شبکه تحقیقات بیماری های ویروسی ایران

مرکز تحقیقات ویروس شناسی بالینی
دانشگاه علوم پزشکی تهران

بررسی عفونت نهفته هپاتیت B در سیر بیماری مزمن؛ تعاریف و کنترل

دکتر سید محمد جزایری

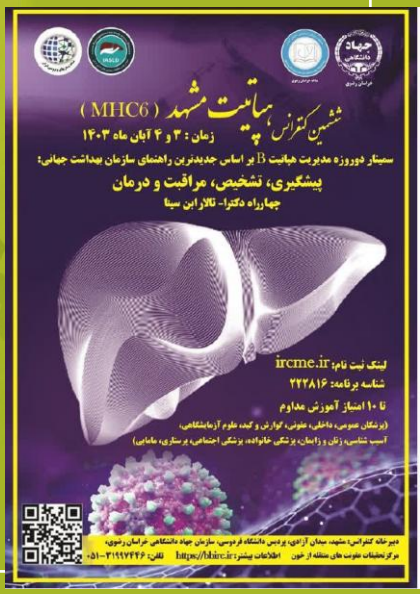
شبکه تحقیقات بیماریهای ویروسی ایران

مرکز تحقیقات ویروس شناسی بالینی

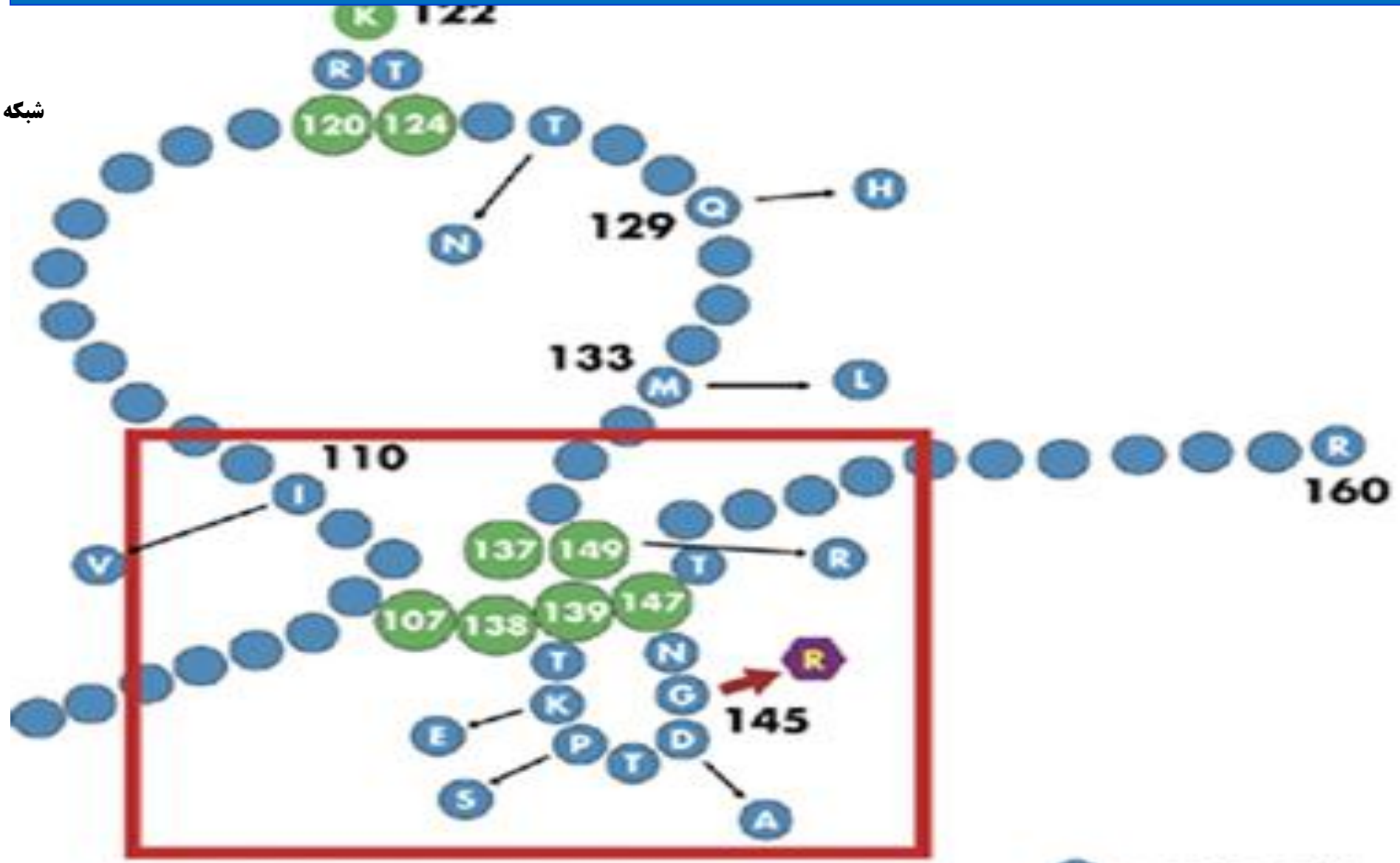
دانشگاه علوم پزشکی تهران

آبان ۱۴۰۳

مشهد



Proposed model of the major hydrophilic region (MHR) of HBsAg



