Hepatitis B Immunity in HIV: Case Vignette

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Disclosures

No financial conflicts of interests or relationships to disclose

Case of Unexpected Hepatitis B

45 year-old man with HIV on ABC/3TC/dolutegravir, PMH multiple STIs including latent syphilis and chronic kidney disease (baseline Cr 1.5) 2º to tenofovir DF.

- Admitted to hospital with profuse diarrhea and dizziness. Stool enteric battery: (+) Shigella
- ALT 279 and AST 166
- Medicine sent hep B serologies → (+) Hep B surface Ag
- HBV DNA 31 million IU/mL

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Case of Unexpected Hepatitis B

- Diagnosed with HIV in April 2003 and had completed hepatitis A/B immunizations at STD Clinic (Feb 2000-April 2003)

Date	Anti-HBs Ab (IU)	HBsAg
May 2003	17.3	Negative

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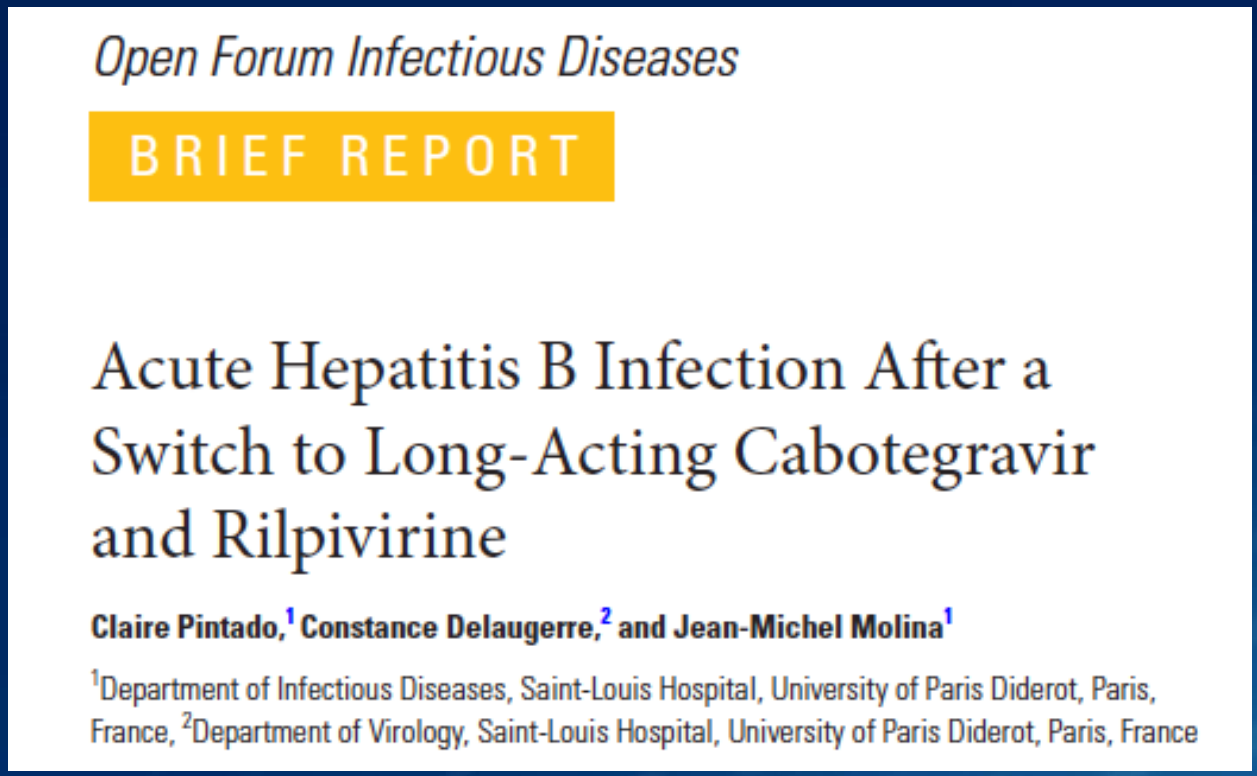

Open Forum Infectious Diseases

BRIEF REPORT

Acute Hepatitis B Infection After a Switch to Long-Acting Cabotegravir and Rilpivirine

Claire Pintado,[1] Constance Delaugerre,[2] and Jean-Michel Molina[1]

[1]Department of Infectious Diseases, Saint-Louis Hospital, University of Paris Diderot, Paris, France, [2]Department of Virology, Saint-Louis Hospital, University of Paris Diderot, Paris, France

- Enrolled in FLAIR trial of cabotegravir + rilpivirine monthly injections
- Found to have acquired acute HBV – ALT peaked to 594. HBsAg and core IgM (+). HBV DNA 229 million IU/ml.
- HBV susceptible → non-response to standard vaccine series

Pintado et al, *Open Forum Infect Dis* 2020; Sep 25;7(9):ofaa367.

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Additional Cases of Unexpected HBV

- Total of 3 new HBV cases in Madison x past year
  - Newly **HBsAg (+)**
  - Hx **absent or low anti-HBs titer** (<10-12 IU/L)
  - Two core Ab negative (previously vaccinated), one core Ab positive (previously exposed)
  - **No tenofovir** (TAF or TDF) in their ART regimen

Antibody Levels and Protection after Hepatitis B Vaccine: Results of a 22-Year Follow-Up Study and Response to a Booster Dose

Brian J. McMahon,[1,2] Catherine M. Dentinger,[2,a] Dana Bruden,[2] Carolyn Zanis,[2] Helen Peters,[2] Debbie Hurlburt,[2] Lisa Bulkow,[2] Anthony E. Fiore,[3] Beth P. Bell,[3] and Thomas W. Hennessy[2]

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Background. The duration of protection in children and adults (including health care workers) resulting from the hepatitis B vaccine primary series is unknown.

