

Isolated Hepatitis B Core Antibody in People with HIV Infection

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Disclosures

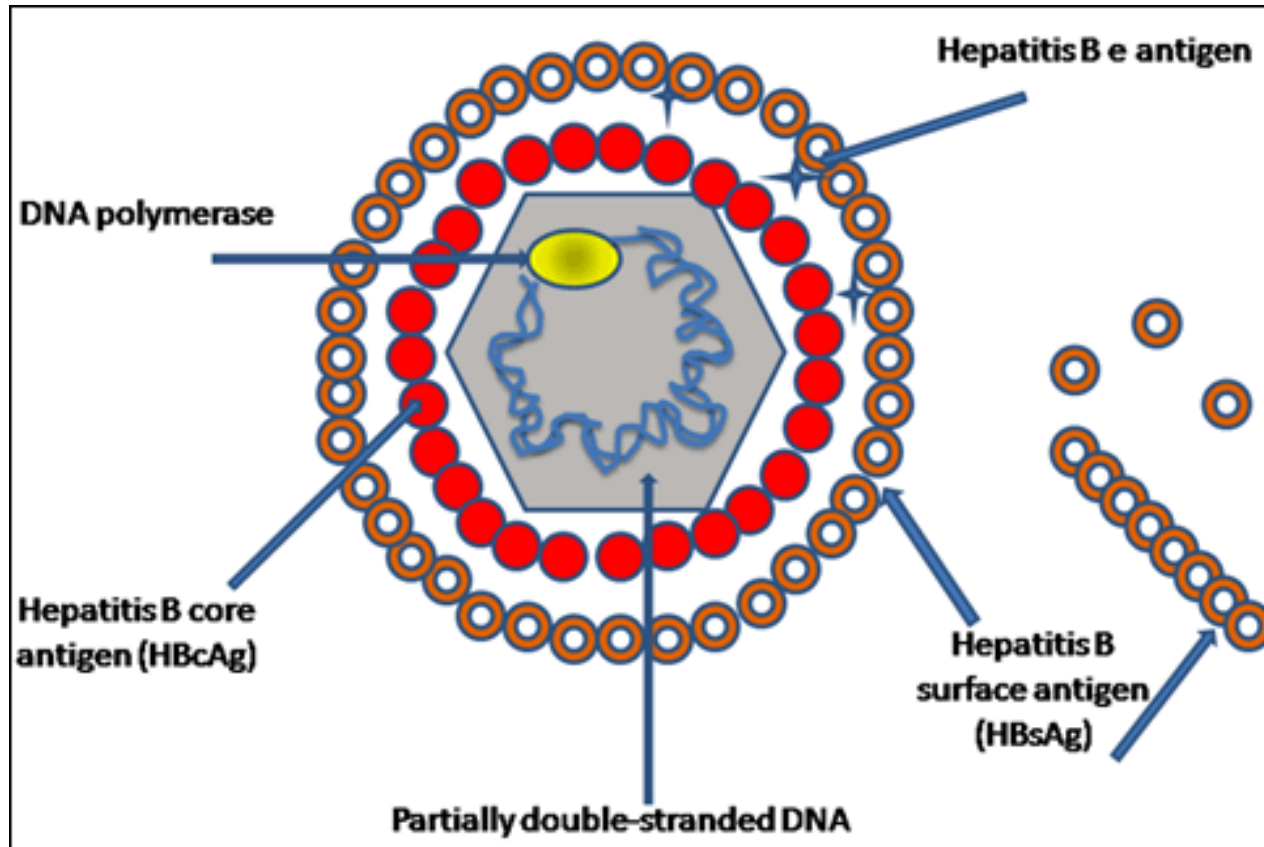
No financial conflicts of interest or relationships to disclose.

