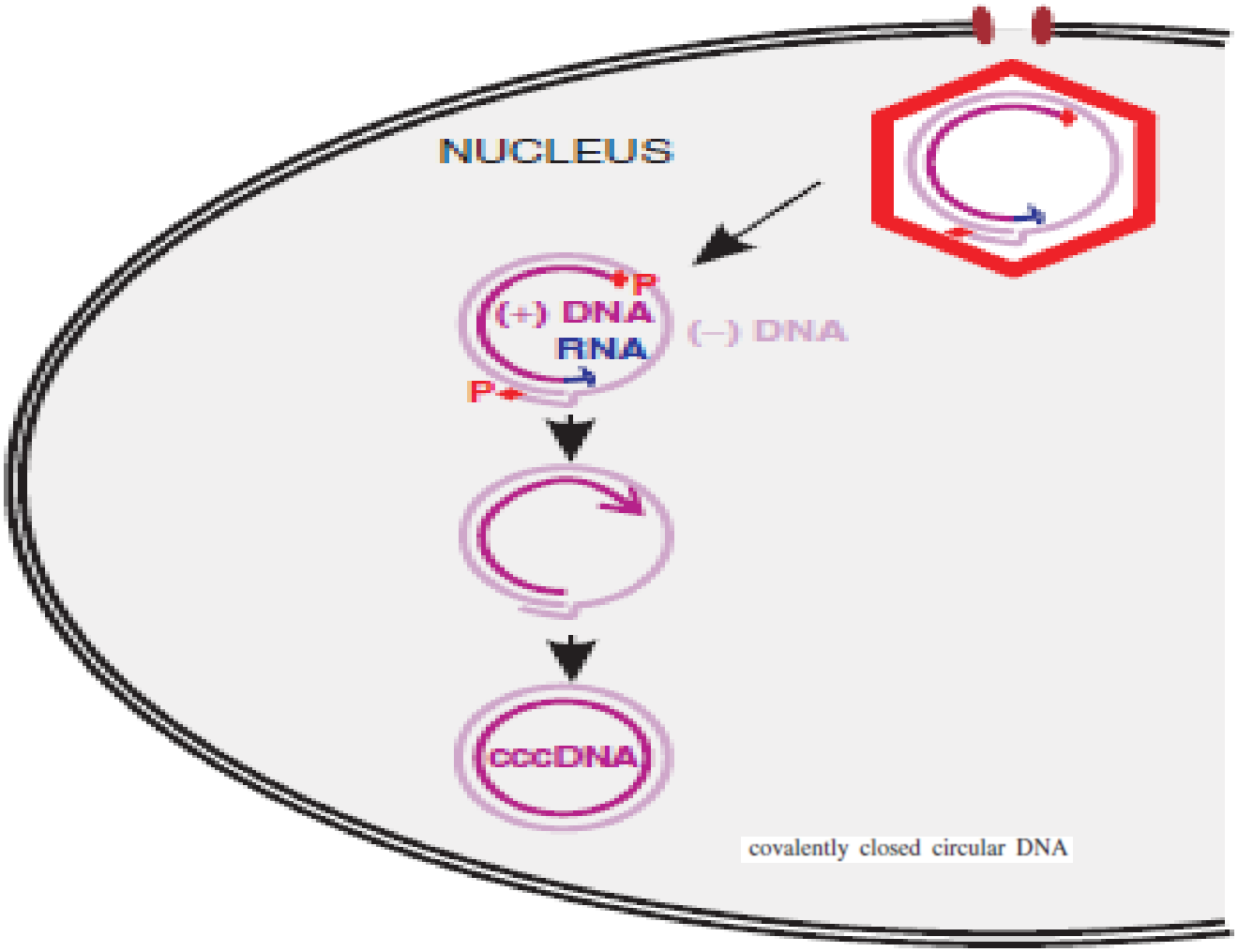


Figure 18.11 *Release of HBV genome from the capsid and conversion into cccDNA.*

HBsAg

-appears in the blood late in the incubation period and before the prodromal phase of acute type B hepatitis;

usually lasts for 3-4 weeks and can persist for

up to 5 months

Viral loads are usually in excess of 10^5 copies/ml in the presence of active viral replication, as indicated by the presence of e antigen.

