U.S. Vaccines: Table 1
Hepatitis B (Adapted from CDC 08/2021)
(For Combination Vaccines, See Table 2)

Vaccine	Trade Name	Abbreviation	Manufacturer	Route	Doses in Routine Series	Approved Ages	Comments
Hepatitis B	Engerix-B®	HepB	GlaxoSmithKline	IM	3	Pediatric: Birth-19 years Adult: ≥20 years	Recombinant, Adj.
	Recombivax HB®	HepB	Merck	IM	3	Pediatric: Birth-19 years Adult: ≥20 years	Recombinant, Adj.
	Heplisav-B®	HepB	Dynavax Technologies	IM	2	≥18 years	Recombinant, Adj.
Vaccine	**Trade Name**	**Abbreviation**	**Manufacturer**	**Route**	**Doses in Routine Series**	**Approved Ages**	**Comments**
Hepatitis A, Hepatitis B	Twinrix®	HepA-HepB	GlaxoSmithKline	IM	3	≥18 years	Inactivated/Recombinant, Adj. Pediatric HepA + Adult HepB

Above are the available hepatitis B vaccines as listed by the Centers for Disease Control.

The San Diego Immunization Coalition does not endorse any brand preference for ACIP-recommendations.

Notes

- The abbreviations on this table (Column 3) were standardized jointly by staff of the Centers for Disease Control and Prevention, ACIP Work Groups, the editor of the *Morbidity and Mortality Weekly Report* (*MMWR*), the editor of *Epidemiology and Prevention of Vaccine-Preventable Diseases* (the *Pink Book*), ACIP members, and liaison organizations to the ACIP.

  These abbreviations are intended to provide a uniform approach to vaccine references used in ACIP Recommendations and Policy Notes published in the *MMWR*, the *Pink Book*, and the American Academy of Pediatrics *Red Book*, and in the U.S. immunization schedules for children, adolescents, and adults.

  In descriptions of combination vaccines, a hyphen (-) indicates products in which the active components are supplied in their final (combined) form by the manufacturer; a slash (/) indicates products in which active components must be mixed by the user.

- "Doses in a Routine Series" (Column 6) reflects doses administered to a healthy patient at the recommended ages. It doesn't necessarily reflect schedules for patients with health conditions or other high-risk factors, alternative schedules, catch-up schedules, or booster doses not part of an initial series. For some combination vaccines, this column represents the routine number of doses *for that product*, and not necessarily the total number of doses in a complete series for the components. (For example, Kinrix or Quadracel may be used for only 1 dose of multi-dose DTaP and IPV series.)

- "Adj." in the "Comments" column indicates that the vaccine contains an adjuvant.

- A hyphen in an age range means "through" (i.e., "6 weeks-6 years" means 6 weeks through 6 years [to the 7th birthday]).

Hepatitis B Overview, New Data and Model Considerations: HIV, CLD and Cost Effectiveness