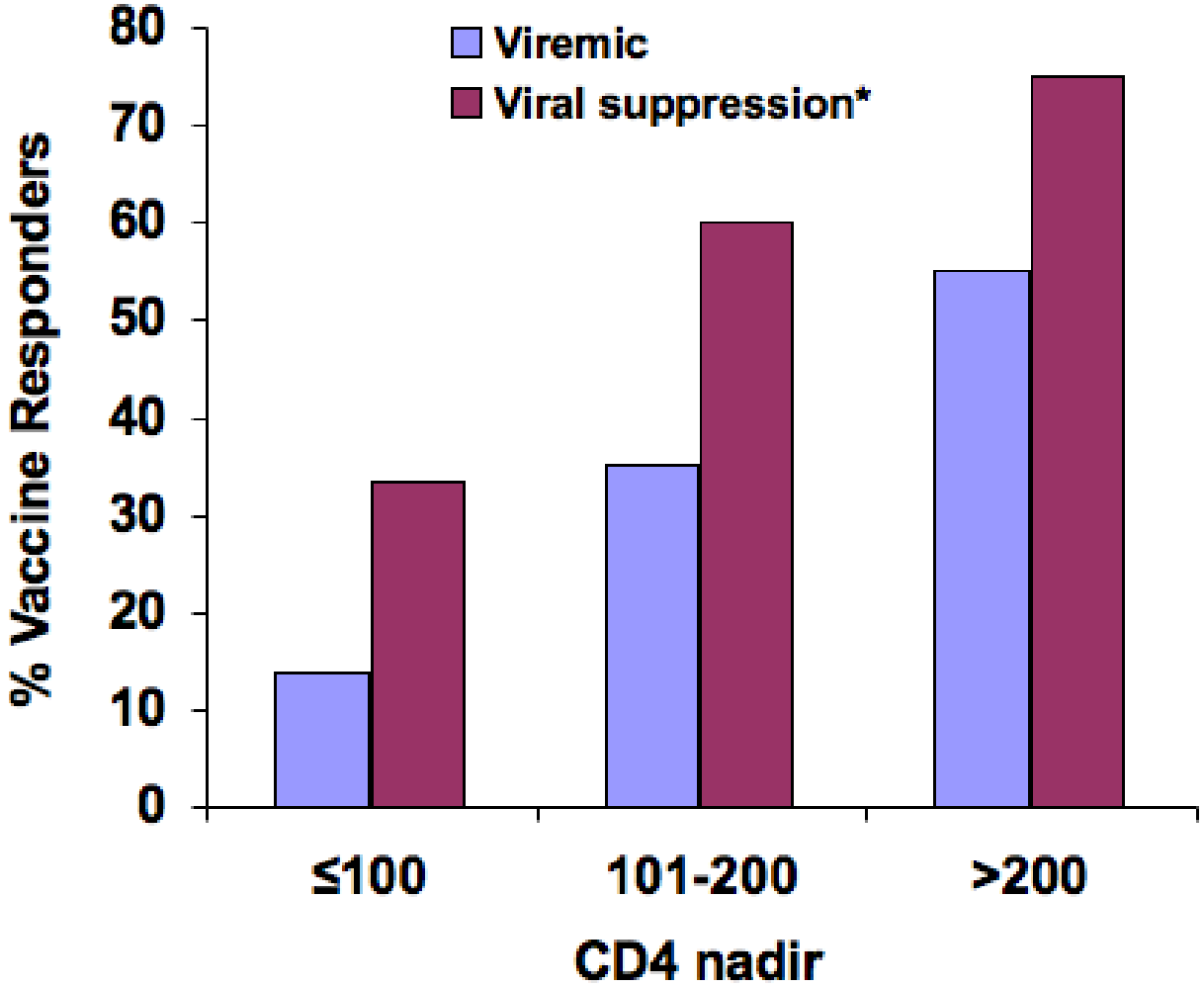
Methods. To determine the protection afforded by hepatitis B vaccine, Alaska Native persons who had received plasma-derived hepatitis B vaccine when they were >6 months of age were tested for antibody to hepatitis B surface antigen (anti-HBs) 22 years later. Those with levels <10 mIU/mL received 1 dose of recombinant hepatitis B vaccine and were evaluated on the basis of anti-HBs measurements at 10–14 days, 30–60 days, and 1 year.

Results. Of 493 participants, 60% (298) had an anti-HBs level ≥10 mIU/mL. A booster dose was administered to 164 persons, and 77% responded with an anti-HBs level ≥10 mIU/mL at 10–14 days, reaching 81% by 60 days. Response to a booster dose was positively correlated with younger age, peak anti-HBs response after primary vaccination, and the presence of detectable anti-HBs before boosting. Considering persons with an anti-HBs level ≥10 mIU/mL at 22 years and those who responded to the booster dose, protection was demonstrated in 87% of the participants. No new acute or chronic hepatitis B virus infections were identified.

Conclusions. The protection afforded by primary immunization with plasma-derived hepatitis B vaccine during childhood and adulthood lasts at least 22 years. Booster doses are not needed.

McMahon et al, *J Infect Dis* 2009; 200:1390–6

Suboptimal HBV Immunogenicity in HIV



Adapted from Kim, *Int J STD AIDS* 2008;19:600-604.