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In contrast, in those with low viral replication, HBsAg- and anti-HBe-positive, viral loads are less than 10^5 copies/ml

One exception mutation .

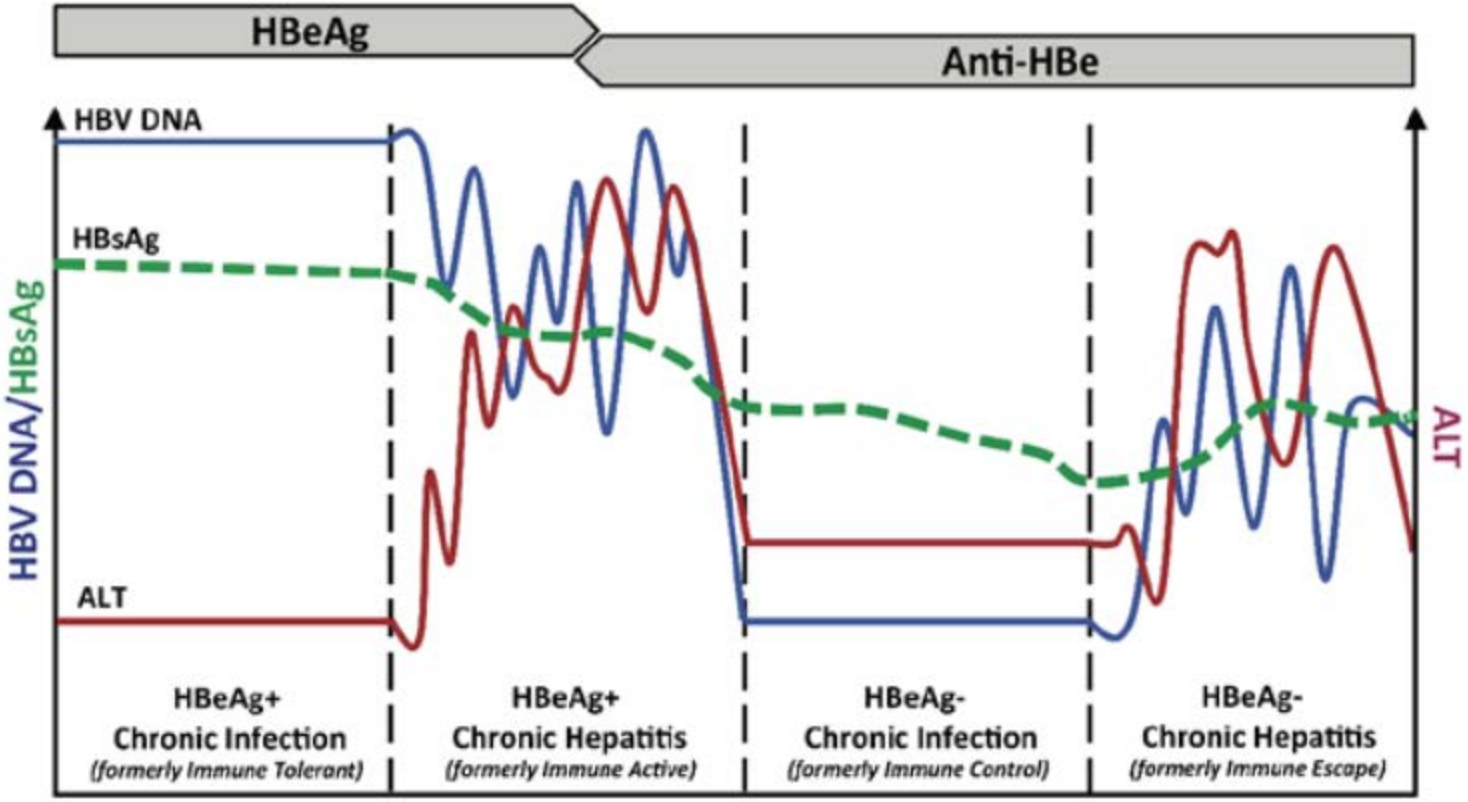

Fig. 1. Disease phases of chronic hepatitis B infection reflecting the updated

Table 1. Phases of chronic HBV as proposed by the EASL Guidelines [2].

