

Hepatitis Screening Strategy and Interpretation of Laboratory Results

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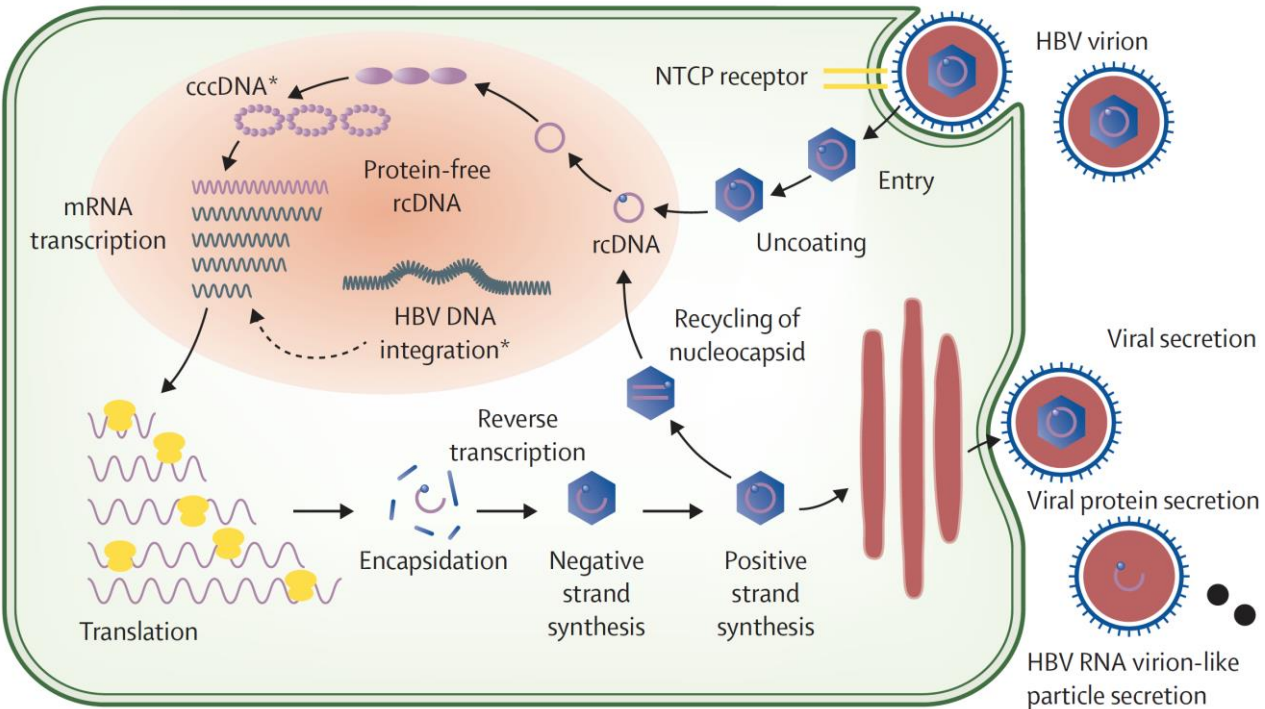
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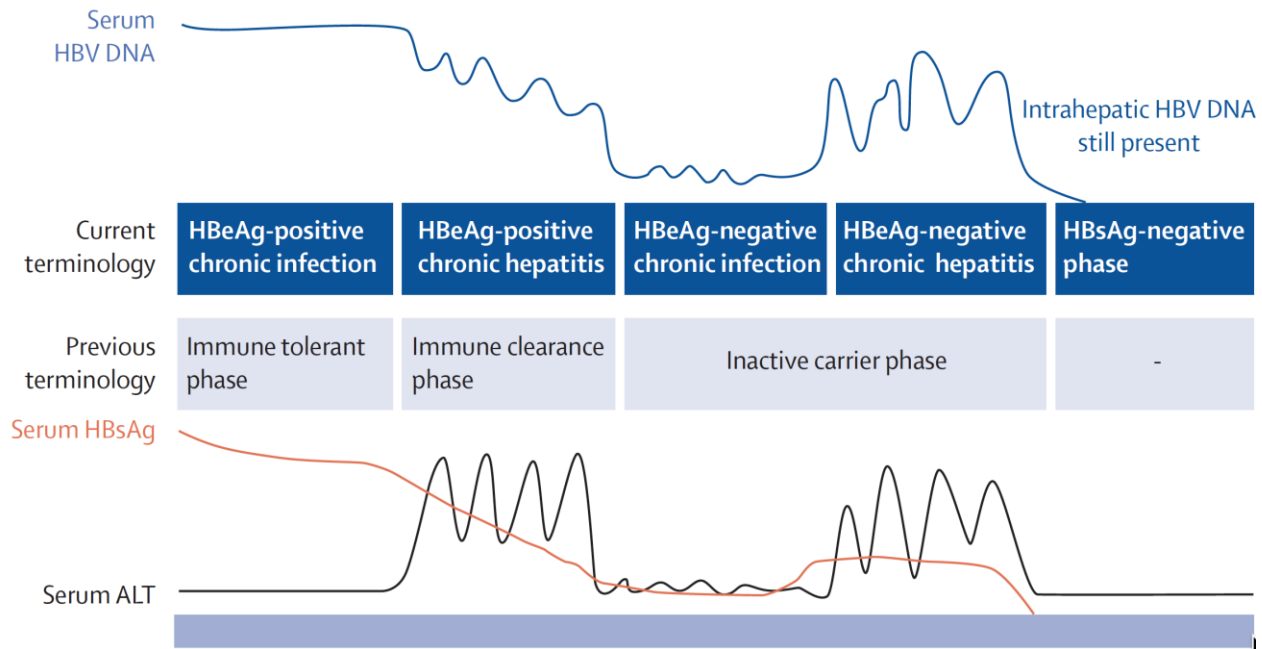
Understanding chronic hepatitis B disease