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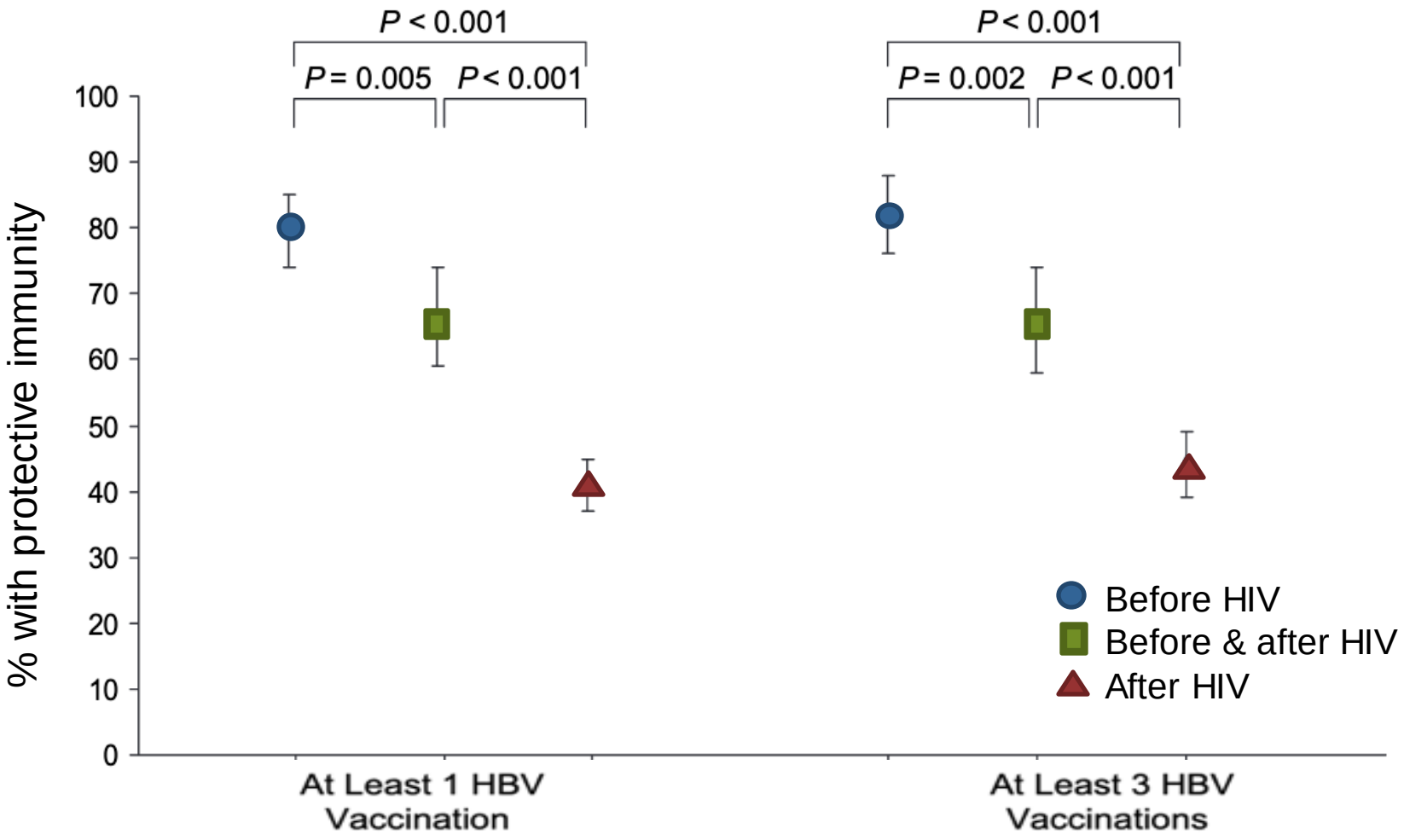
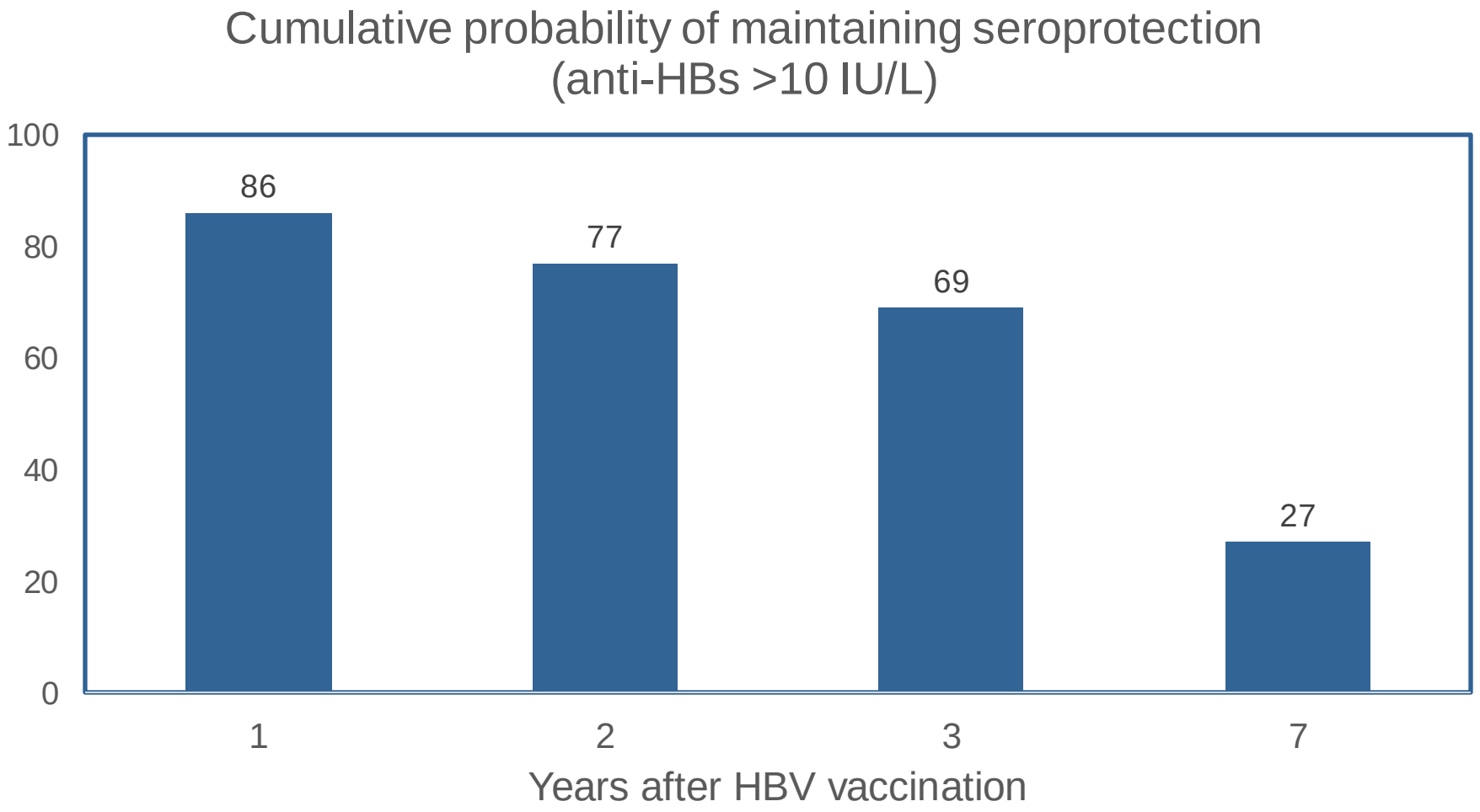
Timing Matters in HBV Immunization in HIV



