



## NORTHWEST AIDS EDUCATION AND TRAINING CENTER

# Isolated Hepatitis B Core Antibody

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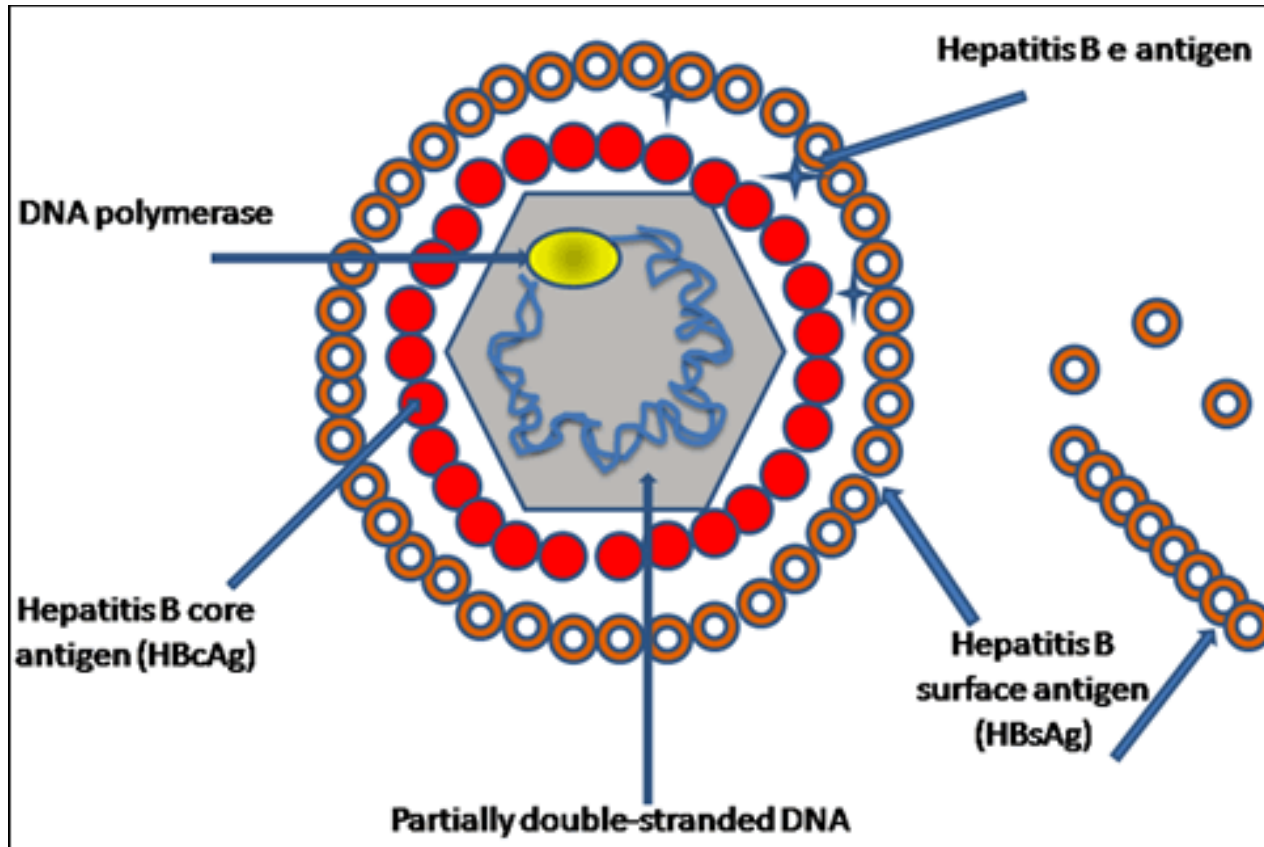
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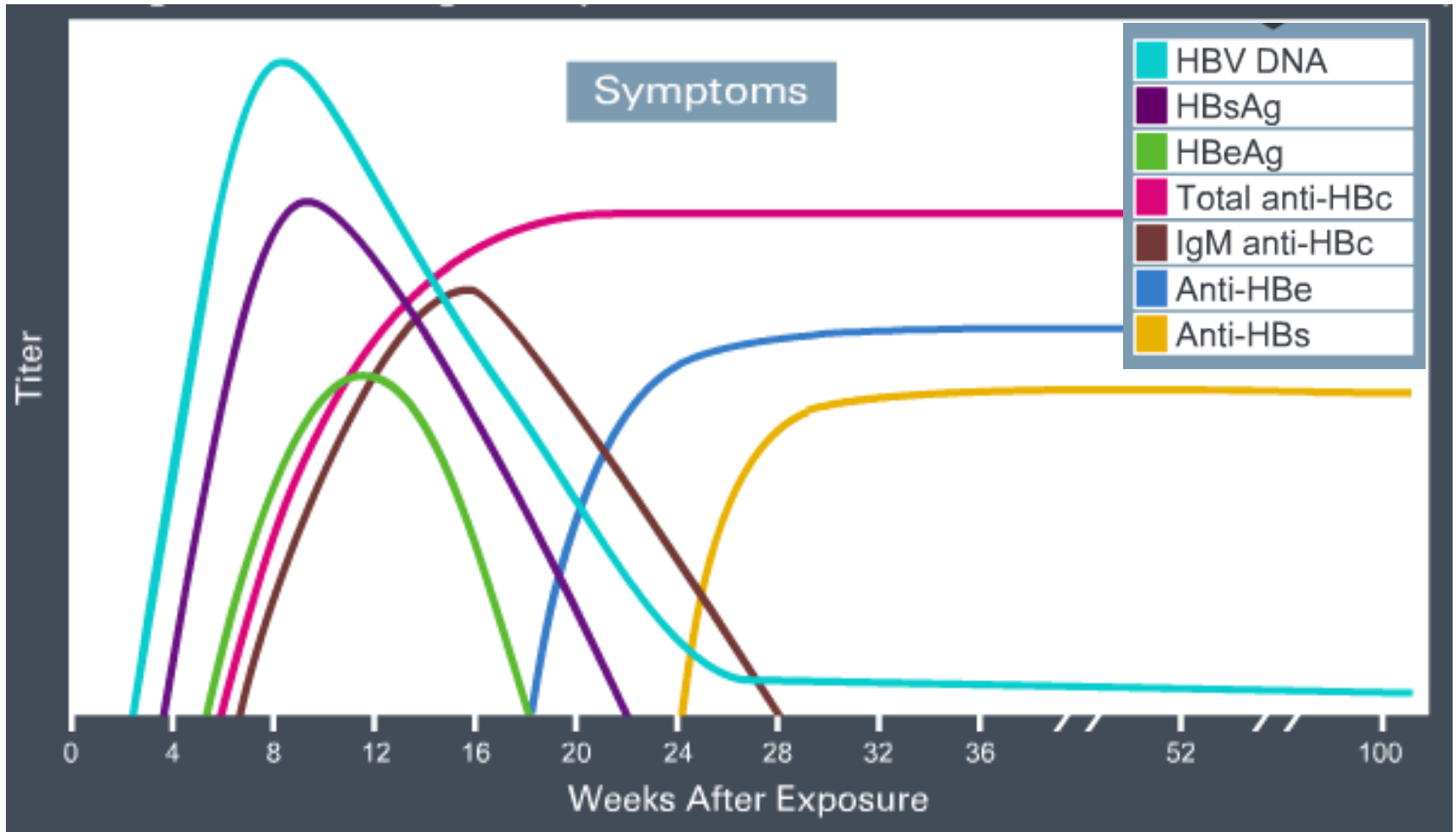
# Isolated Core Antibody