Chronic Hepatitis B Infection: Complex Disease

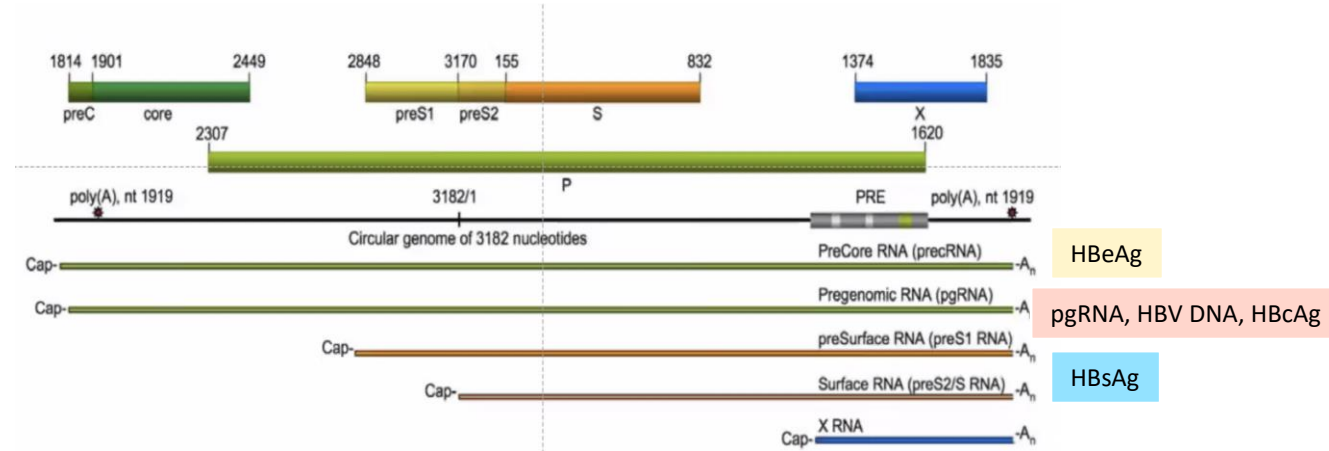
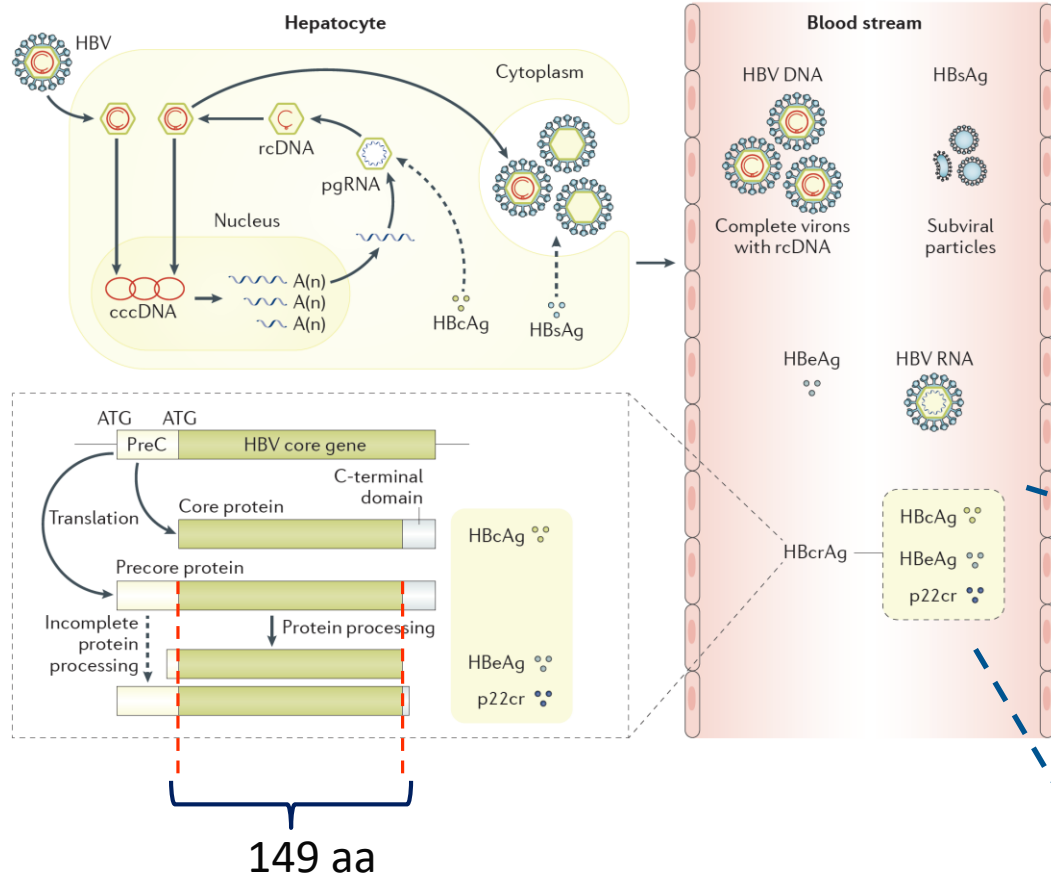
Complex Viral Life Cycle