Adapted from Landrum, *Am J Epidemiol.* 2011 Jan 1;173(1):84-93.

Waning HBV Immunity in Patients with HIV



Adapted from Nicolini et al, AIDS Res Hum Retroviruses. 2018 Nov;34(11):922-928.

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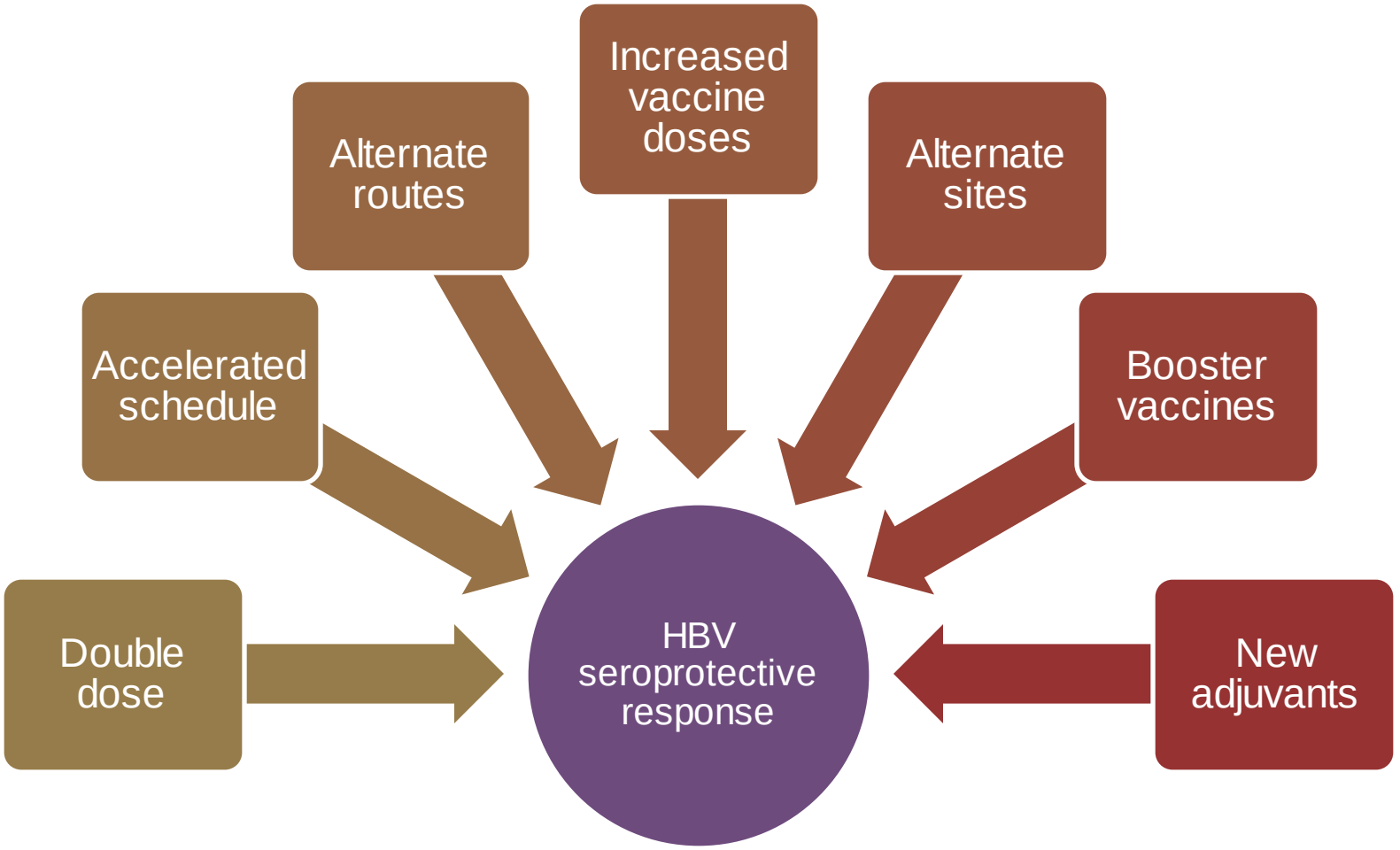
Optimizing HBV Vaccine Immunogenicity in HIV



Adapted from Farooq, Curr HIV/AIDS Rep. 2019 Oct;16(5):395-403.