	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	$>10^7$ IU/ml	10^4-10^7 IU/ml	<2,000 IU/ml**	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

*Persistently or **intermittently HBV DNA levels can be between 2,000 and 20,000 IU/ml in some patients without signs of chronic hepatitis.

HB e

Ab

low viral replication

HBsAg +& anti-Hbe positive

viral loads are **less** than $<10^5$ copies/ml

One exception mutation

Ag

- **active viral replication**
- HBe Ag +ve.
- Viral loads are usually in **excess** of $>10^5$ copies/ml

HB e mutation

which means

they cannot secrete e antigen into serum

HB e mutation

Such individuals will be

anti-HBe-positive

but

have a high viral load and often evidence of chronic hepatitis

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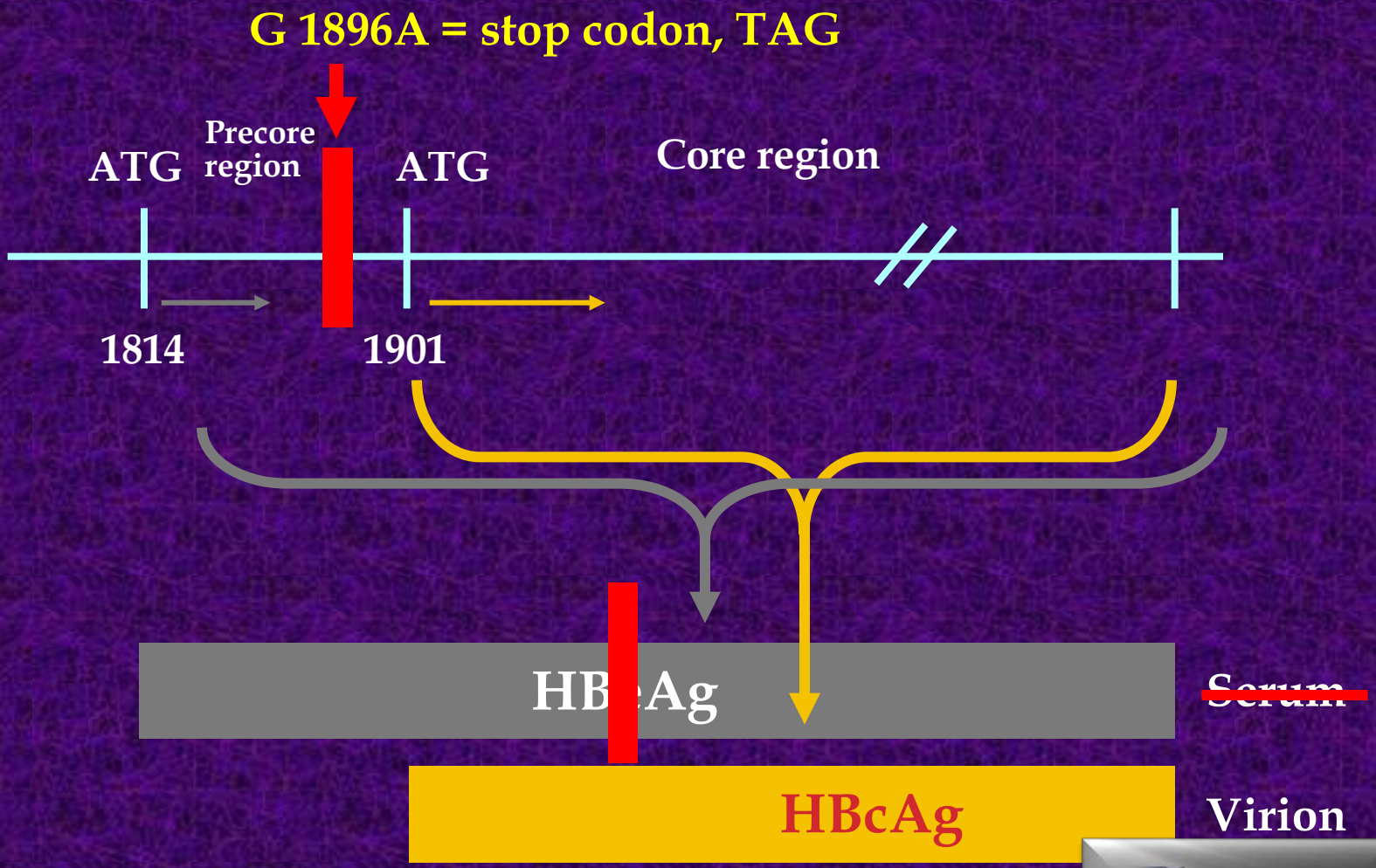
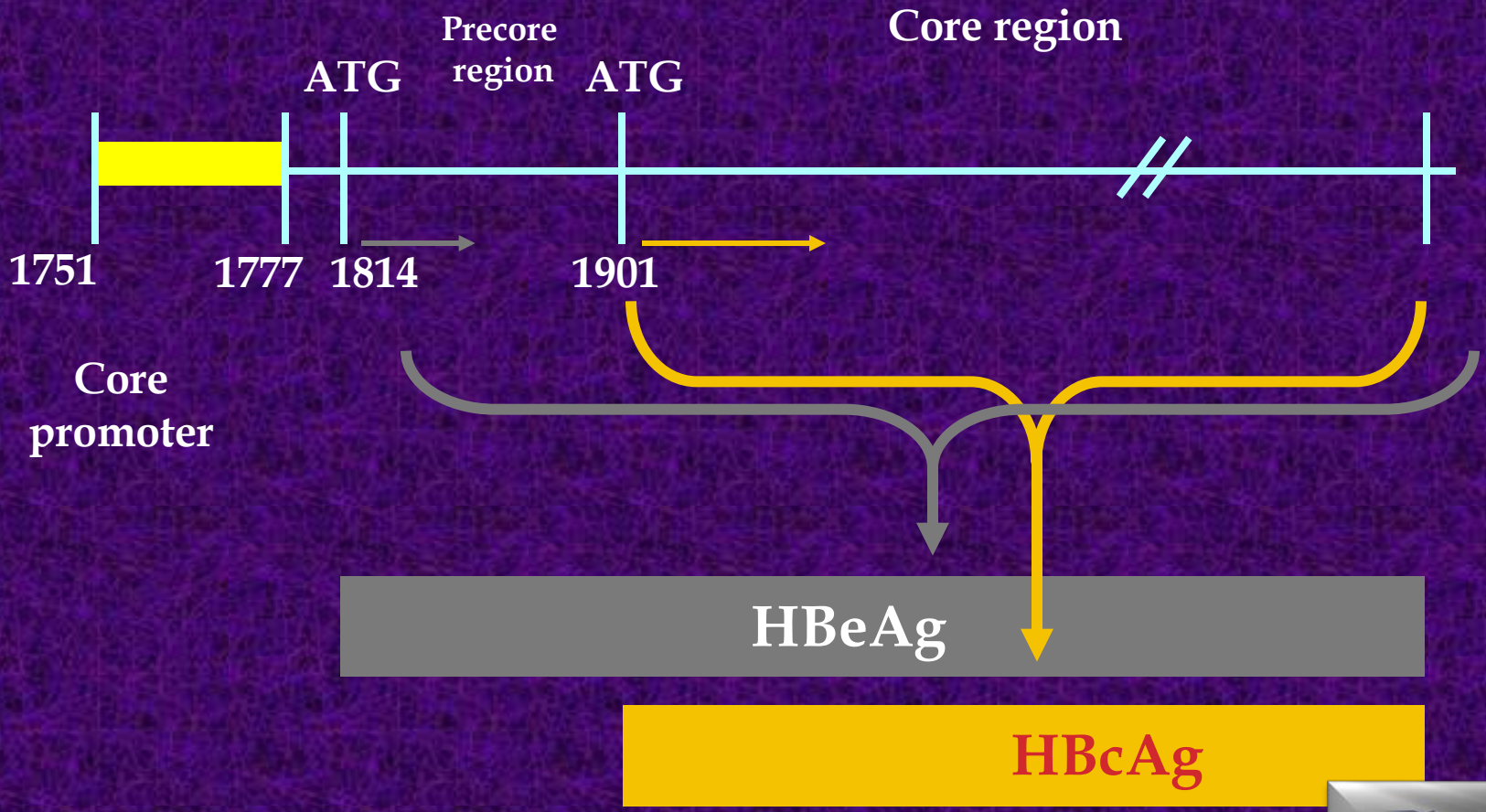
HB e mutation