"a" determinant

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Proposed tree-dimentional features of different HBsAg variants. Jazayeri 2t al, 2013.

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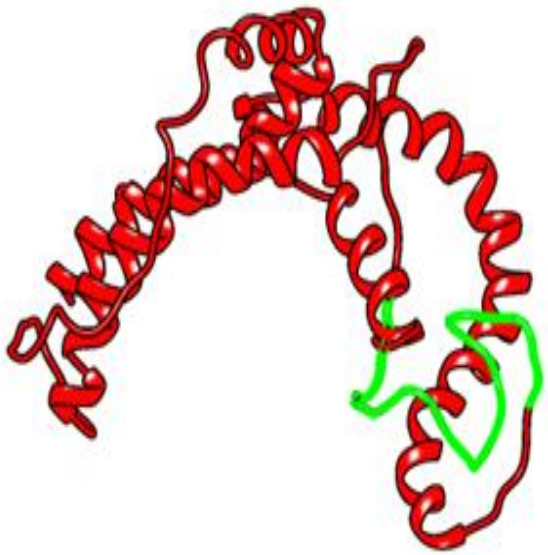
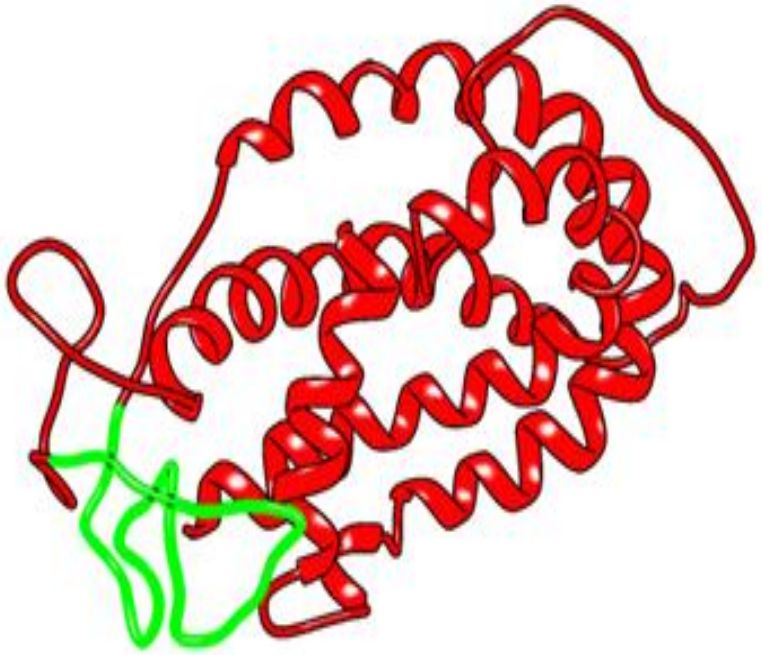
Wild type



Mutant (P127L)



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Occult HBV Infection (OBI)