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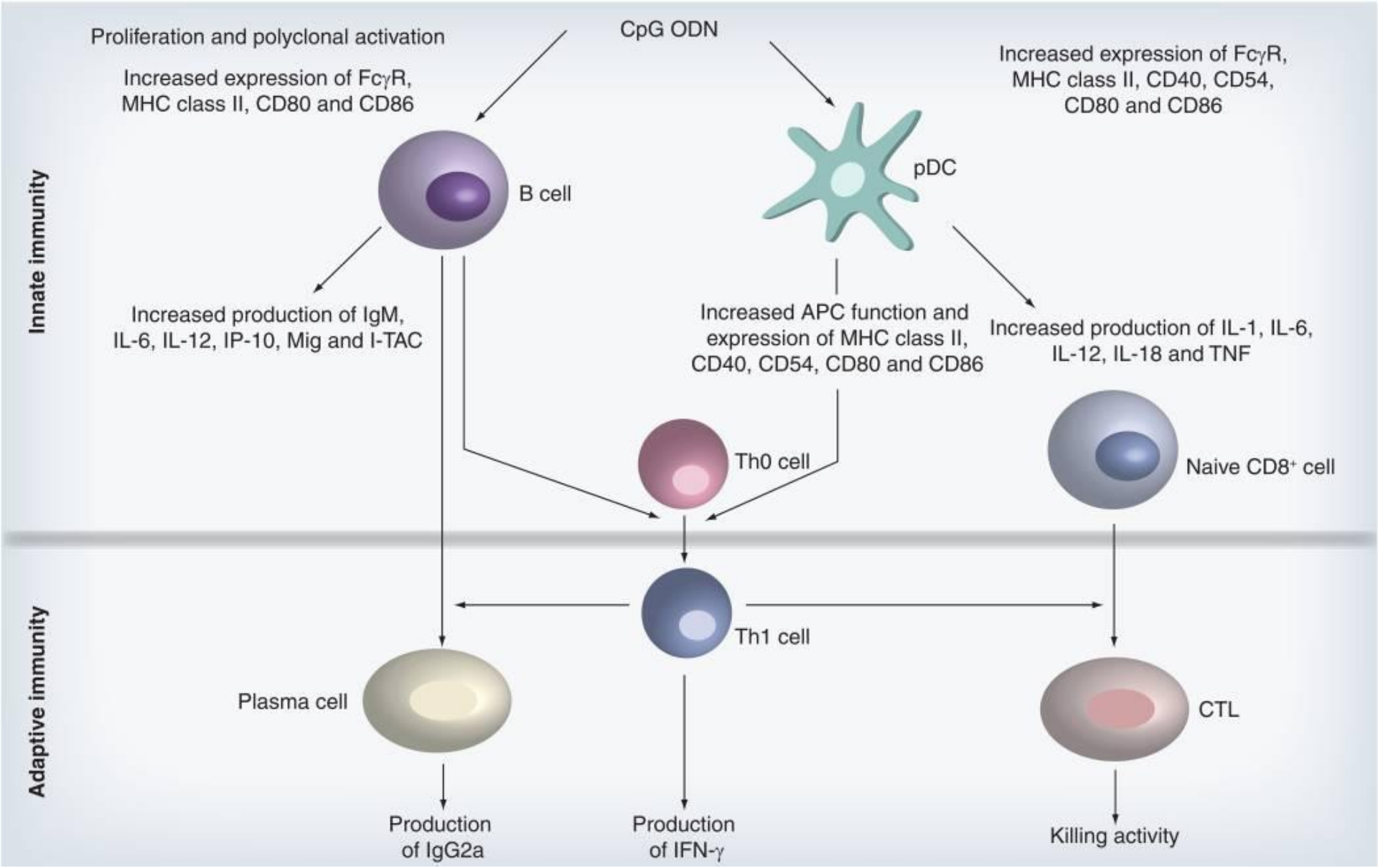
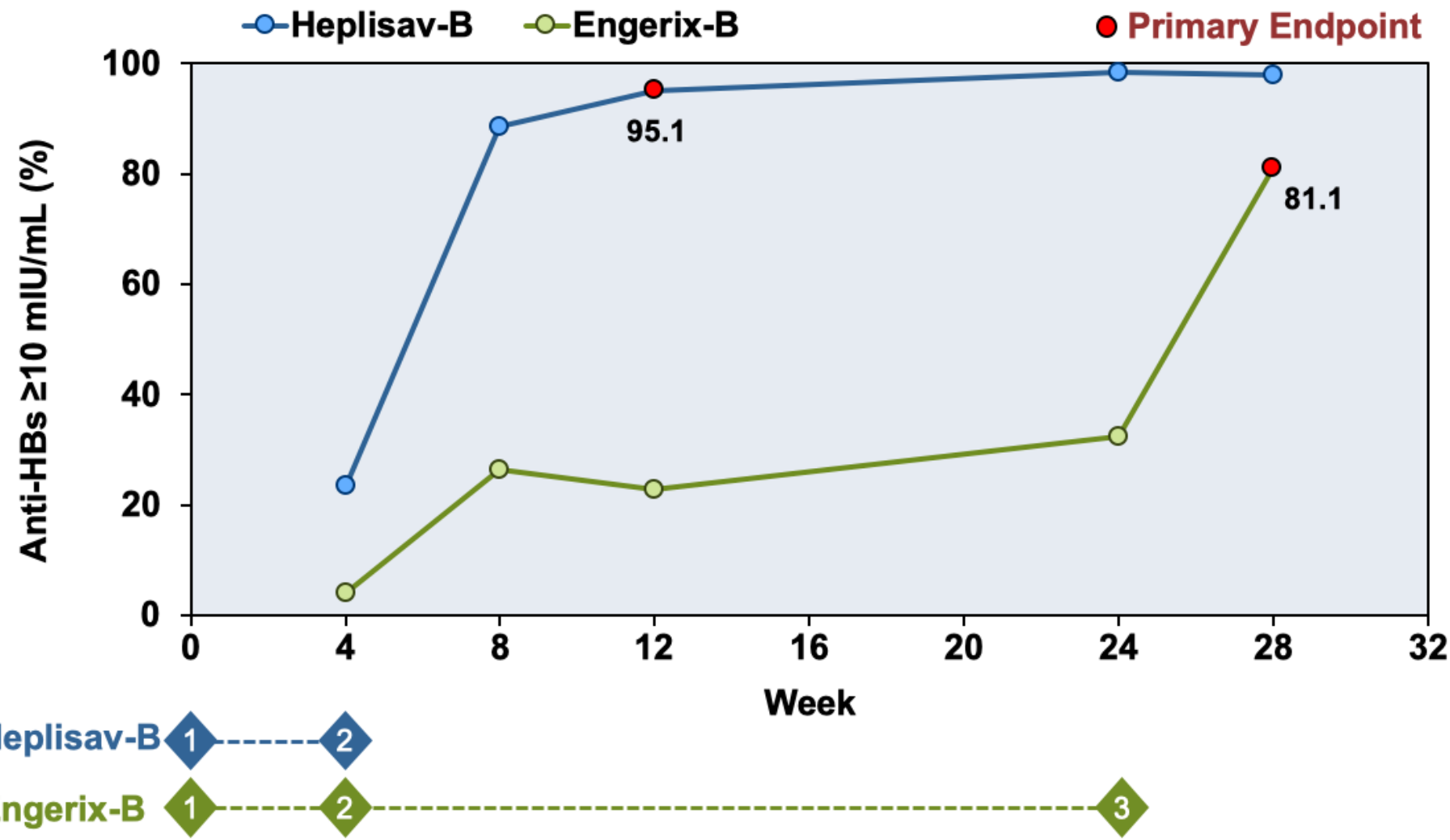