Topics

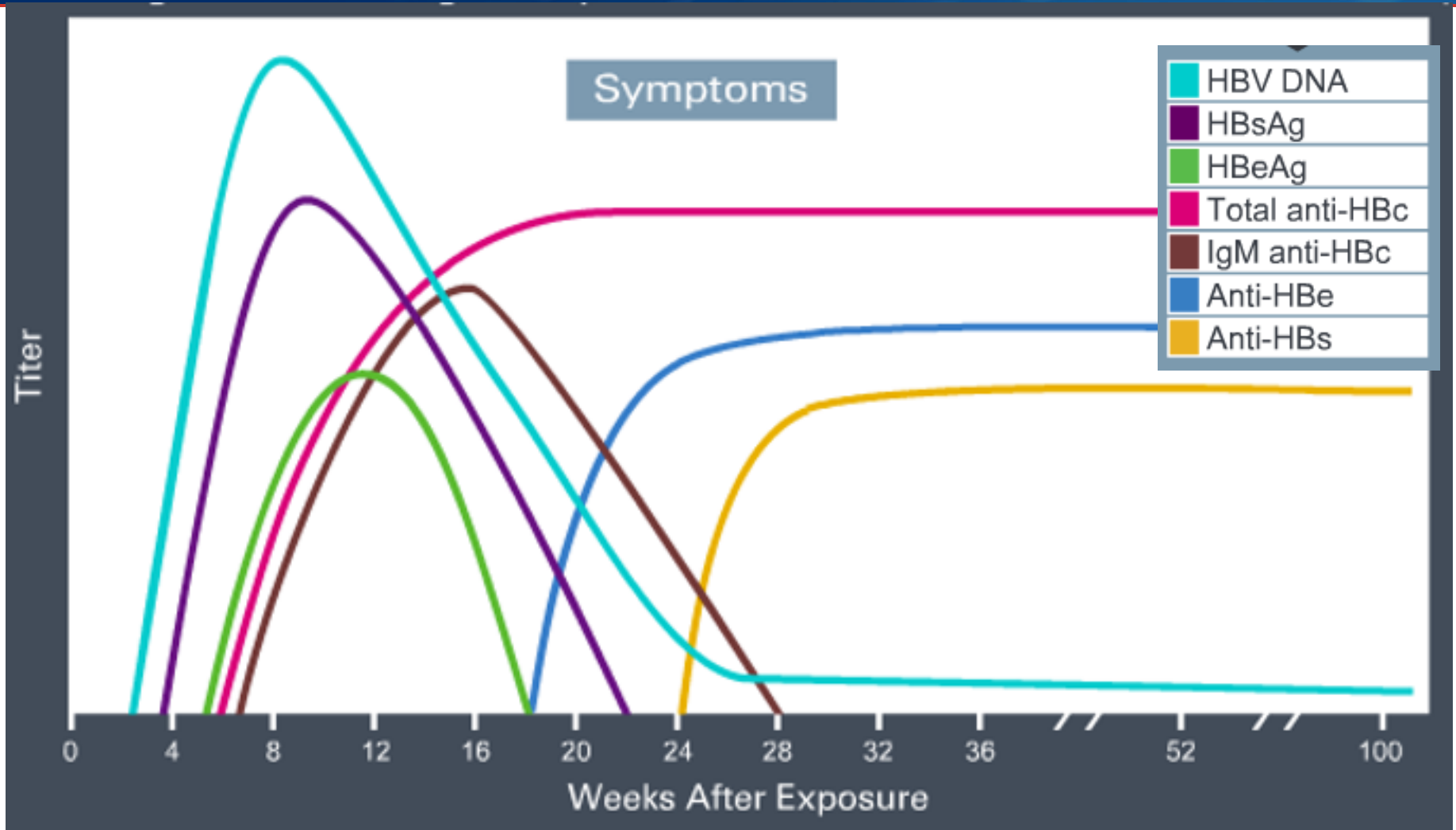
- Virology & Definition
- When isolated anti-HBc is encountered
- Clinical significance – occult HBV infection
- HBV immunization in these patients
- Practical considerations