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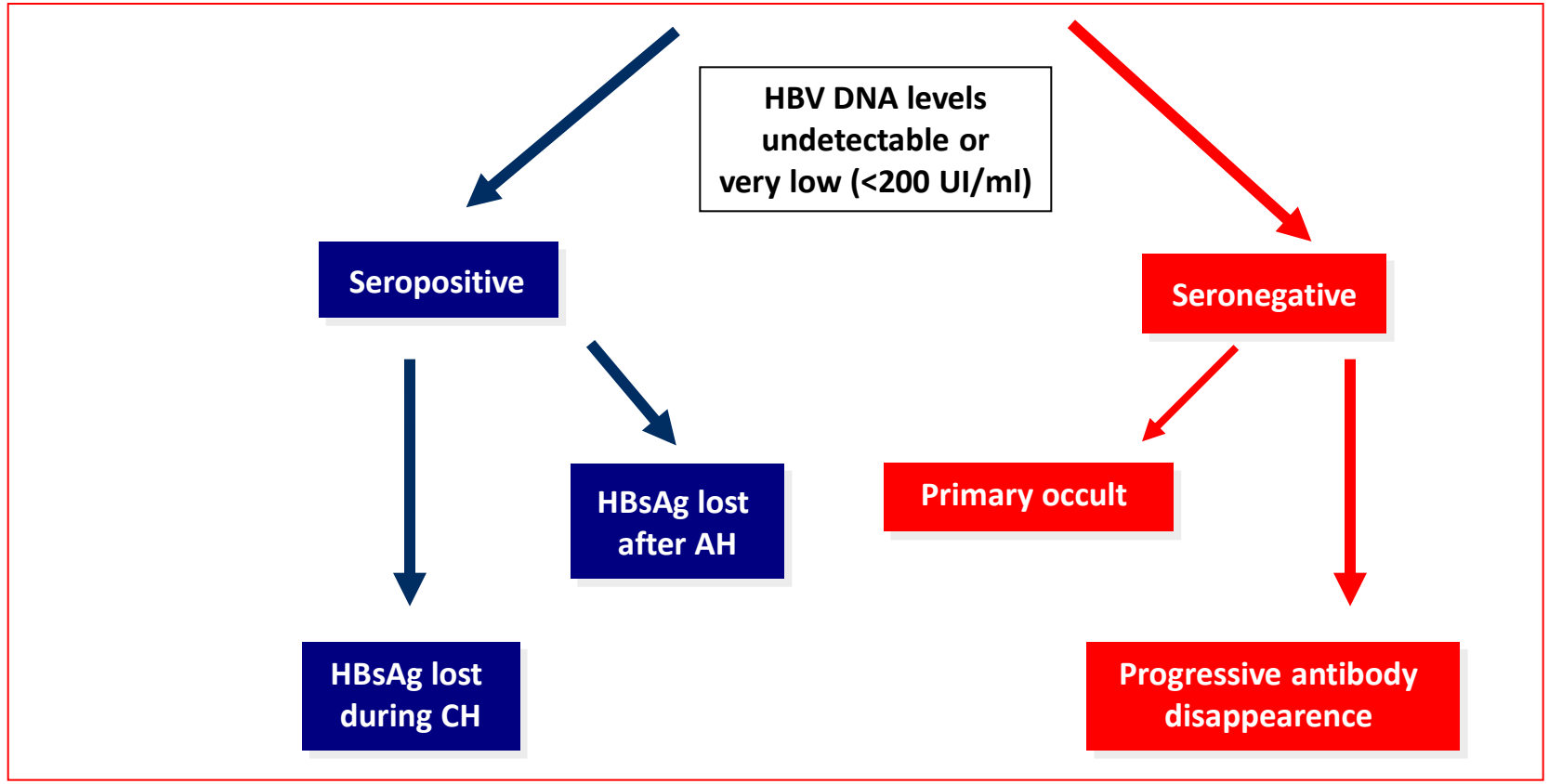
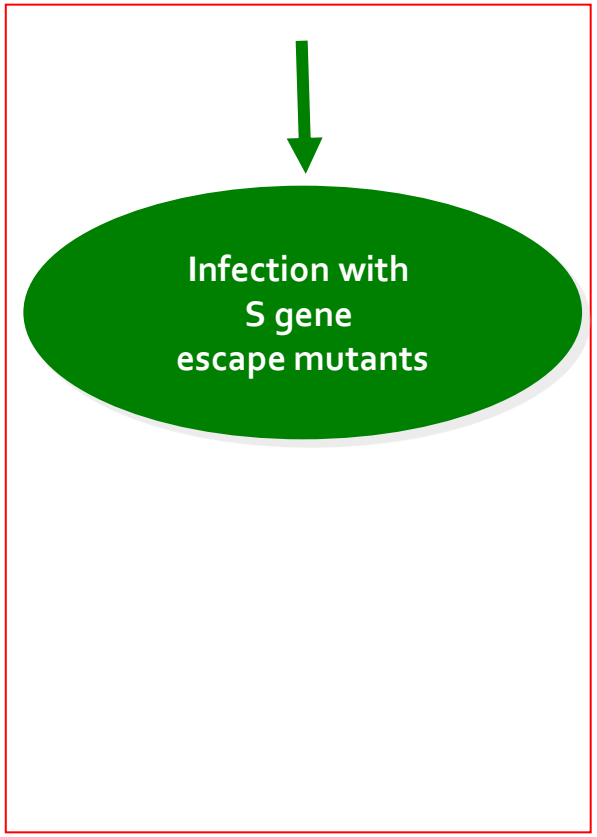
OBI



