CPMC
Sutter Health
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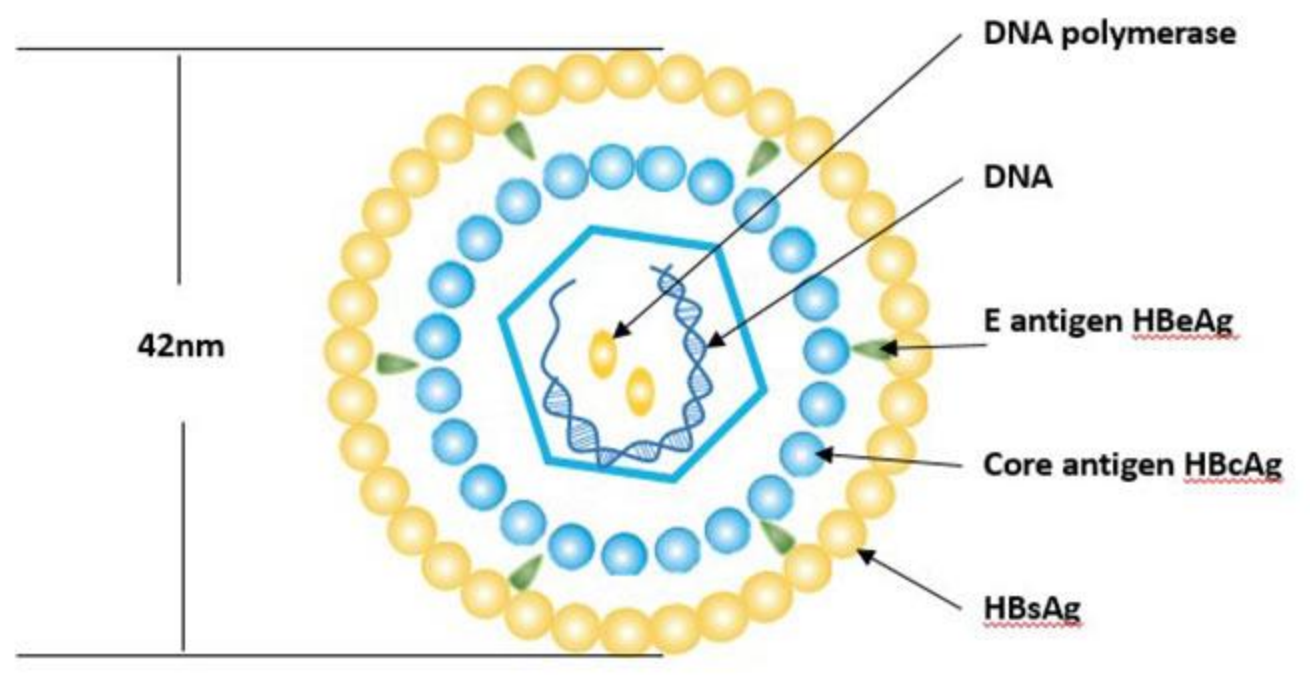
Division of Hepatology

HBV Nomenclature and the Phases of Chronic Infection



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HBV Nomenclature

- HBsAg – structural proteins embedded in viral lipid membrane, involved in cell binding & entry
- HBcAg – structural proteins, comprise the shell of the nucleocapsid that stores viral DNA & polymerase
- HBeAg – secreted, non-structural (not required for replication) protein that modulates host immunity
  - *We group CHB infection into 2 categories based on whether or not replicating virus is able to produce HBeAg.*

Eren et. al., Structure 2018

HBV Nomenclature

- HBcAb – immediate, nearly universal immune response after exposure to HBcAg in viable virions – has no implications for disease severity, control, prognosis, etc.
- HBeAb – made in response to HBeAg as immune system starts to bring HBV replication under control. Appearance of HBeAb = “seroconversion”.
- HBsAb – immune response to HBsAg signaling a much higher level of control of HBV replication. Usually a late-stage event in CHB (vs acute infection).

Eren et. al., Structure 2018

HBV Nomenclature

- A word about mutations…

How

- Pre-core mutation(s)
  - Causes early termination of eAg transcription leading to eAg-negative viral replication

- Basal core promoter mutation(s)
  - Reduces eAg production by up to 70% but increases viral genome replication and increases HCC risk

Tacke et. al., J Virol 2004

Phases of CHB Infection

1. CHB: requires HBsAg for 6 months
2. Immune tolerant: eAg positive, very high DNA, normal ALT, near-normal liver biopsy
3. Immune active: eAg and DNA variable, high ALT, active hepatitis on biopsy
4. eAg negative 'inactive': eAg negative, eAb positive, low ALT, low DNA, near-normal biopsy
5. eAg negative disease: eAg negative, eAb variable, high ALT, variable DNA, active biopsy
6. sAg clearance (resolved): sAg negative, sAb variable, ALT normal, DNA variable

Terrault et. al., Hepatology 2018.