Complex Disease Phase



Conventional and new serum biomarkers



Sommer G & Heise T. *Front Biosci* 2008;13:5533-47

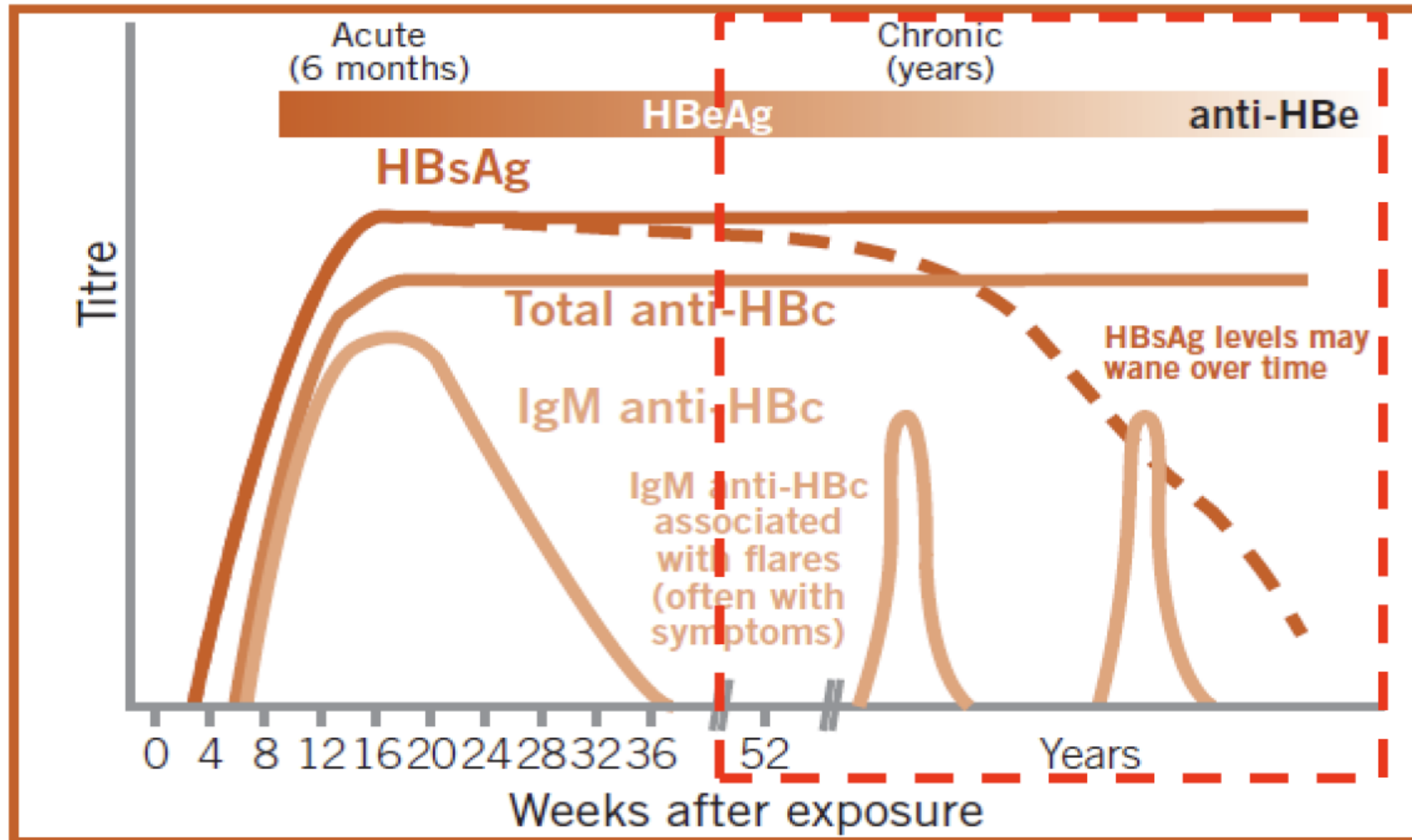


Yuen MF et al., *Nat Rev Dis Primers*. 2018;4:18035

Types of serological markers in blood

Antigen-antibody		Nucleic acid
Antigen	Antibody	
HBsAg (Hepatitis B surface A ntigen)	Anti-HBs (HB surface antibody)	HBV DNA (qualitative or quantitative)
HBcAg (Hepatitis B core A ntigen) Does not appears in blood	IgM anti-HBc (HB core antibody IgM)	
	Total anti-HBc (IgM plus IgG)	
HBeAg (Hepatitis B e A ntigen)	Anti-HBe (Hepatitis B e antibody)	

Serological profile of chronic HBV infection



Clinical interpretation of individual serological markers

Test	Clinical interpretation
HBsAg (hepatitis B surface antigen)	<p><u>Hallmark of infection</u> Positive in the early phase of acute infection and persists in chronic infection</p> <p>Quantification of HBsAg is a potential alternative marker of viraemia and it is also used to monitor the response to antiviral treatment</p>
Anti-HBc IgM (hepatitis B core antibody)	<p>IgM subclass of anti-HBc and observed during <u>acute infection</u> (used to differentiate between acute and chronic HBV infection)</p> <p>Might become positive during severe exacerbation of chronic infection</p>
Anti-HBc (total)	<p>Develops around 3 months after infection (most constant marker of infection)</p> <p>Total anti-HBc (IgM, IgA and IgG) indicates <u>resolved infection</u></p>
HBeAg (hepatitis B e antigen)	<p>Viral protein usually associated with <u>high viral load</u> and <u>high infectivity</u></p>
Anti-HBe (hepatitis B e antibody)	<p>Antibody to HBeAg usually indicates decreasing HBV DNA</p> <p>But present in the immune-control and immune-escape phases</p>
Anti-HBs (hepatitis B surface antibody)	<p>Neutralizing antibody that confers protection from infection</p> <p>Recovery from acute infection (with anti-HBc IgG)</p> <p>Immunity from vaccination</p>