„false“ OBI



Reimondo et al, Taormina's statements on occult HBV infection. J Hepatol 2008

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A schematic phylogenetic tree showing the association of occult hepatitis B in different clinical settings . Jazayeri et al, .2012

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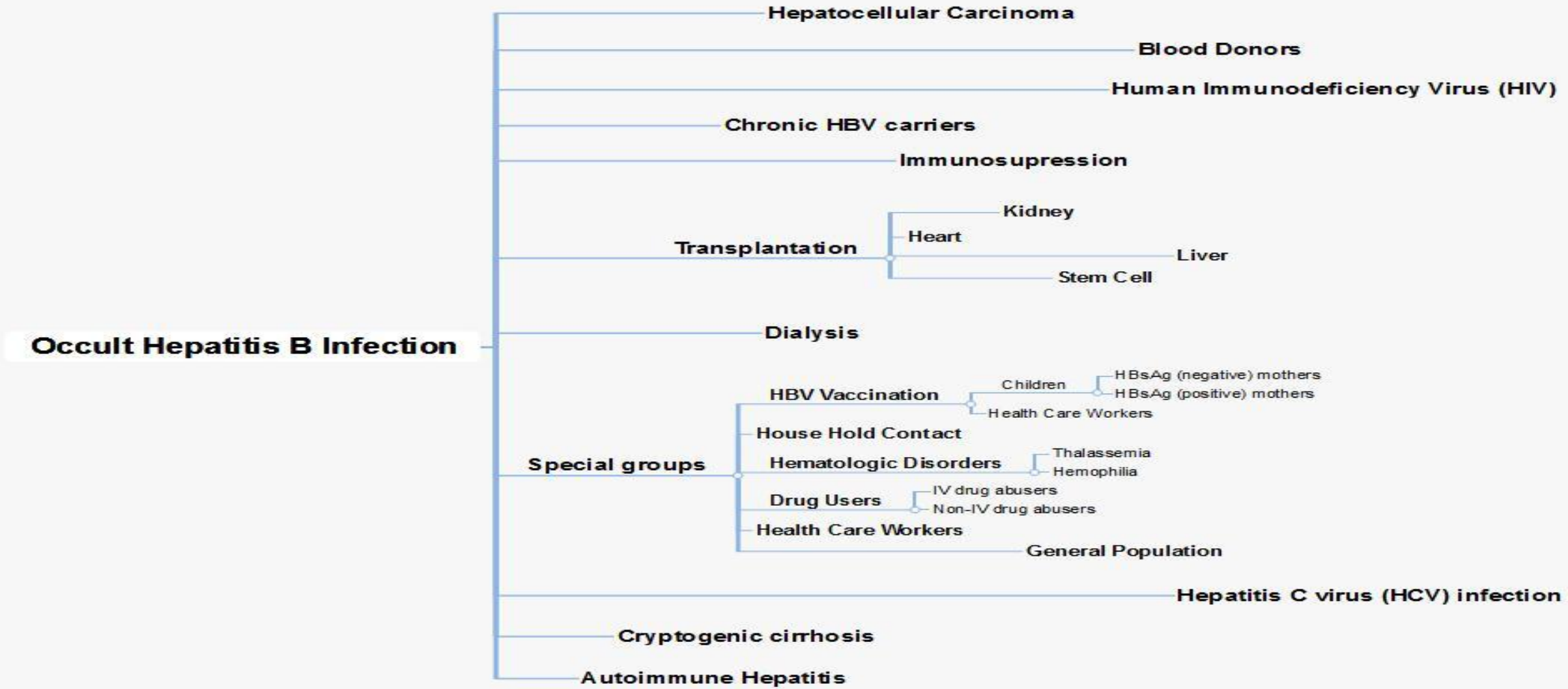