Source: Bode, *Expert Rev Vaccines* 2011;10(4):499-511.

Novel Adjuvanted Hep B vaccine: *Heplisav-B*



Source: Halperin SA, et al. Vaccine. 2012:30:2556-63.

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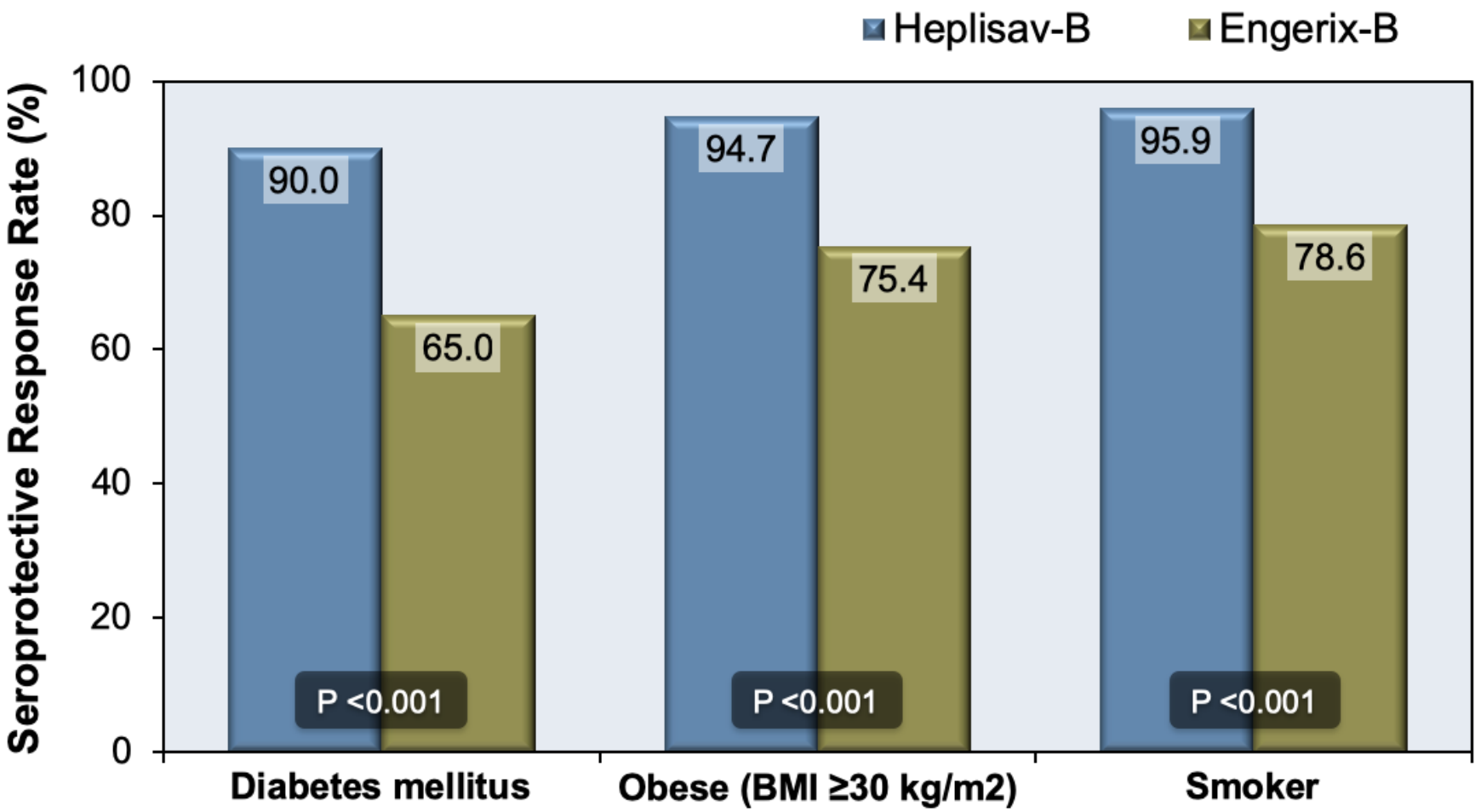
HepB-CpG (*Heplisav-B*) in Adults ages 18-70



Source: Jackson S, et al. Vaccine. 2018:36:668-74.

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CPG 7909 Adjuvant plus Hepatitis B Virus Vaccination in HIV-Infected Adults Achieves Long-Term Seroprotection for Up to 5 Years

C. L. Cooper,[1] J. B. Angel,[1] I. Seguin,[1] H. L. Davis,[2,3] and D. W. Cameron[1]

[1]Division of Infectious Diseases, University of Ottawa at the Ottawa Hospital, Ottawa Health Research Institute, and [2]Coley Pharmaceutical Group, Ottawa, Canada; and [3]Coley Pharmaceutical Group, Wellesley, Massachusetts

Background. Human immunodeficiency virus (HIV)–infected persons are hyporesponsive to hepatitis B virus (HBV) vaccination. CPG 7909 is an oligodeoxynucleotide containing immunostimulatory CpG motifs that activate human B and plasmacytoid dendritic cells via Toll-like receptor 9. We previously reported that addition of CPG 7909 to a commercial HBV vaccine enhanced the kinetics, magnitude, and longevity of the seroprotective response over 48 weeks. We now report data for the 5-year period following vaccination.