- Virology & terminology
- Definition & Risk Factors
- Scenarios where we see isolated anti-HBc
- HBV immunization in these patients
- Occult hepatitis B
- Clinical significance
- Practical considerations

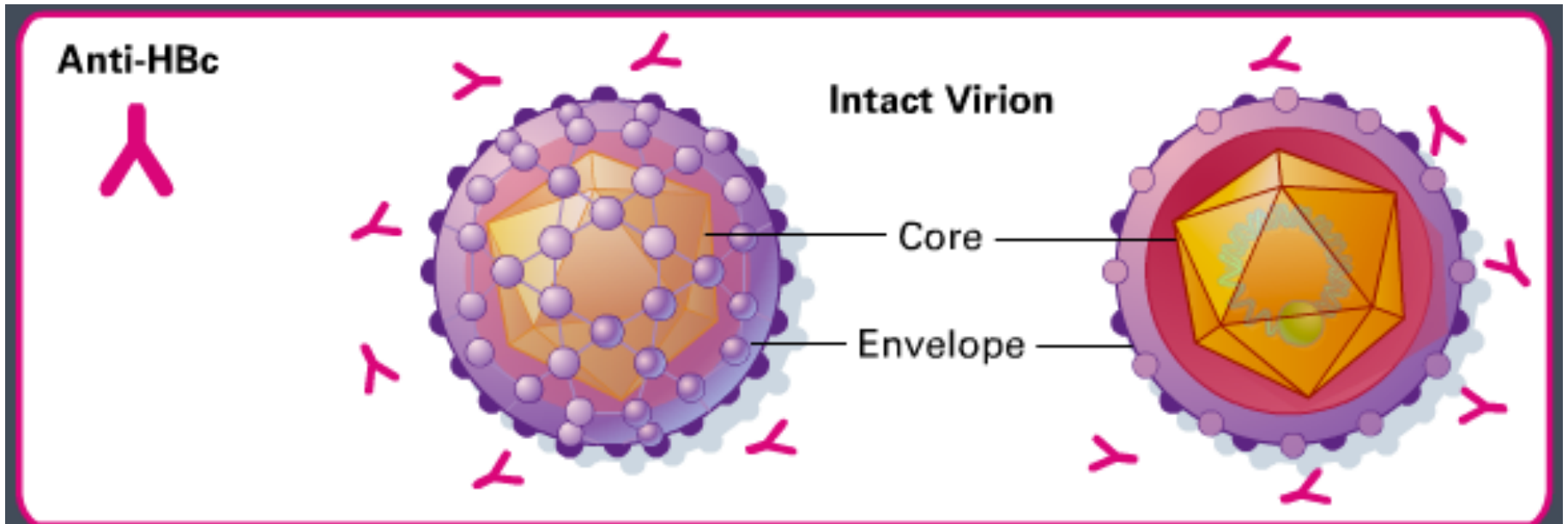
# Hepatitis B virus Terminology



# Virologic & Serologic Responses to HBV



# Core Antibody



**Anti-HBc does not react to the core of the intact virion since the core is completely surrounded by the envelope. Thus, anti-HBc does not play a direct role in controlling or preventing HBV infection.**

# Isolated Hepatitis B Core Antibody in HIV-infected Patients

- Definition: anti-HB core(+) but anti-HBs and HBs antigen negative
- Common profile – found in 20-45% in HIV-infected case series
- **Factors** associated with isolated core Ab:
  - HIV infection
  - Chronic hepatitis C infection
  - Older age
  - CD4 count <100 cells/mm<sup>3</sup>
  - Antiretroviral therapy: less likely to be isolated core

Gandhi, *J Infect Dis*. 2005;191:1435-41.

French, *J Infect Dis* 2007;195:1437-42.

Sun, *J Viral Hepat* 2010;17:578-87.

Witt, *Clin Infect Dis* 2013;56:606-12.

# Isolated Hepatitis B Core Antibody in HIV-infected Patients

- Seen in 1 of these 4 scenarios:
  - 1) “**Window phase**” of acute HBV infection between loss of HB surface antigen and emergence of anti-HB surface Ab;
  - 2) Remote **resolved HBV infection** with waning of anti-HB surface Ab to level <10 IU;
  - 3) Chronic infection, i.e. **occult HBV** with HB surface Ag that has escaped detection either due to low production or mutations in envelope protein;
  - 4) **False positive** → actually never exposed to HBV

Chakvetadze, *Clin Infect Dis*. 2010;50:1184-86.

Al-Mekhaizeem, *CMAJ*. 2001;165:1063-4.

Knoll, *World J Gastroenterol*. 2006;12:1255-60.

# Isolated Hepatitis B Core Antibody HBV Immunization

- Immunization can presumably help distinguish the latter 3 scenarios:

Scenario	Vaccine Response
Resolved HBV, waned sAb	Anamnestic response
Occult (chronic) HBV	No response
False positive	Primary response

- BUT most isolated core Ab patients do NOT mount an anamnestic response



# Isolated Hepatitis B Core Antibody HBV Immunization

Study	n/% Isolated Core	% Anamnestic	Predictors of Anamnestic Vaccine response
Gandhi <i>JID</i> 2005	45% (n=44)	24% (7/29)	Anti-HBe(+): 45% vs. 7%
Jongjirawisan <i>JAMT</i> 2006	20% (28/140)	7% (2/28)	
Chakvetadze, <i>CID</i> 2010	N=40	32.5% (13/40)	No baseline factors predictive. Among 7 nonresponders, only 1 had detectable HBV DNA
Kaech, <i>J Infect</i> 2012	12% (73/605)	22% (8/37)	Anti-HBe(+): OR 9.1, $p=0.06$