Kelvin McKoy, M.D., M.B.A.
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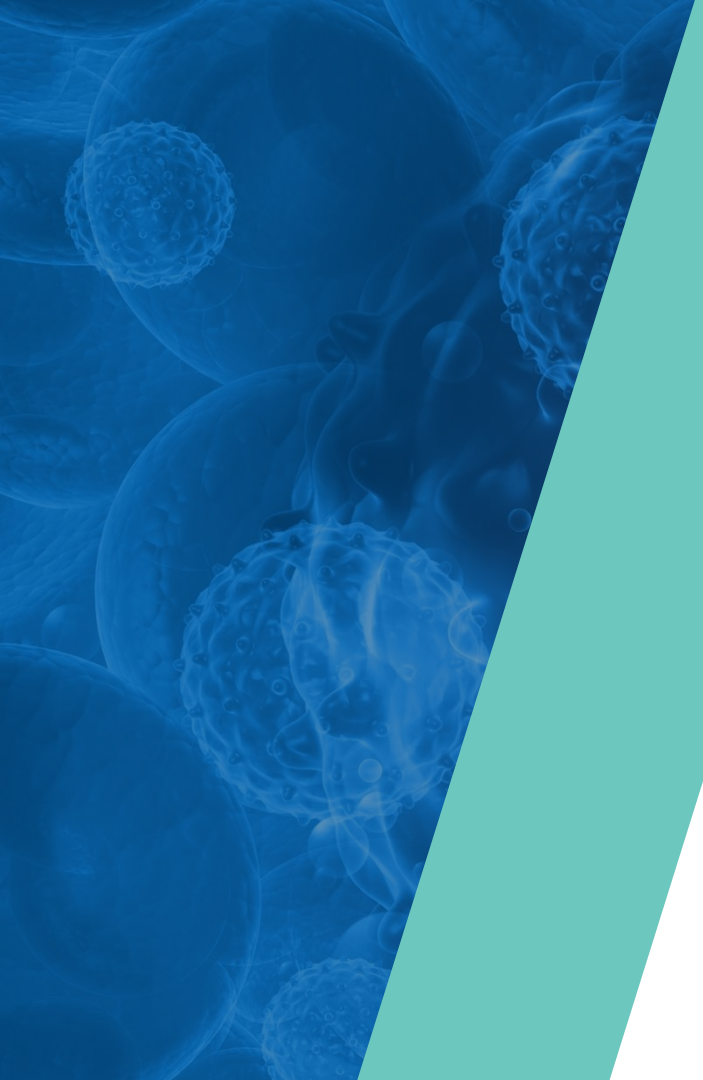
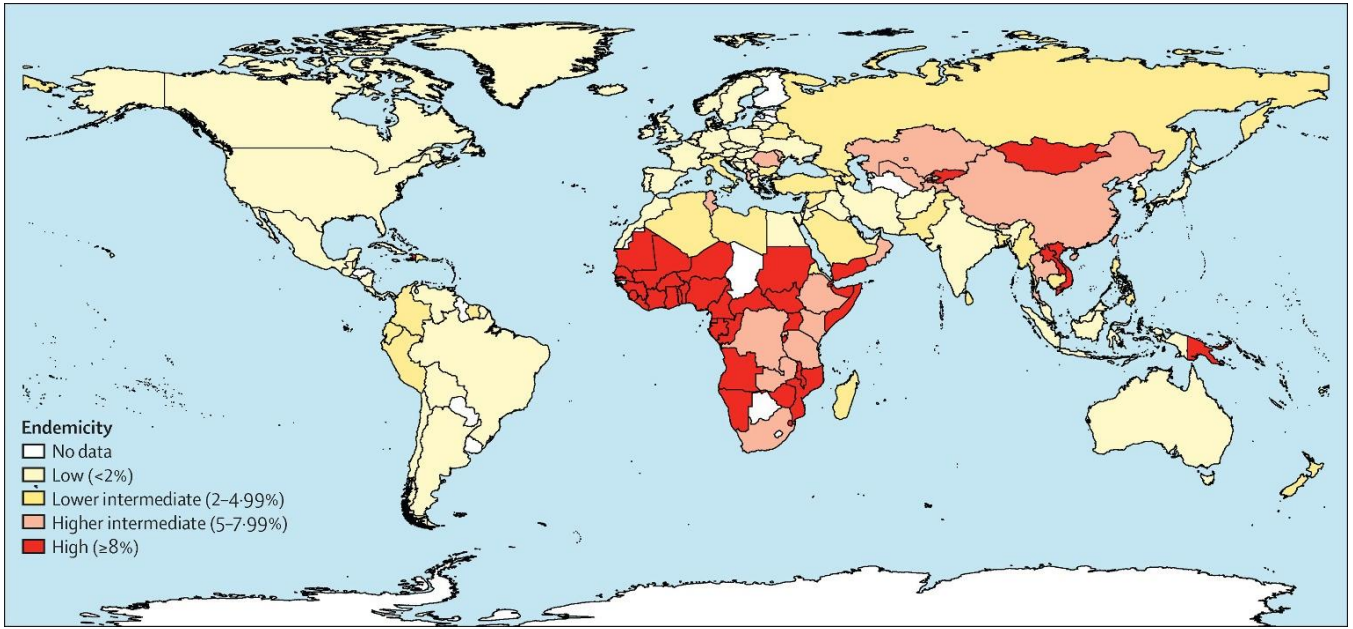