Phases of CHB Infection

- 24 year-old male
- eAg+, eAb-
- DNA 8 logs
- ALT 20

- ***Immune tolerant***
- *Immune active*
- *Inactive*
- *eAg negative disease*
- *Resolved CHB*

Phases of CHB Infection

- 29 year-old male
- eAg+, eAb-
- DNA 7 logs
- ALT 120

- *Immune tolerant*
- ***Immune active***
- *Inactive*
- *eAg negative disease*
- *Resolved CHB*

Phases of CHB Infection

- 49 year-old female
- eAg-, eAb+
- DNA 1 log
- ALT 22

- *Immune tolerant*
- *Immune active*
- ***Inactive***
- *eAg negative disease*
- *Resolved CHB*

Phases of CHB Infection

- 49 year-old female
- eAg-, eAb+
- DNA 4 logs
- ALT 52

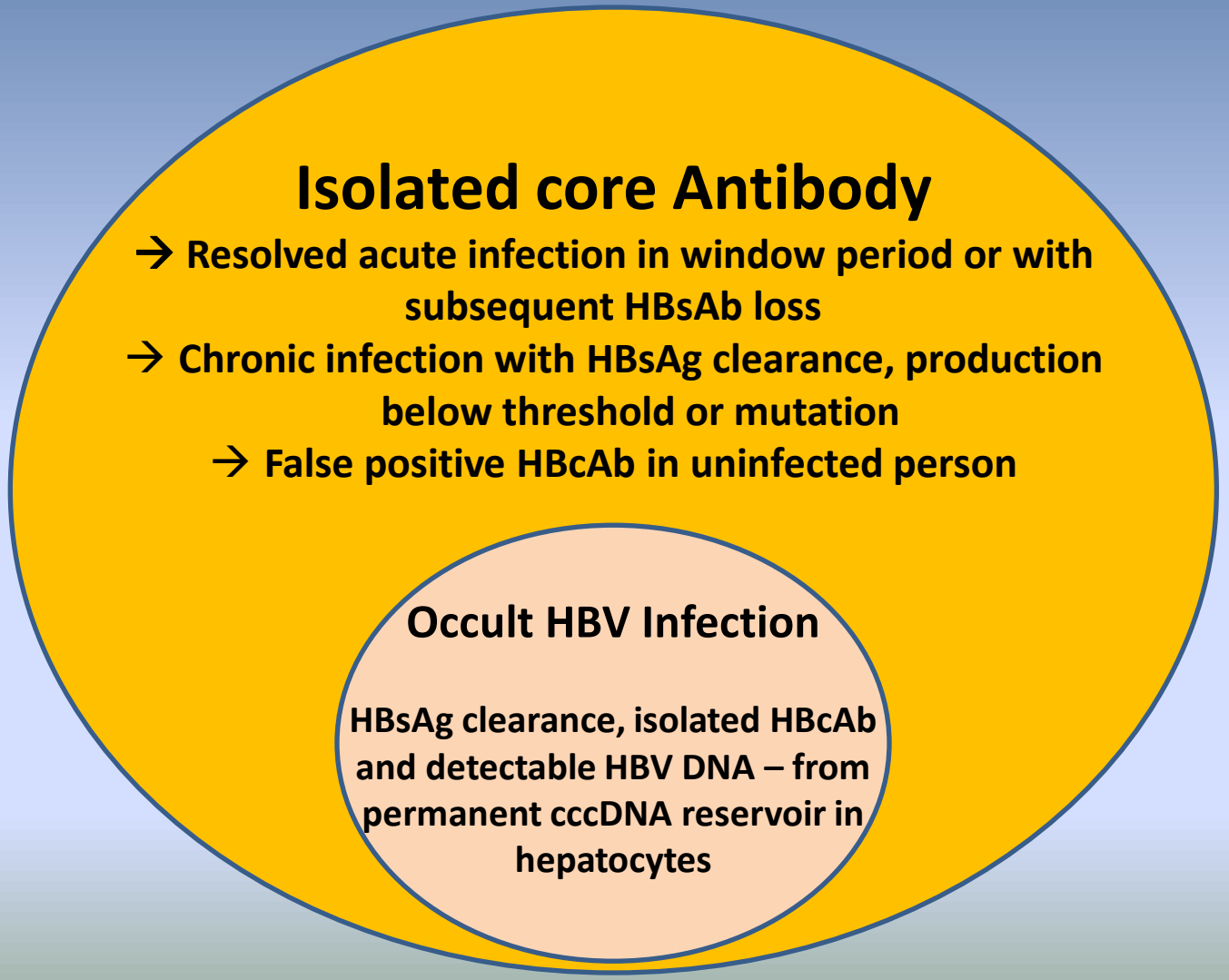
- *Immune tolerant*
- *Immune active*
- *Inactive*
- ***eAg negative disease***
- *Resolved CHB*

Phases of CHB Infection

- 79 year-old female
- sAg-, sAb-
- DNA 1 log
- ALT 22

- *Immune tolerant*
- *Immune active*
- *Inactive*
- *eAg negative disease*
- ***Resolved CHB***

HBV Nomenclature



HBV Nomenclature

- HBV “double negative” patients
  - Clearance of eAg-producing ‘wild type’ virus
  - Emergence of PC/BCM eAg-negative mutant
  - Absence of established immune response to eAg
  - Often in the setting of antiviral therapy
  - Low likelihood of successful treatment withdrawal
  - Higher risk of flare off of treatment?

Questions

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