- Our experience at Madison Clinic: 46% (13/28) anamnestic after single 20 mcg dose of hep B vaccine.
- Anti-HBe(+) status not predictive of this response but appeared to be associated with higher titer of anti-HBs post-vaccination.
- Presence of anti-HBe infers prior HBV exposure & presence of immunologic memory → less likely isolated core is false(+)

# Isolated Hepatitis B Core Antibody Occult HBV Infection in HIV-infected Patients

- Defined by negative surface Ag, (+)HBV DNA level
- Generally not common – prevalence variable, depending on population & assays
  - More recent US-based case series: prevalence ranges from ~2-10% among isolated core pts
  - True prevalence may be underestimated because case series have been small with single time-point HBV measurement & some on HBV-active antivirals
- HBV viral levels detected typically low <1000 IU/mL range

Gandhi *JAIDS*. 2003;34:439-40.

French, *J Infect Dis* 2007;195:1437-42.

Knoll, *World J Gastroenterol*. 2006;12:1255-60.

Shire *JAIDS*. 2003;36:869-75.

# Isolated Hepatitis B Core Antibody Occult HBV Infection in HIV-infected Patients

Pei et al. *Virology Journal* 2014, **11**:9  
<http://www.virologyj.com/content/11/1/9>



VIROLOGY JOURNAL

**CASE REPORT**

**Open Access**

Spontaneous reactivation of hepatitis B virus replication in an HIV coinfecting patient with isolated anti-Hepatitis B core antibodies

Rongjuan Pei<sup>1,2\*</sup>, Sebastian Grund<sup>3</sup>, Jens Verheyen<sup>2</sup>, Stefan Esser<sup>4</sup>, Xinwen Chen<sup>1</sup> and Mengji Lu<sup>1,2</sup>

# Isolated Hepatitis B Core Antibody Clinical Significance

- Isolated core Ab appears to be a stable pattern over time in most (84%) individuals
  - If retested, still present (i.e. window phase or false positive unlikely)
  - If it changes at all, transitions to/from pattern of **natural immunity** (anti-HBs and anti-HBc positive)
  - Transition to/from chronic HBV infection (gain or loss of HBsAg) is rare
- Not consistently associated with:
  - ALT/AST elevations (independent of HCV coinfection)
  - Liver stiffness by FibroScan (independent of HCV coinfection)

Witt, *Clin Infect Dis* 2013;56:606-12.

Perez-Rodriguez, *World J Gastroenterol.* 2009;15:1237-41.

Knoll, *World J Gastroenterol.* 2006;12:1255-60.

Chakvetadze, *Med Mal Infect.* 2013;43:222-5.

# Practical Considerations

## What Do the Guidelines Say?

- **DHHS 2014 OI Guidelines:**

“Some specialists recommend that HIV-infected individuals with anti-HBc alone be tested for HBV DNA. If positive for HBV DNA they should be treated as chronically infected; if negative they should be considered still susceptible to HBV and vaccinated accordingly.”

- **HIVMA 2014 Primary Care Guidelines:**

“Patients who are negative for HBsAg and HBsAb but positive for anti-HBc should be screened for chronic HBV infection by determination of HBV DNA; those without evidence of chronic infection should consider vaccination (strong recommendation, low quality evidence).”

# Practical Considerations

## Expert Opinion

- **Screen Isolated anti-HBc for Occult HBV with HBV DNA level:**
  - Not on tenofovir, emtricitabine or lamivudine (off ART)
  - ALT or AST elevated
  - Chronic hepatitis C
  - Not responding to vaccination
- **Hepatitis B Immunization for isolated anti-HBc:**
  - Can do either boost & check or complete series
  - Can consider anti-HBe assessment to differentiate boost/check or simply complete series
  - **Vaccinate early** (before patient's CD4 gets <350)
  - Always **check anti-HBs** 1-2 months after vaccination completed
  - Keep in mind: Magnitude & duration of HBV vaccine response is often lower in HIV-infected patients due to a variety of factors (low CD4, detectable HIV RNA, occult HBV, other health concerns)