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Reported prevalence of OHB in different clinical settings. Jazayeri, 2012

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Clinical Setting	OHB Prevalence (%)
Blood Donors	0.05-13
HIV	0- 89
HCV	6.7-91,
HCC	12-80
Immunosuppression	3.3-37.8
Dialysis	0-58
Chronic HBV carriers	5-55
Cryptogenic cirrhosis	4.8-40
Transplantation	
Liver	36-64
Stem Cell	0-50
Kidney	0-3.3
HBV vaccinated	2.7-28
Family contact of HBsAg positive carriers	8.8- 28.8
General Healthy Population	0.7- 34
Haemophilia	5.3- 51.2

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WHO Definition

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- People who have cleared hepatitis B surface antigen: they are HBsAg negative but HBV DNA positive, although at very low levels (invariably <200 IU/mL); most are also total anti-HBc positive.

OBI Definition By WHO

- Occult HBV infection: defined as persistence of HBV DNA in the liver or serum among people for whom HBsAg is not detectable in the blood).
- People who have cleared HBsAg but are anti-HBc positive may reactivate if given potent immunosuppressive drugs.

OBI Risk Definition By WHO

- Subjects with occult infection are a potential source of new infections in blood transfusion services when HBsAg is used as the sole marker of infection in donor populations.

OBI Risk Definition By WHO

- HBV reactivation may occur spontaneously or may be triggered by cancer chemotherapy and other immunosuppressive therapy and may lead to fatal acute-on-chronic hepatitis, and pre-emptive nucleos(t)ide analogue therapy is therefore used.

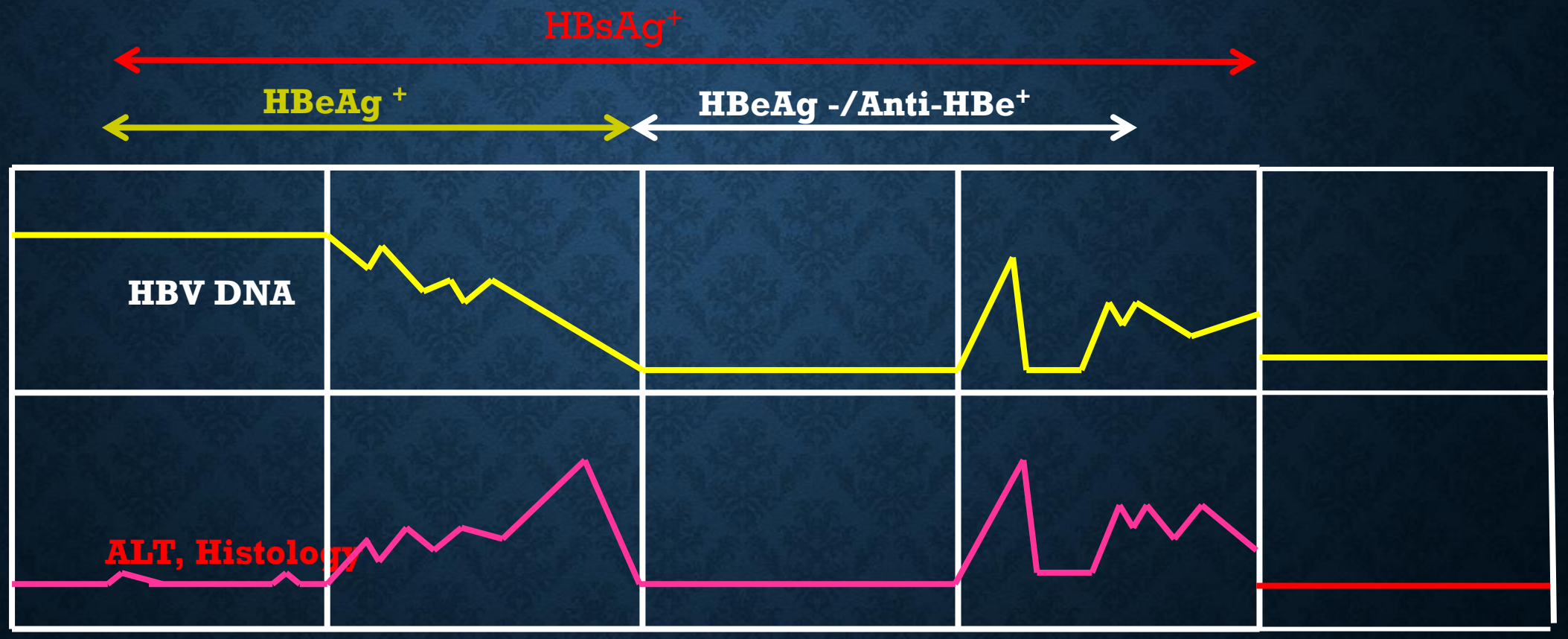
Nomenclature and biomarkers characteristic of the different phases of hepatitis B

