Hepatitis B Immunity in HIV: Case Vignette

H. Nina Kim, MD MSc
Associate Professor of Medicine
University of Washington

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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
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)

<table>
<thead>
<tr>
<th>Date</th>
<th>Anti-HBs Ab (IU)</th>
<th>HBsAg</th>
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<tbody>
<tr>
<td>May 2003</td>
<td>17.3</td>
<td>Negative</td>
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• 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
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,2a 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. Hennessy2

1Liver Disease and Hepatitis Program, Alaska Native Tribal Health Consortium, and 2Arctic Investigations Program, Division of Emerging Infections and Surveillance Services, National Center for Preparedness, Detection, and Control of Infectious Diseases, Centers for Disease Control and Prevention (CDC), Anchorage, Alaska; 3Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC, Atlanta, Georgia

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 $\geq 10$ mIU/mL. A booster dose was administered to 164 persons, and 77% responded with an anti-HBs level $\geq 10$ 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 $\geq 10$ 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.
Suboptimal HBV Immunogenicity in HIV

Timing Matters in HBV Immunization in HIV

Waning HBV Immunity in Patients with HIV

Cumulative probability of maintaining seroprotection (anti-HBs >10 IU/L)

Optimizing HBV Vaccine Immunogenicity in HIV

- Alternate routes
- Increased vaccine doses
- Alternate sites
- Booster vaccines
- New adjuvants
- Accelerated schedule
- Double dose

HBV seroprotective response

Proliferation and polyclonal activation
Increased expression of FcγR, MHC class II, CD80 and CD86

CpG ODN

Increased expression of FcγR, MHC class II, CD40, CD54, CD80 and CD86

Innate immunity

B cell

Increased production of IgM, IL-6, IL-12, IP-10, Mig and I-TAC

pDC

Increased APC function and expression of MHC class II, CD40, CD54, CD80 and CD86

Th0 cell

Naive CD8+ cell

Th1 cell

Plasma cell

Production of IgG2a

Production of IFN-γ

CTL

Killing activity

Novel Adjuvanted Hep B vaccine: *Heplisav-B*

![Graph showing comparison between Heplisav-B and Engerix-B](source-url)

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

![Bar chart showing seroprotective response rates for HepB-CpG in adults with diabetes, obesity, and smoking.](chart.png)

- **Diabetes mellitus:**
  - Heplisav-B: 90.0%
  - Engerix-B: 65.0%
  - *P* < 0.001

- **Obese (BMI ≥ 30 kg/m²):**
  - Heplisav-B: 94.7%
  - Engerix-B: 75.4%
  - *P* < 0.001

- **Smoker:**
  - Heplisav-B: 95.9%
  - Engerix-B: 78.6%
  - *P* < 0.001

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. Cameron1

1Division of Infectious Diseases, University of Ottawa at the Ottawa Hospital, Ottawa Health Research Institute, and 2Coley Pharmaceutical Group, Ottawa, Canada; and 3Coley 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, ≥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.
Time to Loss of HBV Seroprotection

Log-Rank p=0.004

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

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

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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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.
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