Clinical interpretation of combination of serological markers

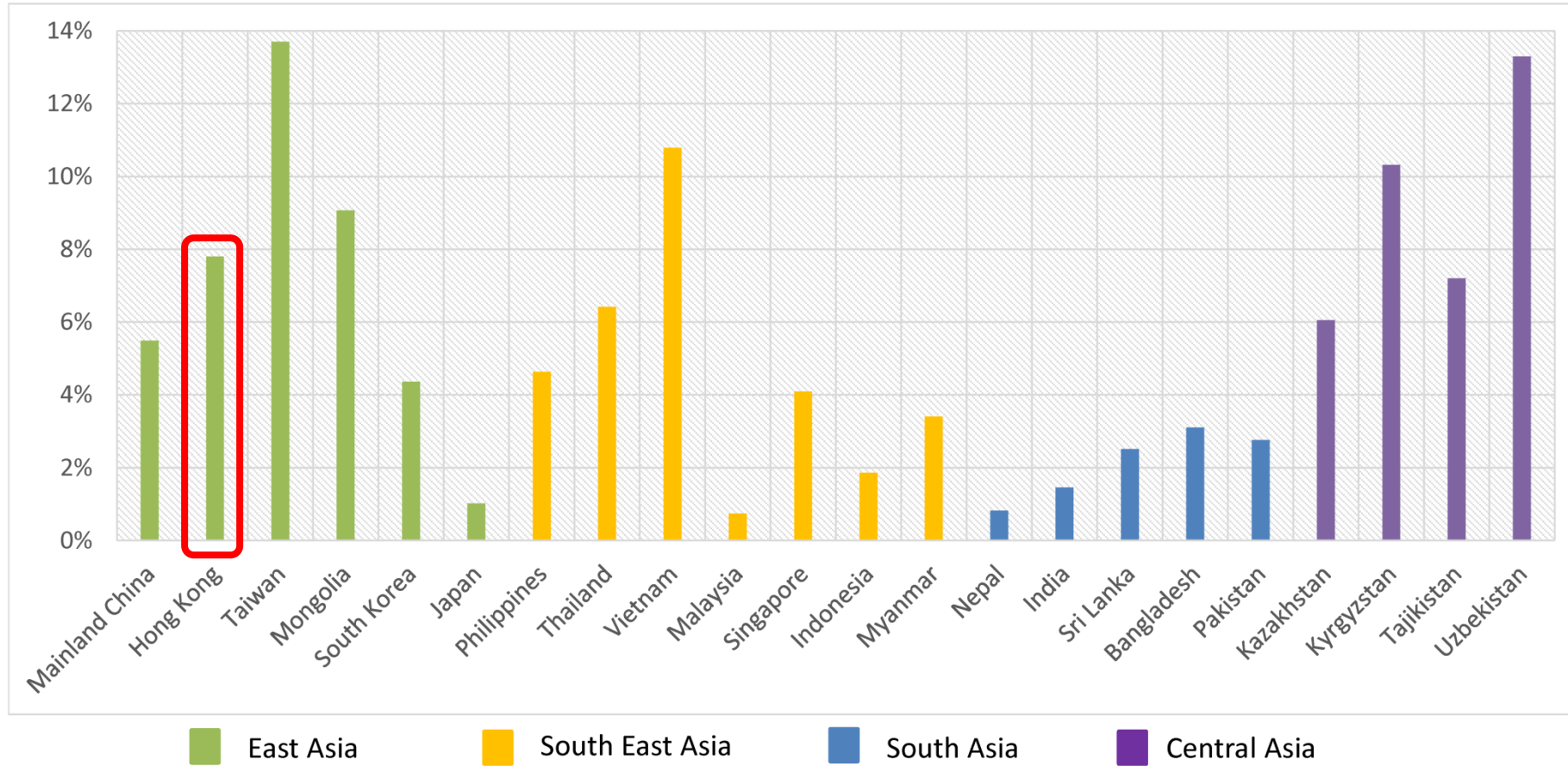
HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
-	-		-	Never exposed
-	+	-	+	Past natural infection, cleared, immunity achieved
-	+	-	-	Past natural infection, cleared, anti-HBs has waned over time
-	-	-	+	Immunity due to vaccination
-	+	+	+	Recent infection, recovered, immunity achieved
+	+	+	-	Acute infection, ongoing
+	+	-	-	Chronic infection (ongoing)

? Occult HBV
(Chronic HBV with
HBsAg seroclearance)

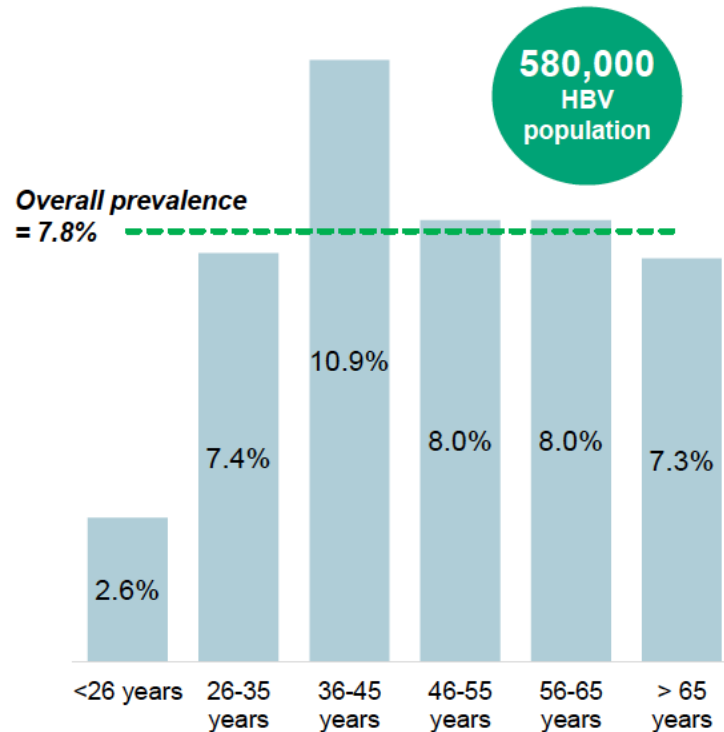
Chronic HBV with
acute exacerbation

- Additional & personal interpretations

Prevalence of CHB in Asia-Pacific Regions



HBV Prevalence by in Hong Kong by Age (n=10,256)