They respond differently to antiviral drugs from those with classical e antigen-positive chronic hepatitis.

HBeAg and Precore Mutation

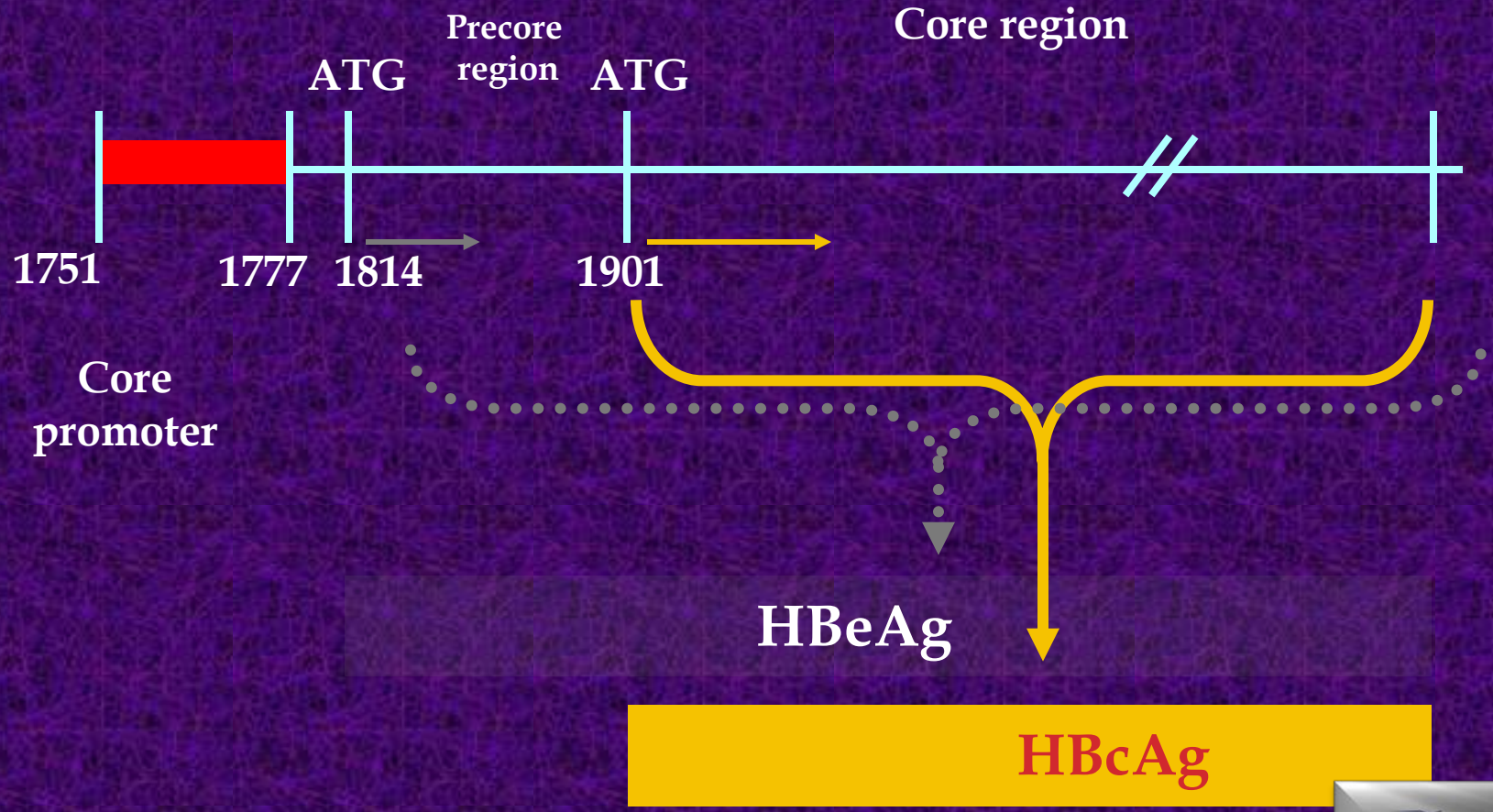


HBeAg and Core Promoter Mutation



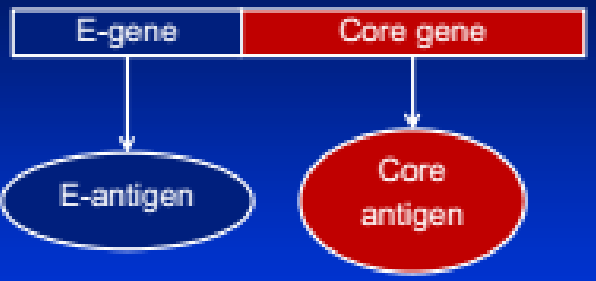
HBeAg and Core Promoter Mutations

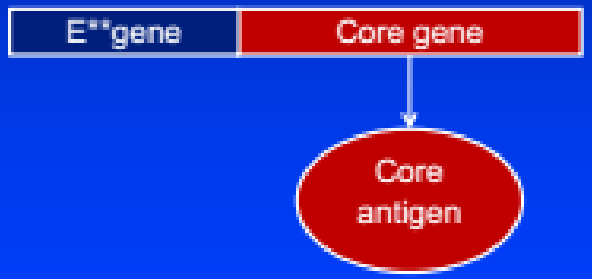
A1762T, G1764A
T1753C, C1766T etc



CHRONIC HBV
WHAT IS E-NEGATIVE ACTIVE HBV

- E-gene located in the pre-core region of HBV
- Not necessary for replication
- Target of the immune response to inactivate HBV



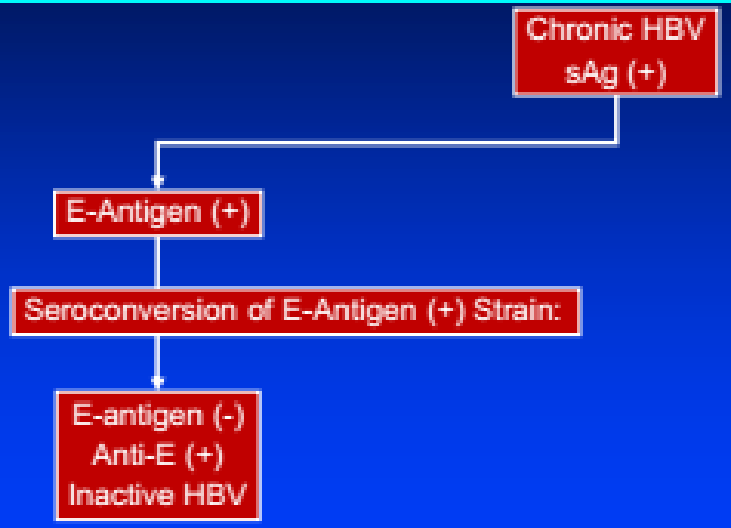


- Mutation of the E-gene
- No detectable E-antigen
- Does not prevent replication
- Prevents the immune response from inactivating HBV

Adapted from: S Ahn et al
Gastroenterol 2003; 125:1370-1378.

Bon Secours
Liver Institute of Virginia

E-ANTIGEN NEGATIVE CHRONIC HBV EVOLUTION



Adapted from: JH Hoofnagle et al.
Hepatology 2007; 45:1056-1075.

The impact of treatment on chronic viral hepatitis

This includes

- **1-improved quality of life**
- **2-regression of fibrosis**
- **3- a reduction in the risk of HCC**
- **4-a reduction in mortality**

Patients with E-antigen negative HBV cannot seroconvert to an inactive state and therefore viral suppression must be considered life long.