Methods. A randomized, double-blind, controlled trial was conducted to determine clinical safety and immunogenicity of HBV vaccine in adult HIV-infected subjects receiving effective antiretroviral therapy. HBV-susceptible subjects, one-half of whom had experienced previous vaccination failure, were vaccinated at 0, 1, and 2 months with a double adult dose of recombinant HBV vaccine, with or without 1 mg of CPG 7909 (19 subjects per arm). Titers of antibody to HBV surface antigen (anti-HBs) were measured at 6-month intervals for up to 60 months.

Results. The proportion of participants achieving and retaining seroprotection (surface antibody titers, $\geqslant$10 mIU/mL) was greater in CPG 7909 recipients ($P < .05$ at all time points). Geometric mean anti-HBs titers were higher in the CPG 7909 group than in the control group (without CPG 7909 adjuvant) at all measured time points.

Conclusions. The immunostimulatory properties of CPG 7909 present an important strategy in achieving long-term protection in HIV-infected patients and other HBV vaccine–hyporesponsive populations.

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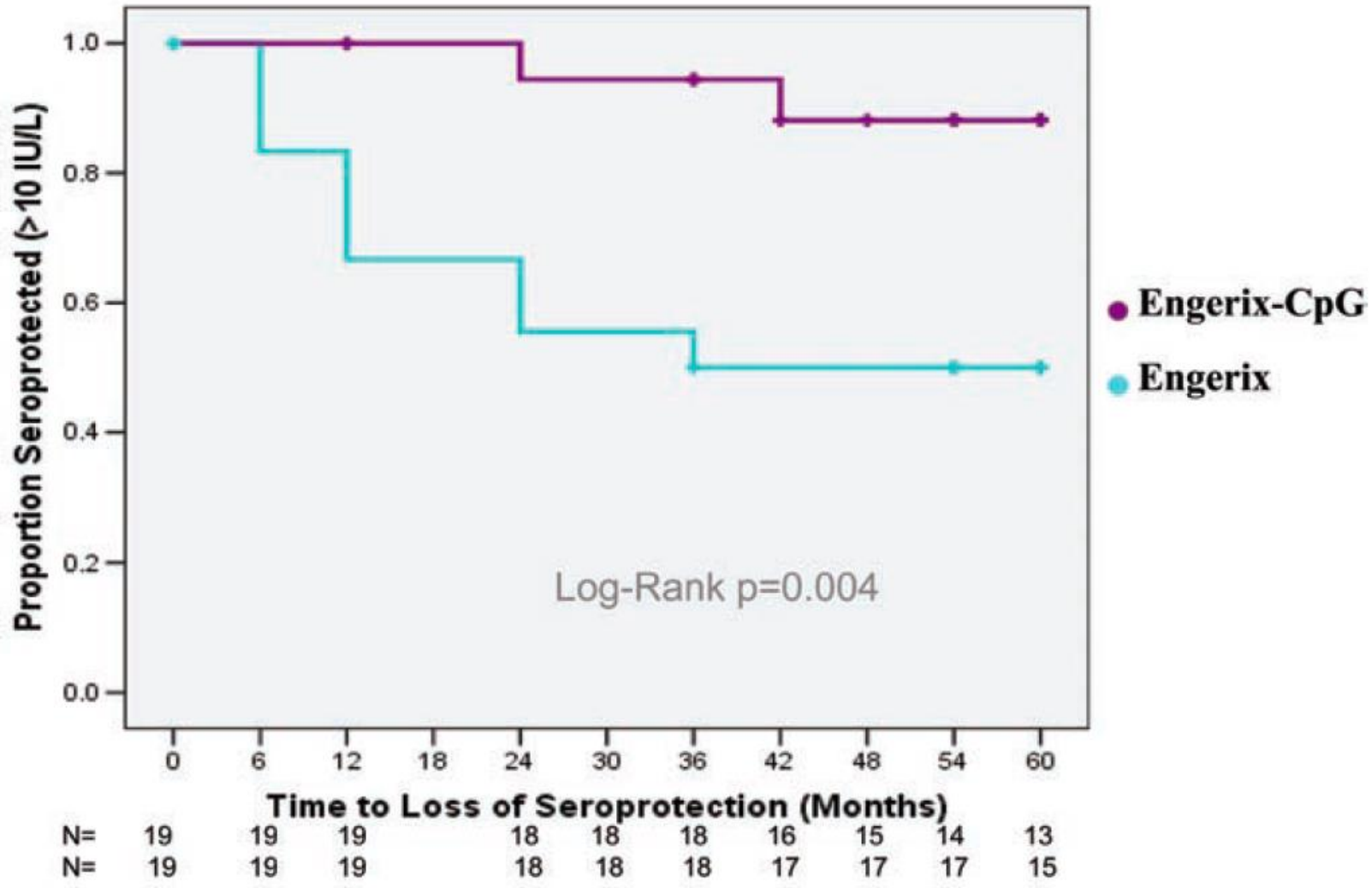
Time to Loss of HBV Seroprotection



Source: Cooper et al, *Clin Infect Dis* 2008; 46:1310–4.

Rate of HBV Immunization among People receiving Care for HIV, 2009-2012

9.7%

See Weiser et al, *Ann Intern Med*. 2018;168:245-254.