Nomenclature		HBeAg-positive infection	HBeAg-positive disease	HBeAg-negative infection	HBeAg-negative disease	Grey zone	Occult hepatitis B
Other terms		Immune tolerant	Immune (re)active	Inactive carrier state	Immune-active or HBeAg-negative disease	Indeterminate	None
Serology	HBsAg	Positive	Positive	Positive	Positive	Positive	Negative
	Quantitative HBsAg	3.5–4.5 log10 IU/mL	3.5–4.5 log10 IU/mL	2.5–3.5 log10 IU/mL	2–3 log10 IU/mL	2–3 log10 IU/mL	Negative
	HBeAg	Positive	Positive	Negative	Negative	Negative	Negative
	Anti-HBe	Negative	Negative	Positive	Positive	Positive	May be positive
	HBV DNA	Typically >10^7 IU/mL	Typically >10^5 to 10^7 IU/mL	<10^3 IU/mL	Typically 10^3 to 10^5 IU/mL	3.3 log10 (2000 IU/mL) to 4.3 log10 (20 000 IU/mL)	Low at detection limit
Biochemistry	ALT	Around ULN	Raised	Around ULN	Raised	Fluctuate around ULN	Around ULN
Histology	Liver biopsy	Minimal necroinflammation or fibrosis	Moderate or severe necroinflammation and varying degrees of fibrosis	Minimal necroinflammation and fibrosis	Moderate to severe necroinflammation or fibrosis	Minimal or low necroinflammation	Usually minimal or low necroinflammation Fibrosis can be present
cccDNA+	(Assumed)	Relatively high copy number per cell	Relatively high copy number per cell	Low copy number or transcriptional activity	Lower copy number but transcriptional activity	Low number and transcription variable	Data uncertain
Integrated HBV DNA	Usually assumed	Present	Present	Present and account for majority of HBsAg	Present and account for majority of HBsAg	Present	Present
HBcrAg	Measured	High levels	High levels	Low or undetected	Lower levels	May be detected	Data not available
HBV RNA	Measured	High levels	High levels	Low or undetected	Lower levels	May be detected	Data not available