- Patients with cirrhosis are at high risk to develop hepatic decompensation if HBV reactivates and liver transaminases flair.

  For this reason it is recommended that all patients with chronic HBV and cirrhosis be treated.
- This includes patients with inactive disease and low levels of HBV DNA

- optimal treatment for a patient with cirrhosis and chronic HBV is an oral antiviral agent.

pregnant women

- If they are HBsurface antigen positive
- HBV DNA should be measured

and

- if this is greater than 200,000 IU/ml

Consider oral antiviral therapy at the start of the third trimester

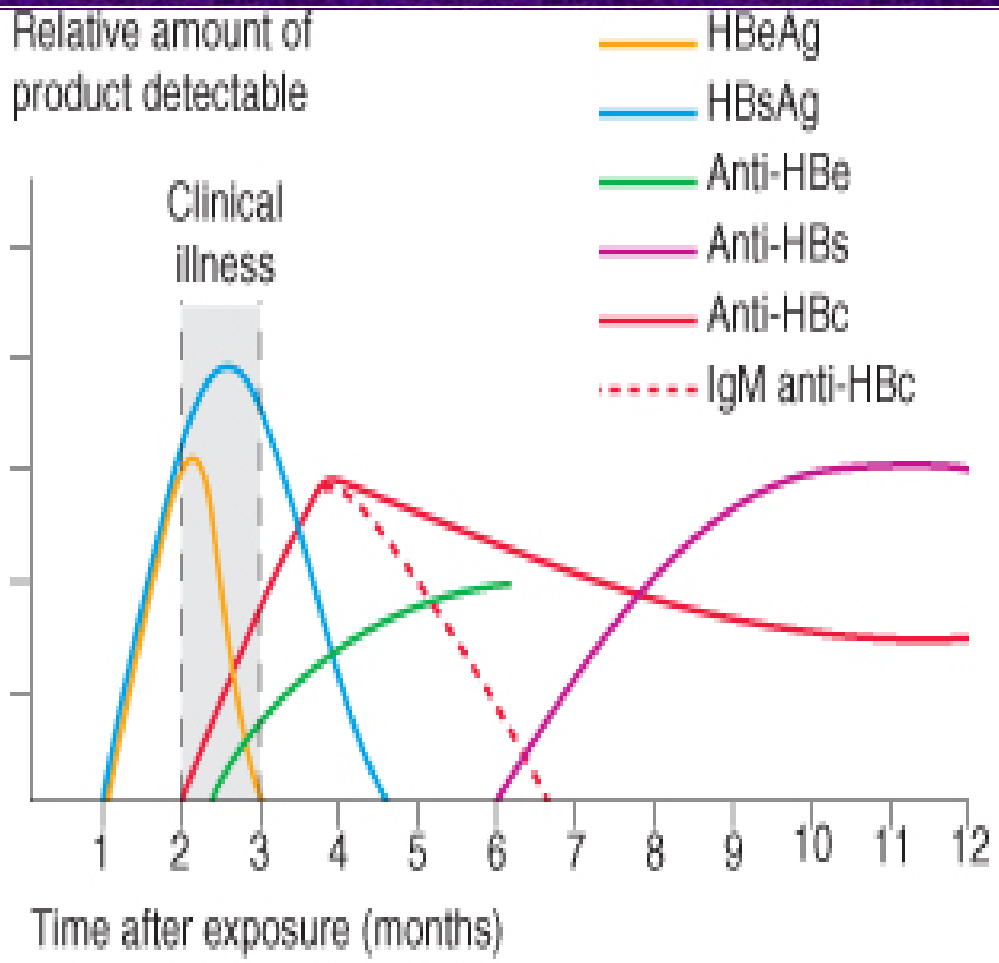
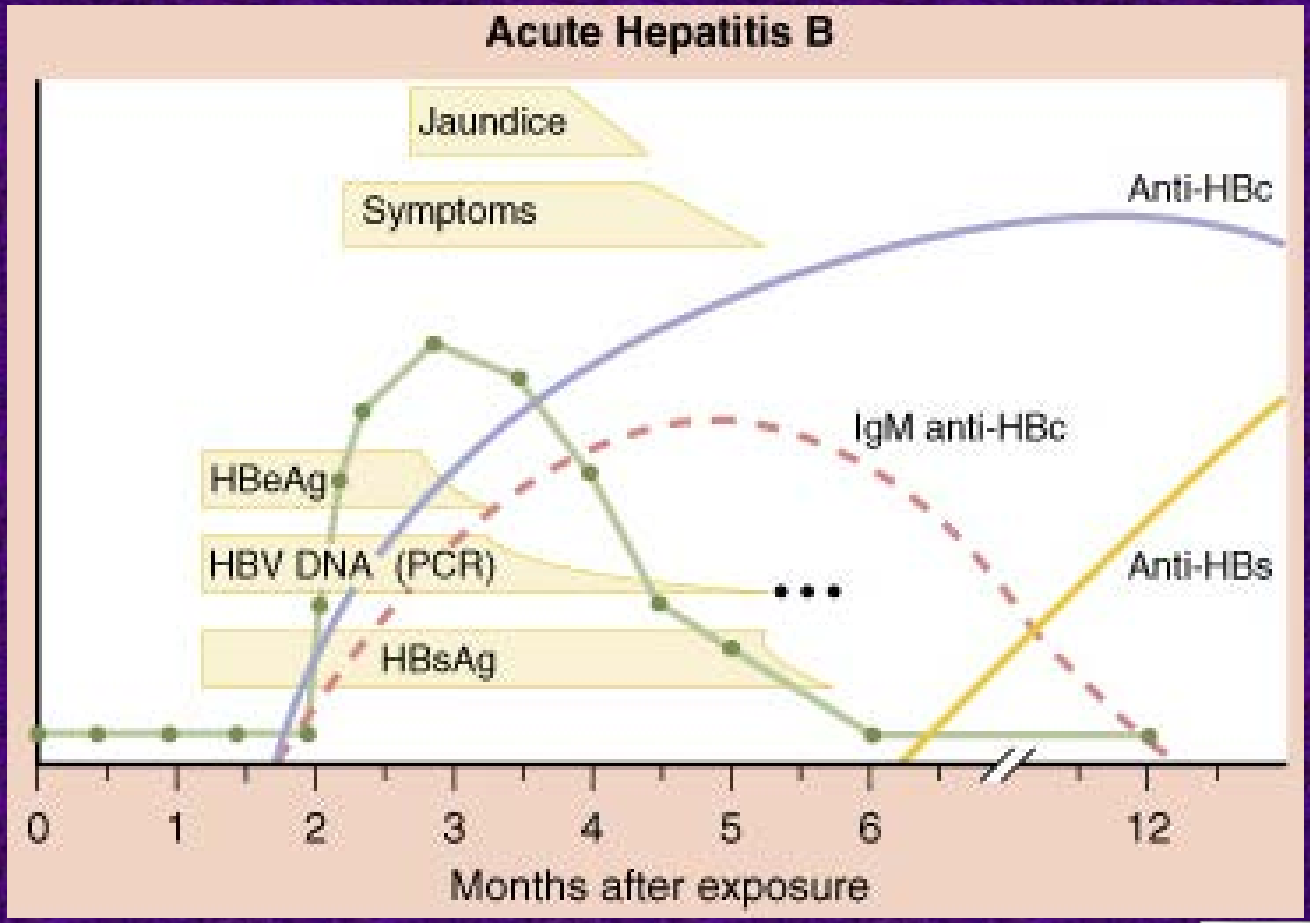


Figure 23.27 Serological responses to hepatitis B virus infection. (HBsAg = hepatitis B surface antigen; anti-HBs = antibody to HBsAg; HBeAg = hepatitis B e antigen; anti-HBe = antibody to HBeAg; anti-HBc = antibody to hepatitis B core antigen)

الاختبارات المصلية لالتهاب الكبد الفيروسي الحاد ب



المصلية لالتهاب الكبد الفيروس الاختبارات الحاد ب
SEROLOGY OF HBV INFECTION