Hepatitis B Disease

Worldwide Distribution of Chronic HBV Infection

Global HBsAg Endemicity 1957–2013

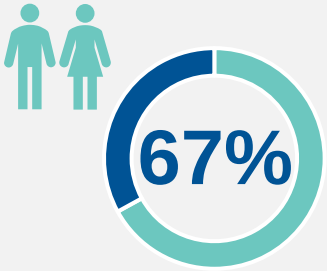


Global assessment of country-level population prevalence of chronic HBV infection shows a wide variation between countries

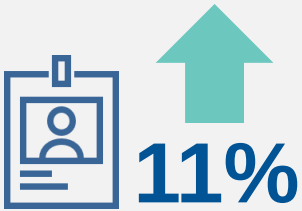
Schweitzer A, et al. *Lancet*. 2015;386:1546-55.

Hepatitis B is on the Rise

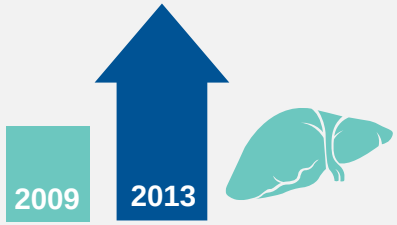
12 million Americans have been infected with HBV and **850,000 to 2.2 million are living with chronic infection**[1]



of people **are unaware** they are infected[2]

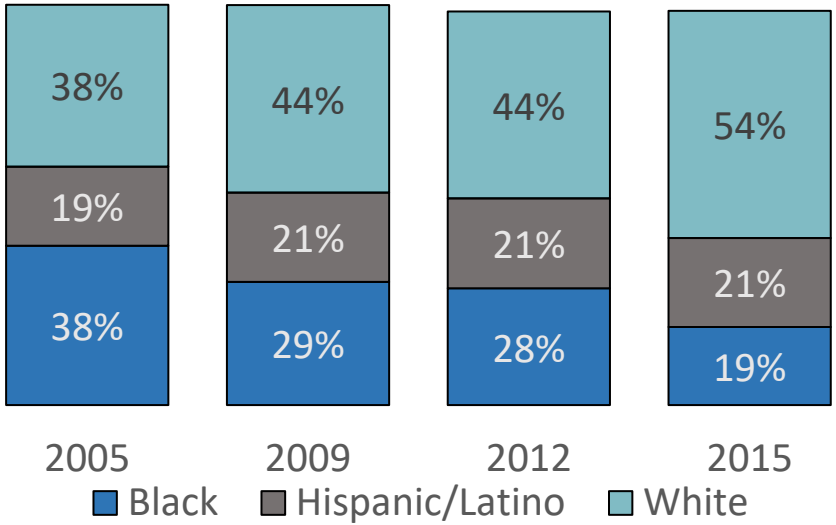


Estimated **new cases** of HBV in the United States have **risen 11%** over a 5-year period[3]



Hepatitis B infections have increased up to **114%** from 2009 to 2013 in some states affected by the opioid and heroin epidemics[4]