HBsAg ++++++++++++++++++++++++++++++++±

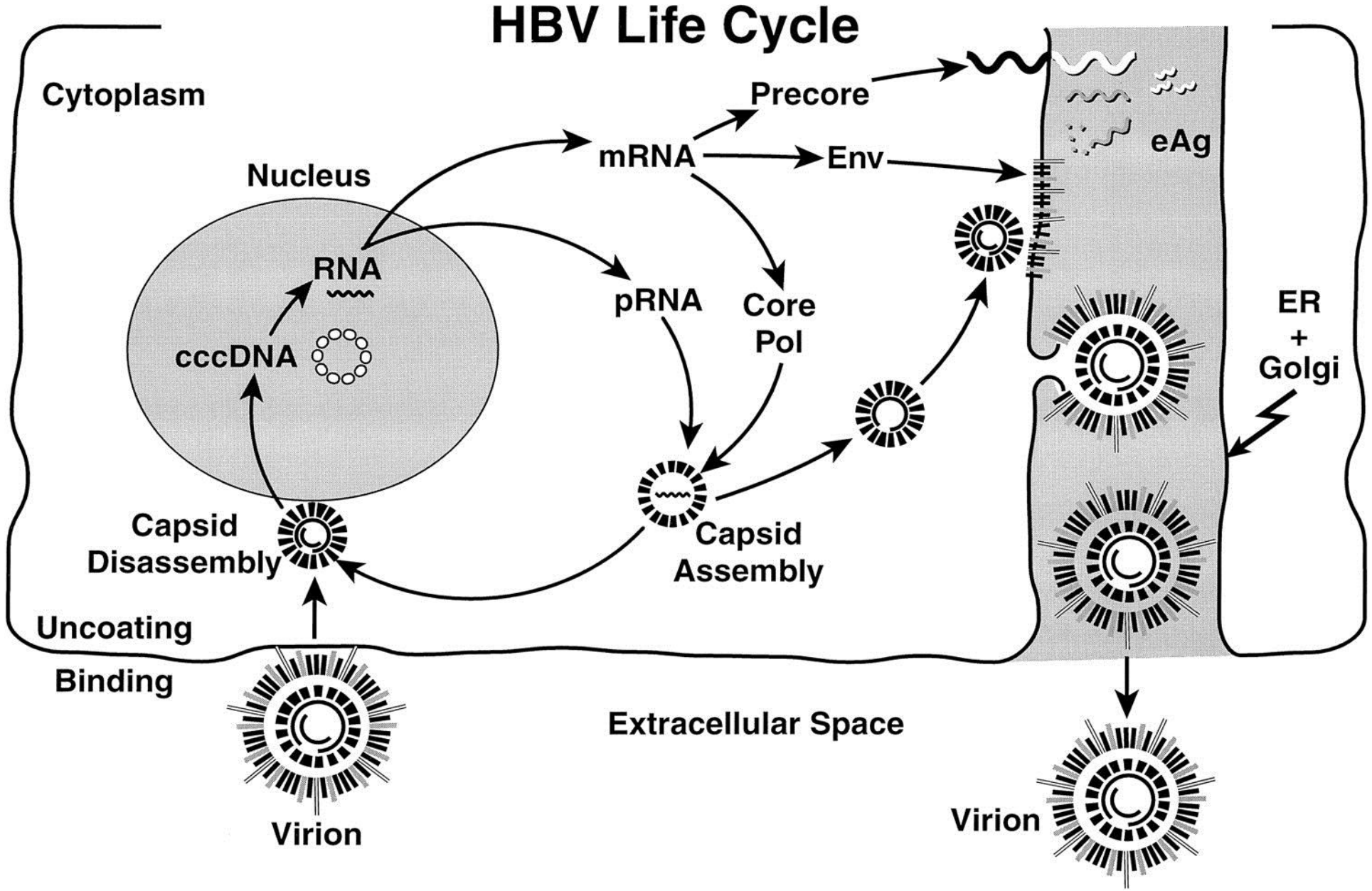
HBeAg ++++++++++++++++++++++++---±---±-----

Anti-HBe ----------++±++±+++



HBV Seroyeild

- Considerable difference between the release of viral structural proteins and the formation of full virions released in the circulation.
- Non-encapsidated viral DNA tends to be rapidly destroyed, whereas in the absence of anti-HBs, surface antigen produced by either infected cells or integrated viral genome may remain in circulation for prolonged periods of time.
- This can explain the presence of rare cases of detectable HBsAg without detectable HBV DNA in chronic HBV infection.


HBV Life Cycle
Cytoplasm
Nucleus
RNA
cccDNA
mRNA
Precore
Env
pRNA
Core
Pol
eAg
ER
+
Golgi
Capsid
Disassembly
Capsid
Assembly
Uncoating
Binding
Virion
Extracellular Space
Virion

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