Hepatitis B virus

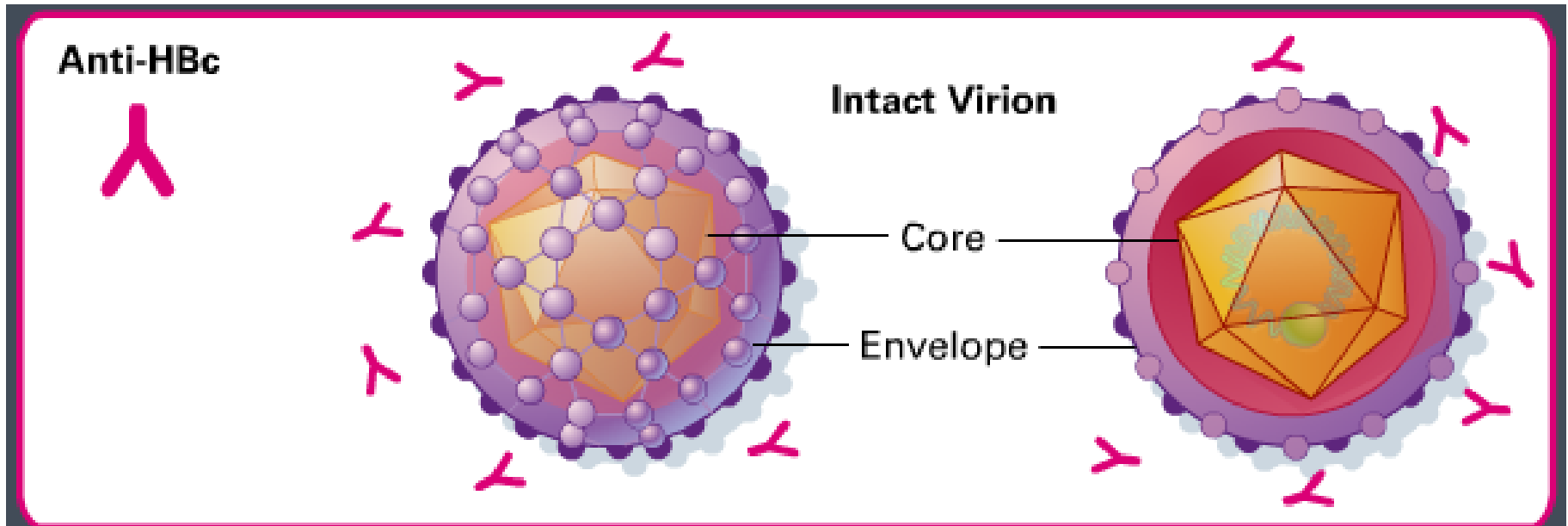
Virology



Natural History of Acute Resolved 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

- Definition: **Anti-HB core Ab(+)** but anti-HBs and HBs antigen negative
- Common profile – found in 20-45% in persons with HIV
- **Factors** associated with isolated core Ab:
 - Chronic hepatitis C infection
 - Older age
 - CD4 count <100 cells/mm³
 - HIV suppression on ART: less likely to be isolated core

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

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

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

Bhattacharya, *J AIDS* 2016;72:e14-17.

Isolated Hepatitis B Core Antibody in HIV

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 rendering sAg undetectable by routine assays;
- 4) Finally, **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

Clinical significance

- Isolated core Ab appears to be a stable pattern over time in most (84%) individuals
 - If retested, still present (i.e. false positive seems unlikely)
 - If it changes, transitions to/from pattern of **natural immunity** (anti-HBs and anti-HBc positive) were typical
 - Transition to/from chronic HBV infection (gain or loss of HBsAg) was rare
- Not 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.

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

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

Bhattacharya, *J AIDS* 2016;72:e14-17.

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Isolated Hepatitis B Core Antibody Occult Hepatitis B in HIV

- Defined by negative surface Ag, (+)HBV DNA level
- Not common – prevalence variable, depending on geography, population & assays
 - US-based case series: prevalence ~2-10% among isolated core pts
 - True prevalence may be underestimated due to
 - ✓ Cross-sectional nature of many studies
 - ✓ Fact that patients may be on HBV-active antivirals
- HBV viral levels detected typically low (<1000 IU/mL range)

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

Tsui, *Clin Infect Dis* 2007;45:736-40.