Changes in Who Is Starting to Inject Drugs (New PWID), 22 cities, 2005–2015



White new PWID in 2015

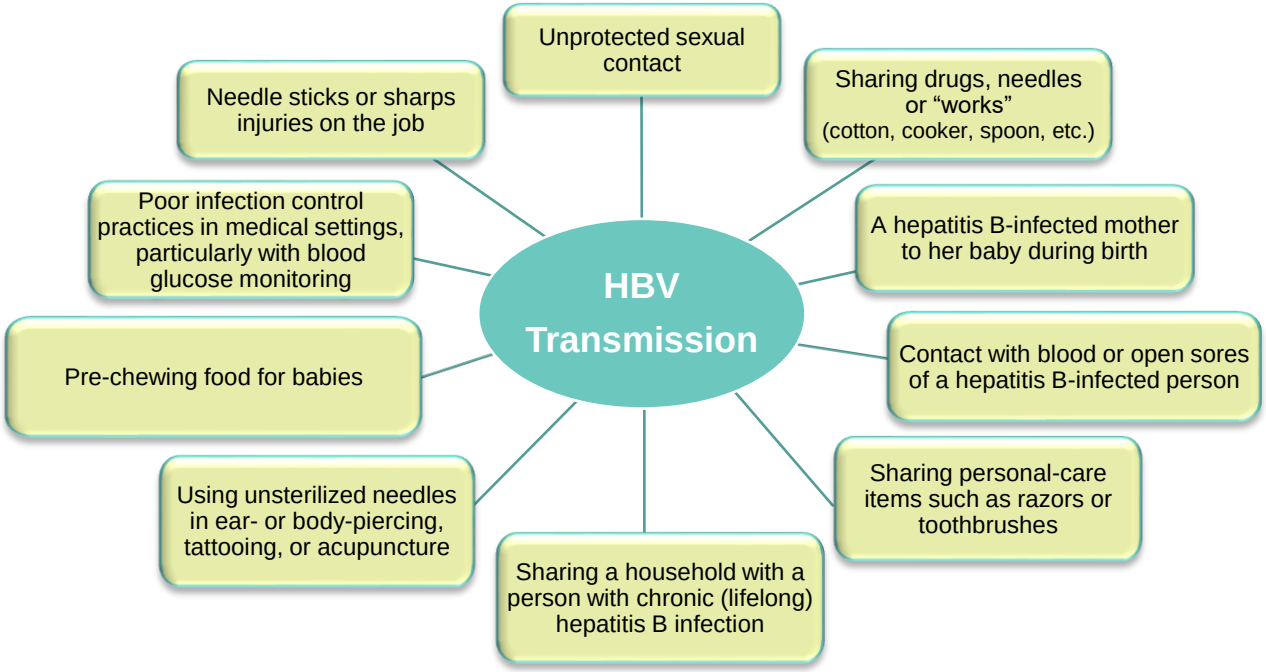
- Higher risk: 46% shared syringes

Black new PWID in 2015

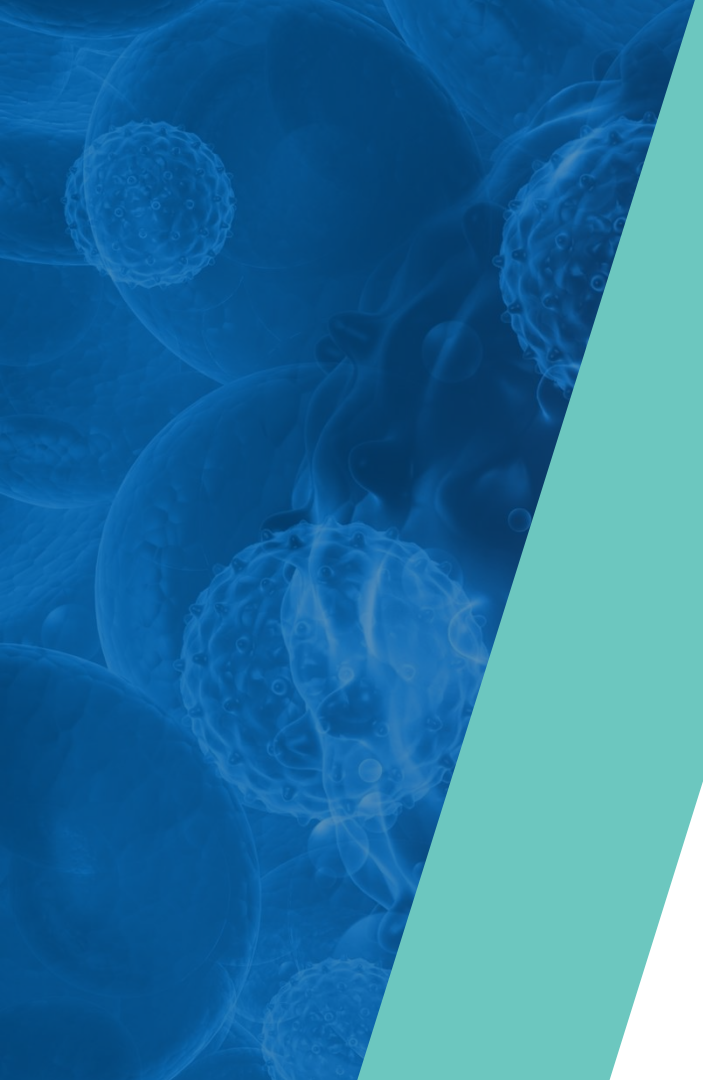
- Lower risk: 28% shared syringes

Wejnert C. Vital Signs: Trends in HIV Diagnoses, Risk Behaviors, and Prevention Among Persons Who Inject Drugs — United States. National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention. Presented at: Turning Research Into Prevention; November 30, 2016.

Hepatitis B Can Be Spread in Many Ways



Immunization Action Coalition. Hepatitis B: Questions and Answers. December 2017. Available at: http://www.immunize.org/catg.d/p4205.pdf. Accessed January 18, 2018.



Current Recommendations & Series Completion Rates