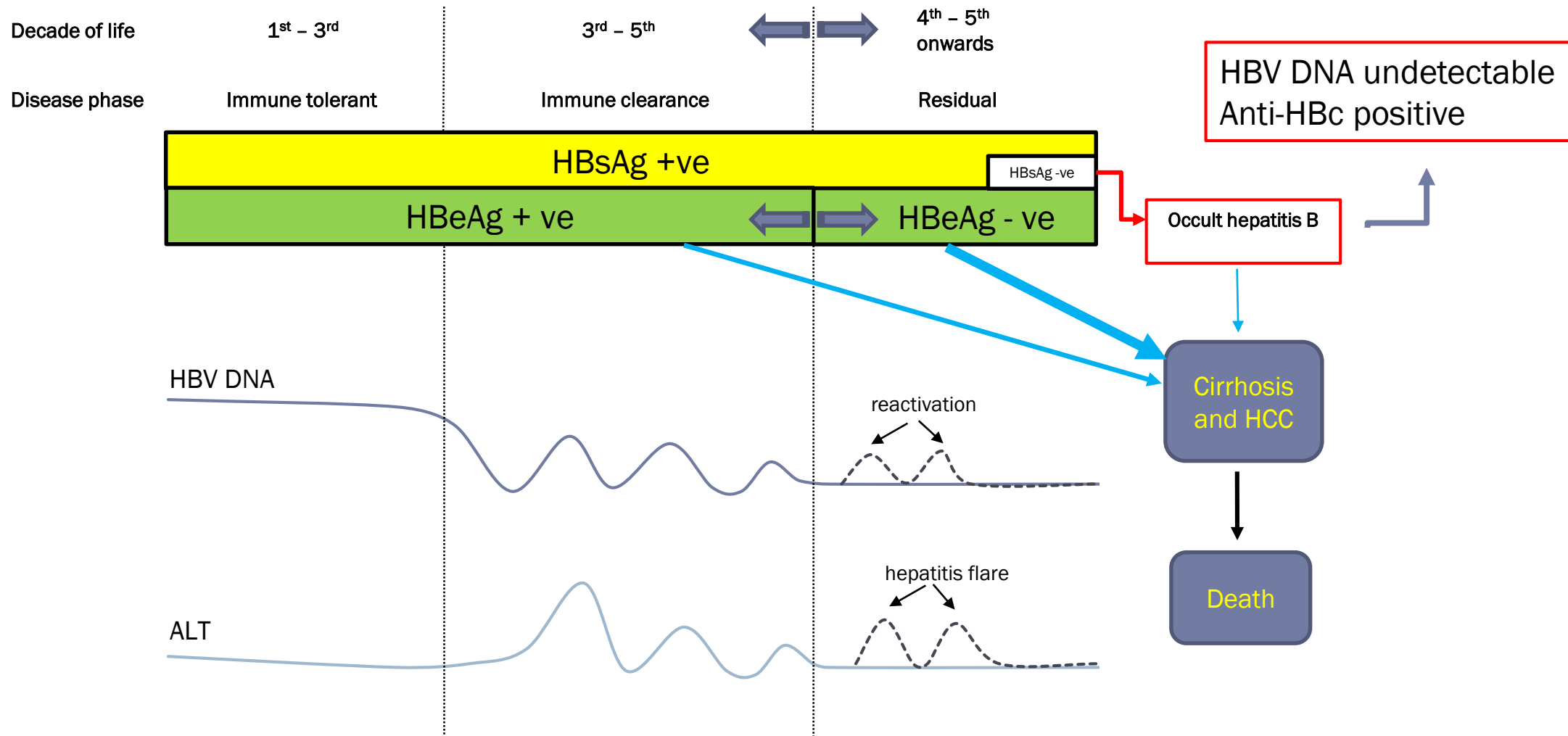


Universal HBV vaccination started in 1988

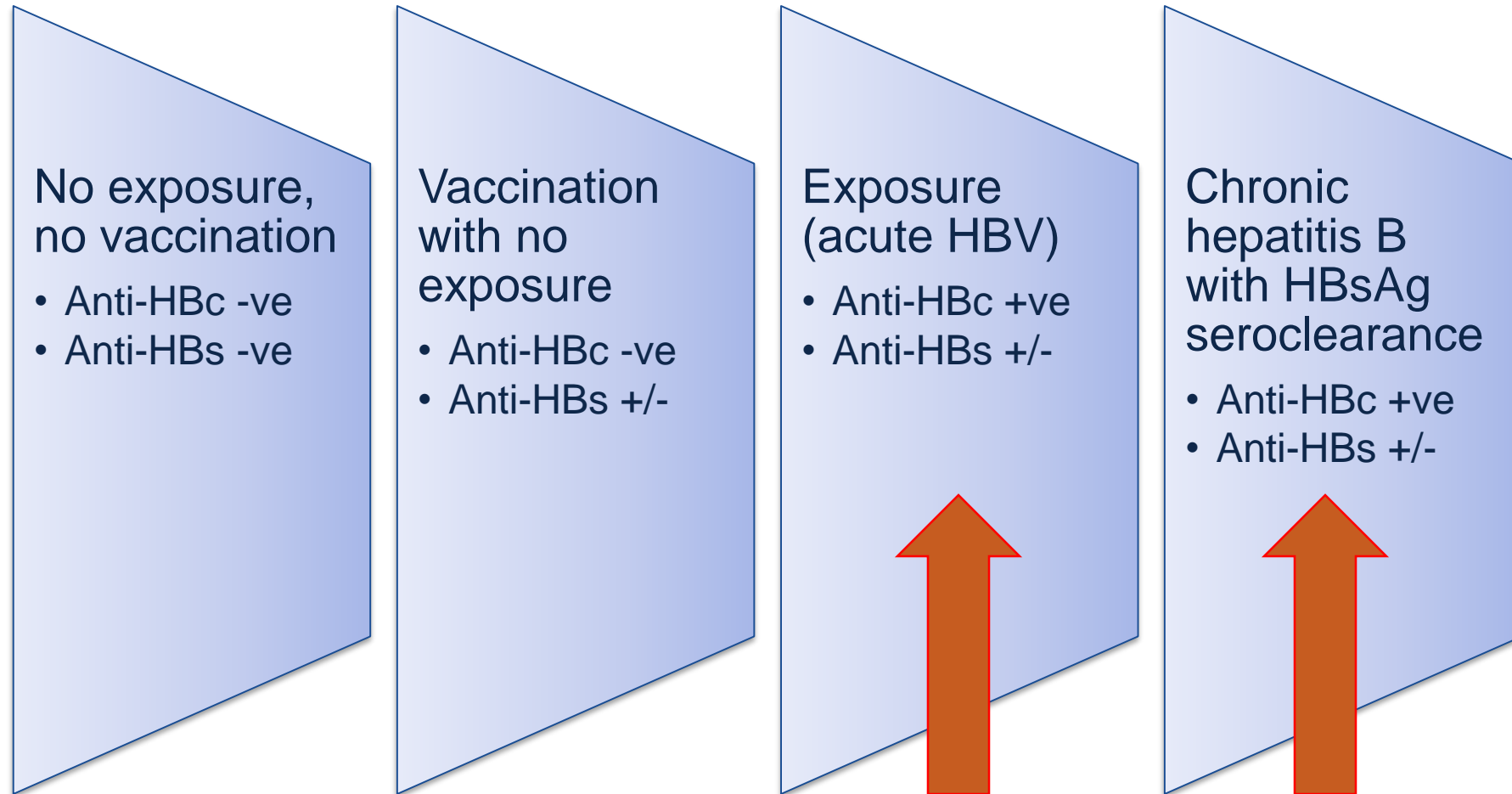
Participants born after 1988:

- HBsAg+ve rate:
 - 3.4%
- HBsAg+ve rate (born in HK):
 - 1.8%

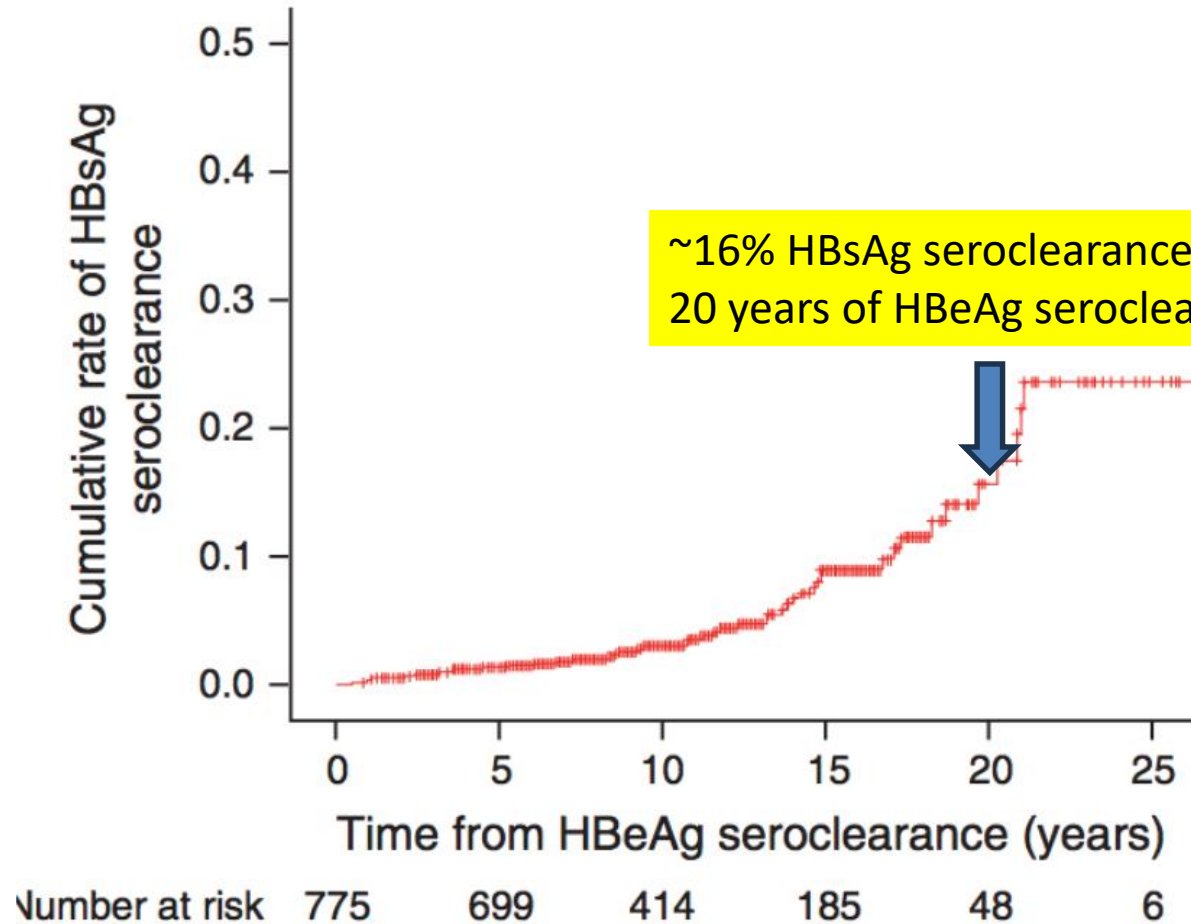
Occult HBV patients: CHB with HBsAg seroclearance



HBsAg –ve: significance of Anti-HBc and Anti-HBs



Cumulative rate of HBsAg seroclearance after HBeAg seroclearance



HBsAg Seroclearance: Intrahepatic viral status serum HBV DNA, liver biochemistry

298 patients with HBsAg seroclearance

Median age of HBsAg seroclearance: 49.6 years

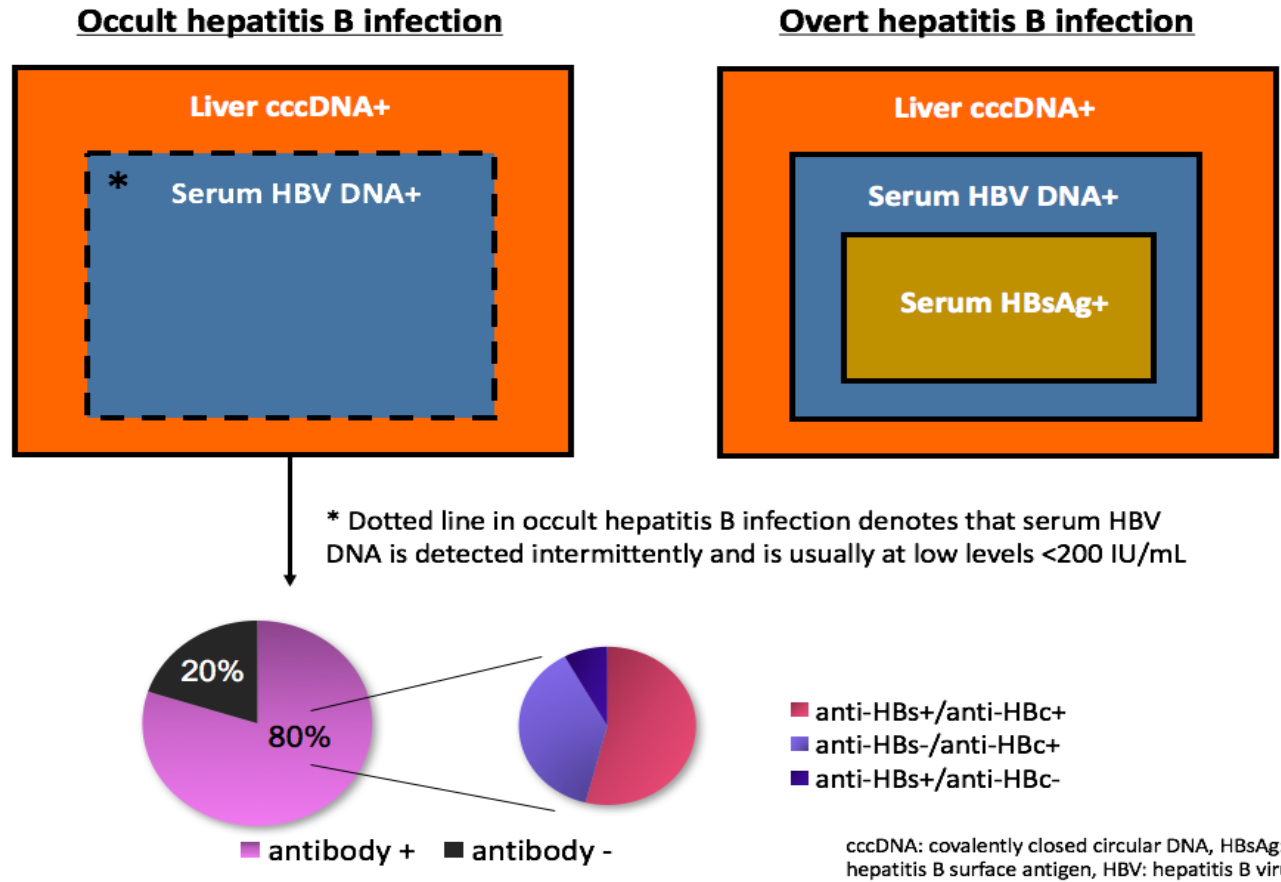
29 patients with liver biopsy: 100% had detectable HBV DNA,
79.3% had detectable cccDNA