Take Home Lessons – Hepatitis B Prevention

- HBV is out there and actively circulating in our patient population
- Vaccinate early (ideally before HIV!). Do not delay in high-risk individuals (multiple sexual partners, IDU)
- Check anti-HBs titers 1-3 months after last dose
- Revaccinate those who do not seroconvert... See DHHS Hep B OI guidelines
- Screen those with new/unexplained ALT/AST elevation for HBsAg as well as HCV Ab (regardless of prior anti-HBs or vaccination status)
- NOTE: HBV antiviral therapy is not failsafe protection against HBV - tenofovir may be more protective but our case developed HBV on lamivudine.
- Thinking of NRTI or tenofovir sparing regimen? Please consider all of the above plus risk of HBV reactivation in chronically infected individuals

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A5379: B-Enhancement Of HBV Vaccination In Persons Living With HIV (BEe-HIVe): Evaluation Of HEPLISAV-B

A5379 is a study looking at hepatitis B vaccination in adults living with HIV. Hepatitis B is a serious viral infection that affects the liver and is transmitted through blood and body fluids. The study will involve individuals who have received a previous hepatitis B vaccination but the vaccine did not respond well and individuals who have never received the vaccination. The study will take place both in the US and internationally. The study will compare how well an individual responds to the vaccine in different groups based on the type of vaccine and number of doses.

Purpose of the Study: Vaccination for hepatitis B in individuals living with HIV does not always work, especially in those with impaired immune systems or ability to fight infection. Prevention of hepatitis B in individuals living with HIV has primarily been done by vaccinating with a series of 3 shots given over 6 months. A new vaccine, called HEPLISAV-B, has been approved that may provide a better response than what has currently been used. The researchers will study whether this vaccine will prove to be more effective than the current standard.

https://actgnetwork.org/studies/

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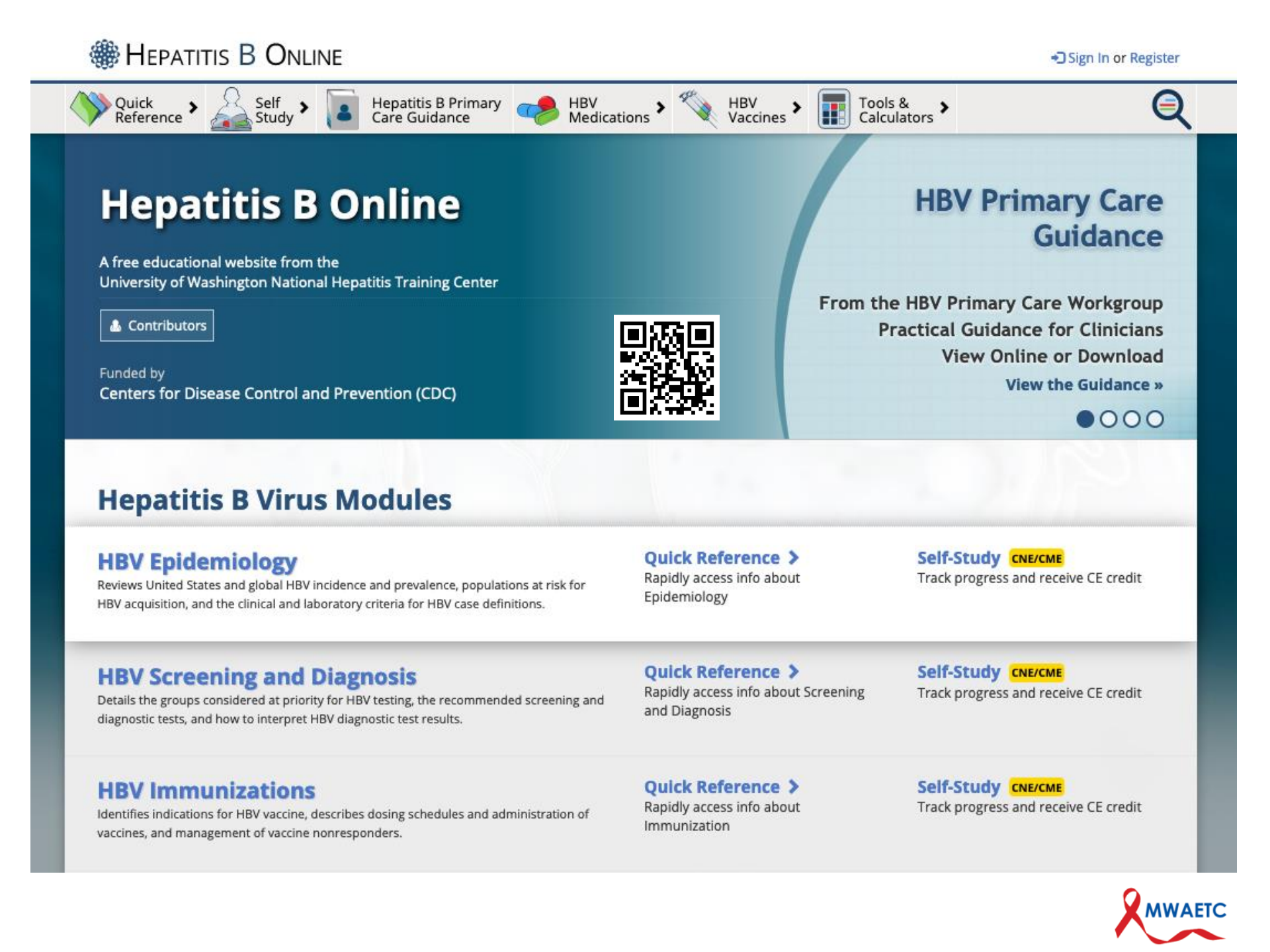
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Details the groups considered at priority for HBV testing, the recommended screening and diagnostic tests, and how to interpret HBV diagnostic test results.
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The content in this presentation are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, HRSA, HHS, or the U.S. Government.

AETC AIDS Education & Training Center Program Mountain West

Question re Isolated anti-HB core?

Check out my archived ECHO talk on this topic which includes how to approach vaccination:

https://tinyurl.com/yasezuh3