CDC Recommends HBV Vaccination for a Variety of Adults, Including Those Commonly Seen in Primary Care Settings[5]

Medical Diagnoses[6]

- Diabetes, aged 19 to 59 years
- Chronic liver disease
- HIV infection
- End-stage renal disease, including predialysis, hemodialysis, and home dialysis patients

Sexual Exposure[6]

- Sexually active patients who are not in a long-term, mutually monogamous relationship
- Patients seeking testing or treatment for a sexually transmitted disease
- Men who have sex with men
- Sexual partners of HBV-positive persons

Occupational Risk[6]

- Persons who have occupational risk of infection, including healthcare and public safety workers
- International travelers
- Employers must offer HBV immunization at no cost to healthcare and public safety workers[6]

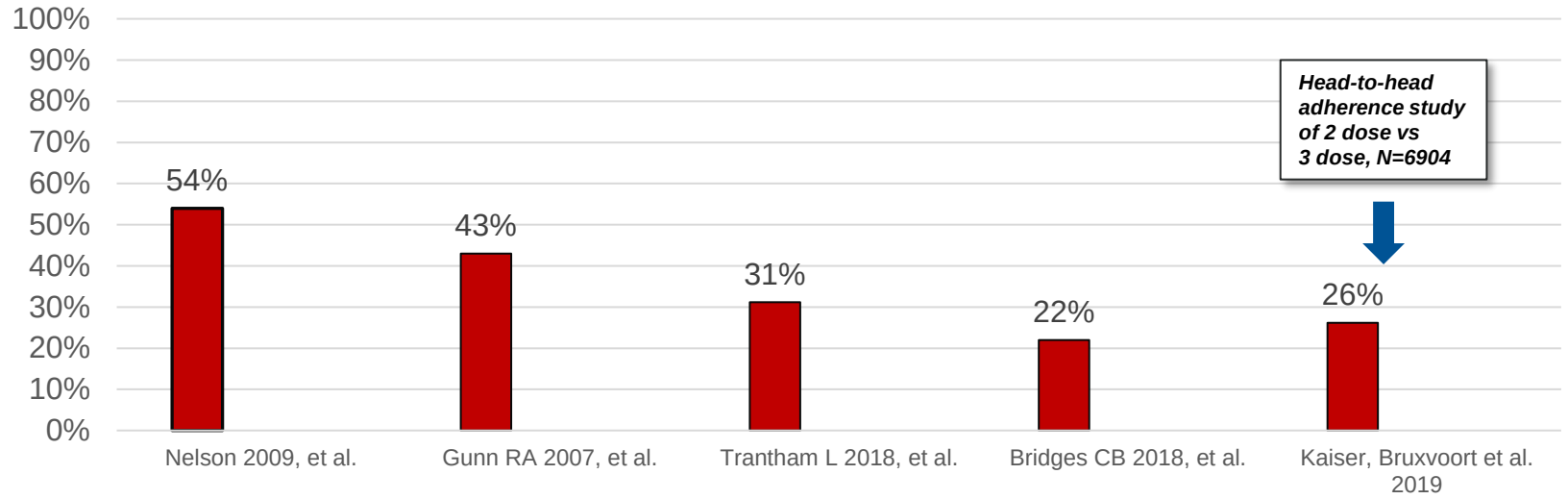
Other Risk Factors[6]