Serum HBV DNA detectability with time after HBsAg
seroclearance

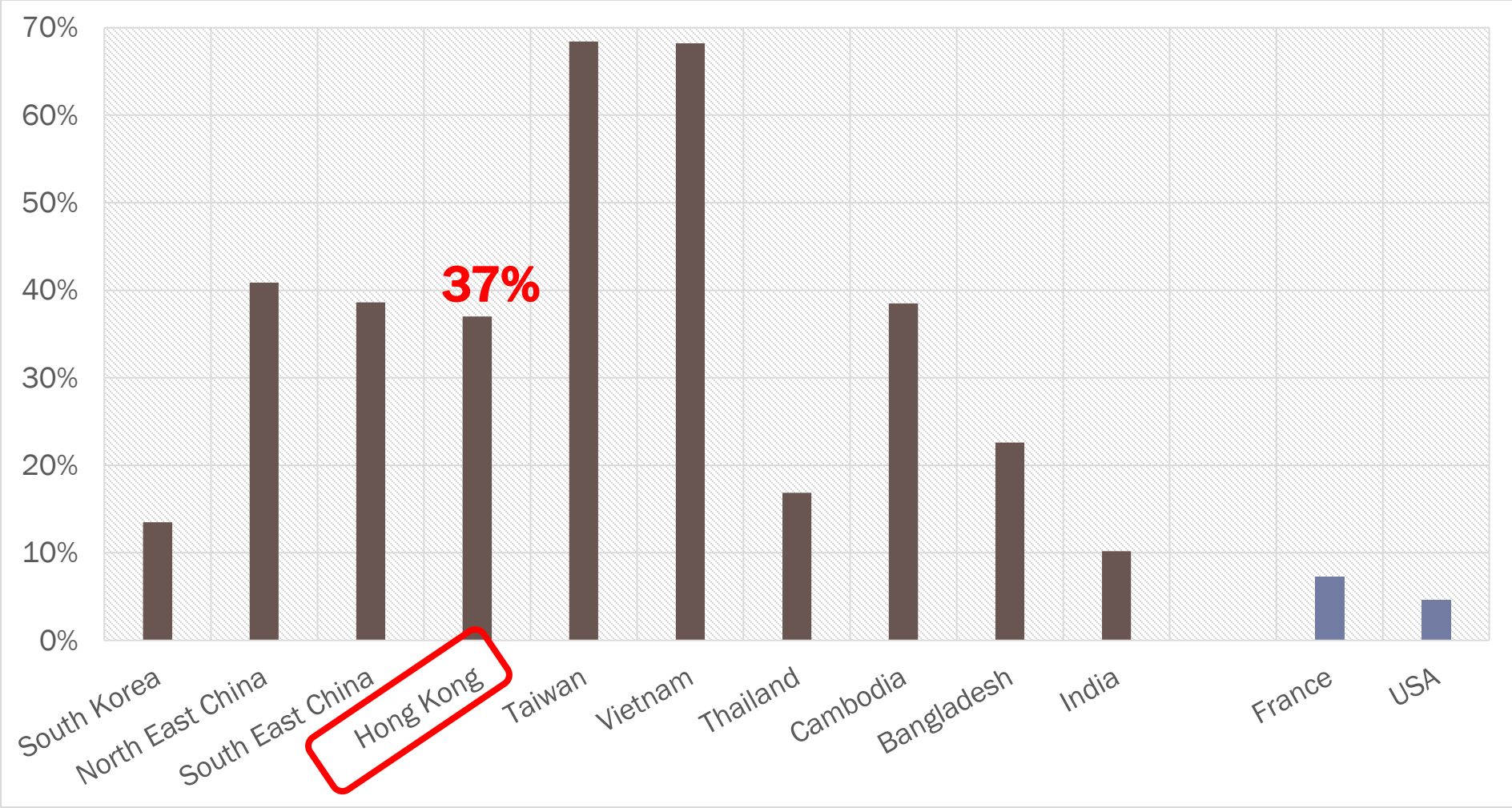
- × 1 yr: 13.4%
- × 5 – 10 yrs: 6.1%
- × >10 yrs: 3.7%