Palacios, *HIV Clin Trials* 2008;9:337-40.

Chang, *Curr HIV/AIDS Report* 2018;15:172-81.



Isolated Hepatitis B Core Antibody Reactivation of Occult HBV with DAA therapy

Fabbri et al. *BMC Infectious Diseases* (2017) 17:182
DOI 10.1186/s12879-017-2287-y

BMC Infectious Diseases

CASE REPORT

Open Access



Reactivation of occult HBV infection in an HIV/HCV Co-infected patient successfully treated with sofosbuvir/ledipasvir: a case report and review of the literature

Gabriele Fabbri*, Ilaria Mastroiosa, Alessandra Vergori, Valentina Mazzotta, Carmela Pinnetti, Susanna Grisetti, Mauro Zaccarelli, Adriana Ammassari and Andrea Antinori



Rituximab-associated hepatitis B virus (HBV) reactivation in lymphoproliferative diseases: meta-analysis and examination of FDA safety reports

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Received 6 July 2010; revised 16 August 2010; accepted 19 August 2010

Background: Rituximab has been associated with hepatitis B virus reactivation (HBV-R). However, the characteristics and scope of this association remain largely undefined.

Methods: We completed a comprehensive literature search of all published rituximab-associated HBV-R cases and from the Food and Drug Administration (FDA) Adverse Event Reporting System (AERS) MedWatch database. Literature and FDA cases were compared for completeness, and a meta-analysis was completed.

Results: One hundred and eighty-three unique cases of rituximab-associated HBV-R were identified from the literature ($n = 27$ case reports, $n = 156$ case series). The time from last rituximab to reactivation was 3 months (range 0–12), although 29% occurred >6 months after last rituximab. Within FDA data ($n = 118$ cases), there was a strong signal for rituximab-associated HBV-R [proportional reporting ratio = 28.5, 95% confidence interval (CI) 23.9–34.1; Empiric Bayes Geometric

Poll

A 50 year-old man with HIV, CD4 678 cells/mm³ and VL is undetectable on ART (abacavir-lamivudine-dolutegravir). His hepatitis B profile demonstrates isolated anti-HBc. LFTs are normal.

What would you do next?

- A. Check HBV DNA level to evaluate for occult HBV.
- B. Start complete HBV immunization series with standard dose.
- C. Give one standard dose and check anti-HBs titer in 4 weeks to determine next steps.
- D. Check anti-HBe antibody to determine next steps.

Isolated Hepatitis B Core Antibody

HBV Immunization

- Immunization can presumably help distinguish the latter 3 scenarios:

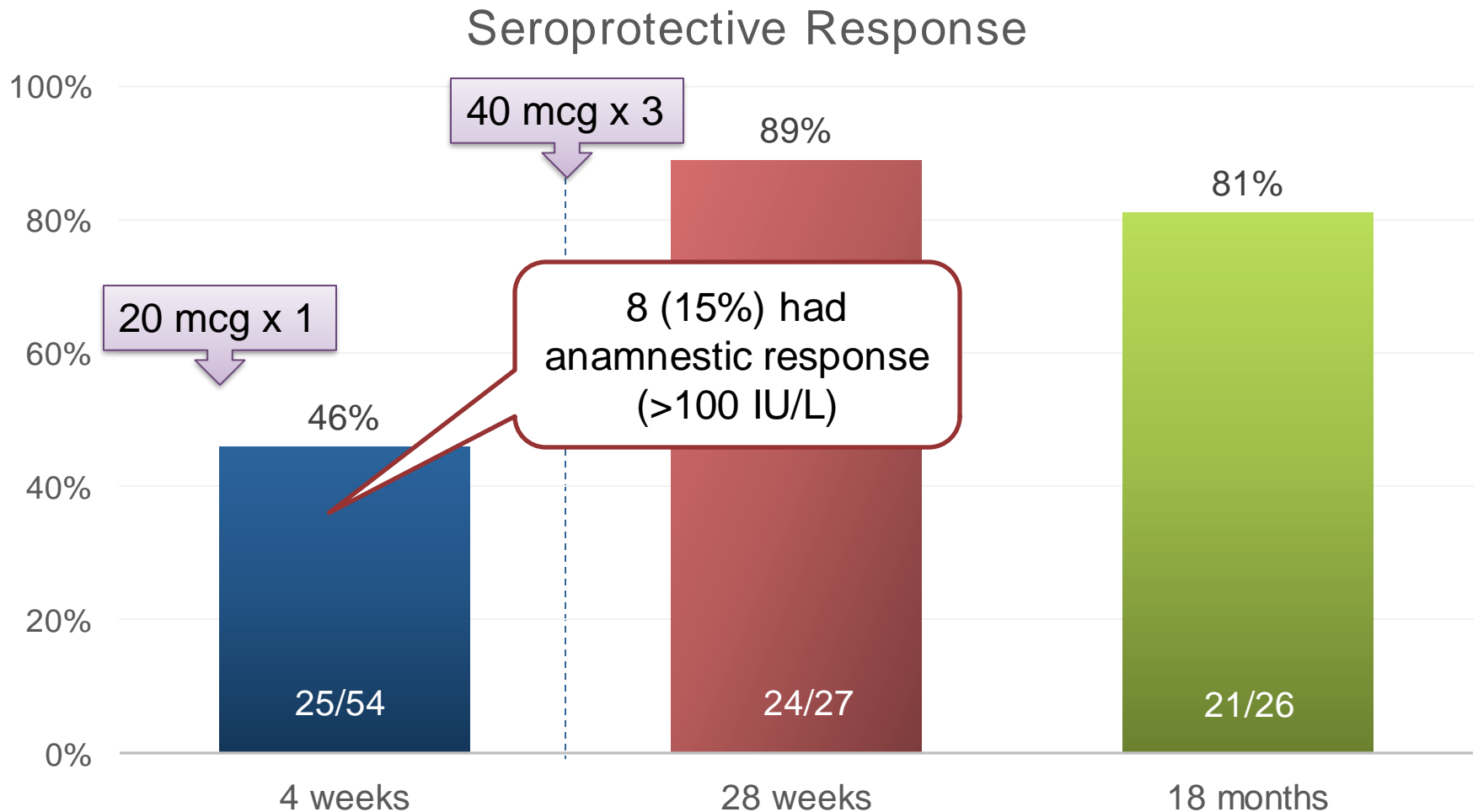
Scenario	Vaccine Response
Resolved HBV, waned sAb	Anamnestic response
Occult (chronic) HBV	No response
False positive	Primary response

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

Isolated Hepatitis B Core Antibody HBV Immunization

Study	Anamnestic Response
Gandhi <i>JID</i> 2005	24% (7/29)
Jongjirawisan <i>JAMT</i> 2006	7% (2/28)
Chakvetadze, <i>CID</i> 2010	32.5% (13/40)
Kaech, <i>J Infect</i> 2012	22% (8/37)
Piroth, <i>JID</i> 2016	8% (8/54)

HBV Immunization of Isolated Core Ab



Practical Considerations

What do the guidelines say?

DHHS OI Guidelines on Hep B (last update June 2019):

- Do not routinely check HBV DNA in patients with isolated core Ab
- Vaccinate with one standard dose of HBV vaccine
- Check anti-HBs titers 1 to 2 months after
- If sAb <100 IU/L, then give full vaccine series (level BII)

HIVMA 2020 Primary Care Guidelines:

- Isolated core Ab patients should receive vaccination

Practical Considerations

Expert Opinion

- **Isolated cores: Screen for occult HBV with HBV DNA level**
 - Not on tenofovir, emtricitabine or lamivudine
 - ALT or AST elevated
 - Chronic hepatitis C – esp. pre-DAA
 - Not responding to HBV vaccination
 - When you're worried re HBV reactivation
- **Hepatitis B Immunization for isolated anti-HBc:**
 - Vaccinate early
 - Always check anti-HBs 1-2 months after vaccination
 - Role of CpG-adjuvanted hep B vaccine...?

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