82% had normal ALT levels

Serology of occult HBV

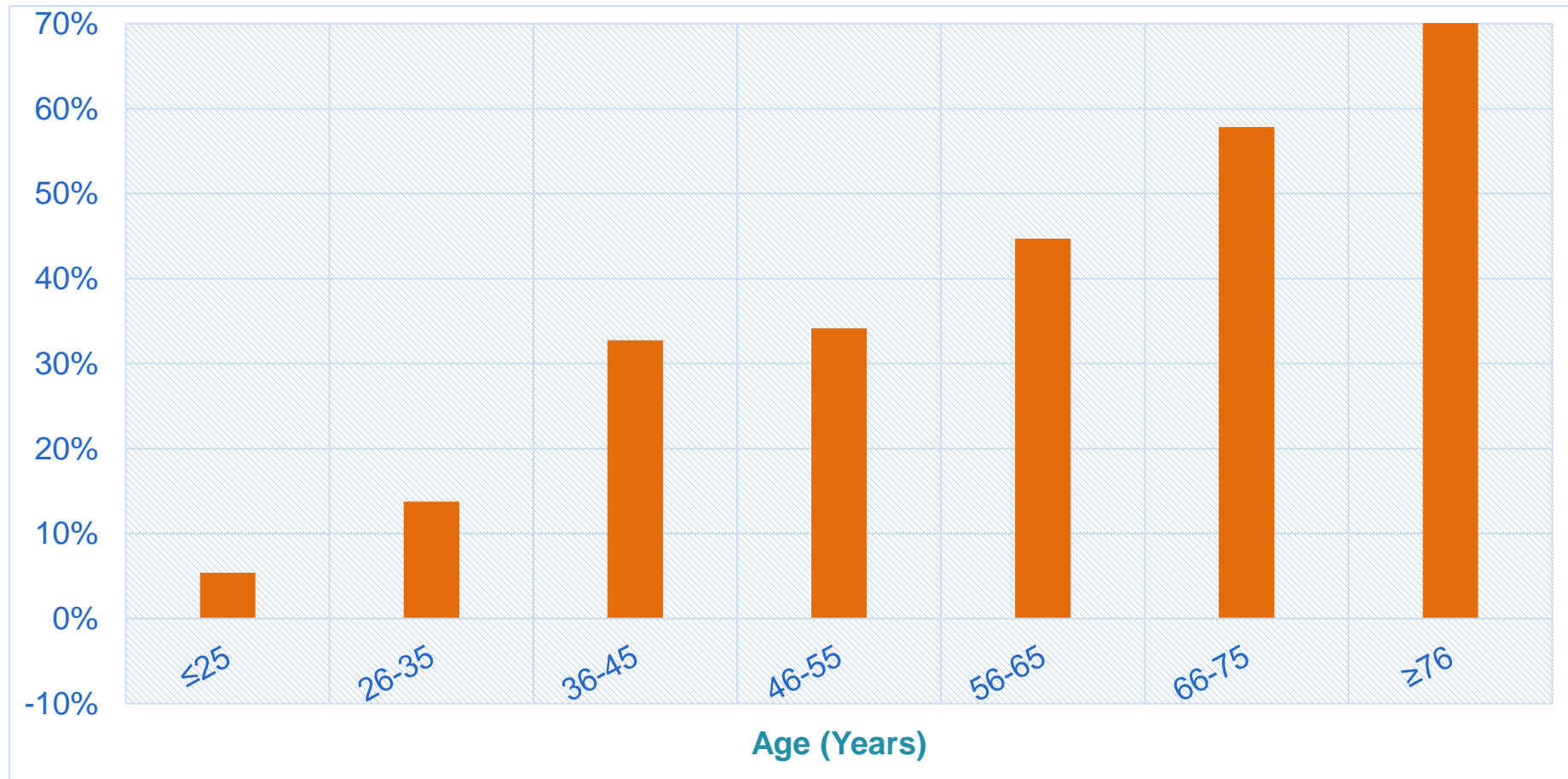


Prevalence of HBsAg -ve but anti-HBc +ve



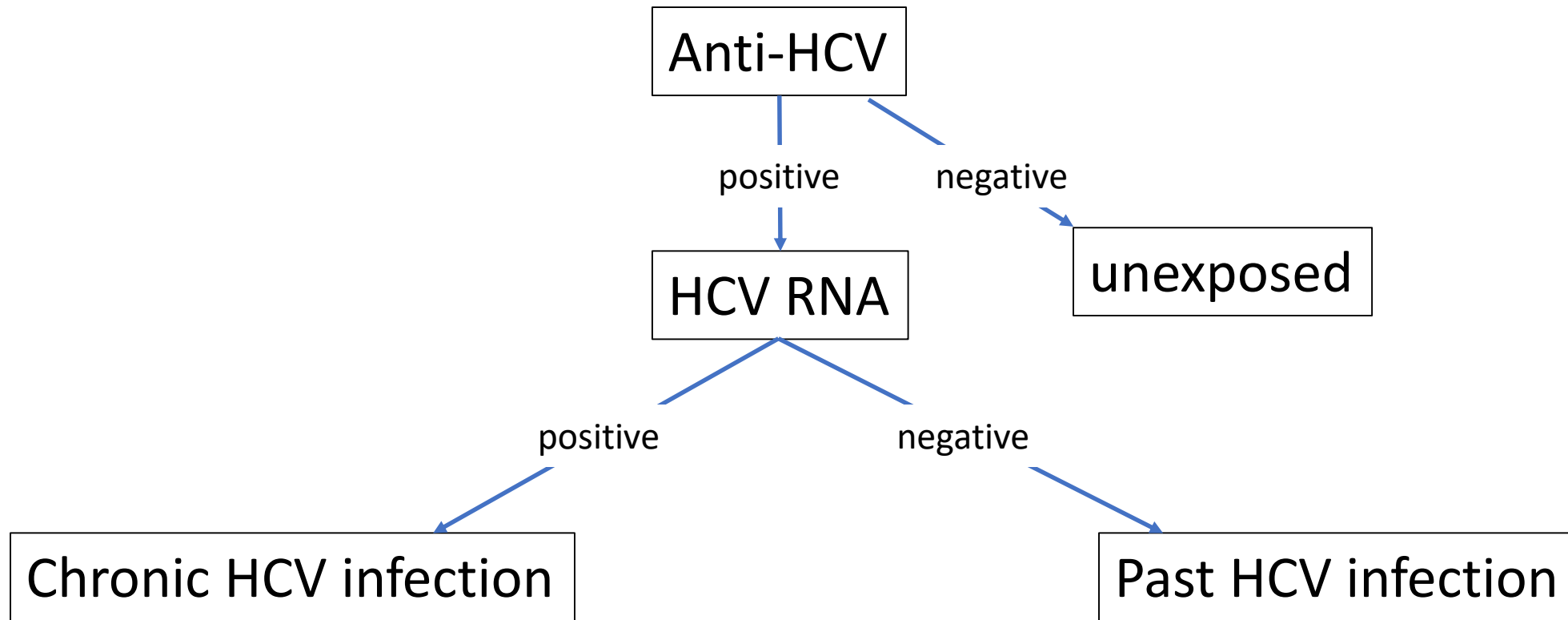
Seto WK, Yuen MF. HBV reactivation during immunosuppressive therapy. In Immunosuppressives: Advances, Applications and Analyses (2017) Nova Publishers

Seroprevalence of anti-HBc in Hong Kong by age



Chronic hepatitis C infection

- Simple diagnosis



Conclusions

- HBV remains to be a significant disease in Hong Kong
- Diagnoses of different HBV scenarios require combination of serological markers
- Although HBV prevalence rate by HBsAg testing is decreasing, entity of occult hepatitis B is increasingly recognized and should not be neglected
- Viral load (HBV DNA) is usually undetectable (or at extremely low detectable level intermittently) in occult hepatitis B
- HCV infection diagnosed by HCV RNA is simple (anti-HCV negative + HCV RNA positive is very uncommon except in immunocompromised patients)

Thank you