- Current or recent injection drug users
- Household contacts of HBV-positive persons
- All patients seeking protection from HBV infection

EFFECTIVE VACCINATION IS CRITICAL TO REDUCING THE SPREAD OF THE DISEASE[5]

Three-Dose HepB Vaccine Series Completion Rates

Multiple studies indicate suboptimal series completion rates for 3 dose adult HBV vaccines

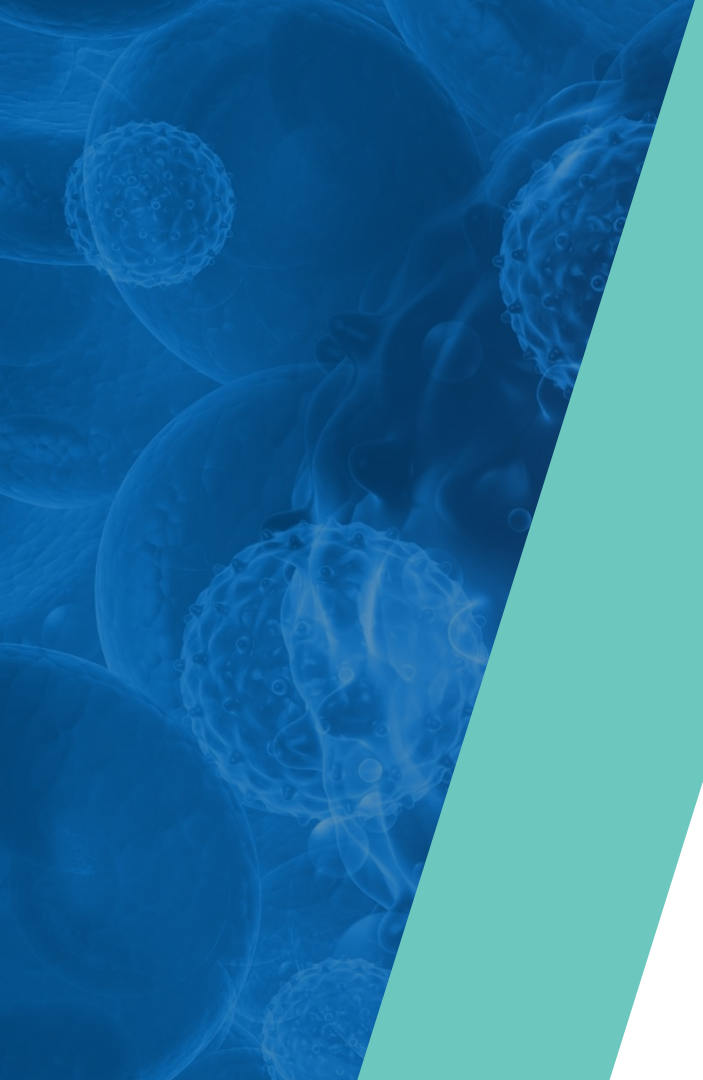


Sources: *Data on file. Dynavax Technologies Corporation,2019; Nelson J, et al. Am J Public Health. 2009;99:S389-S397; Gunn RA, et al. Sex Transm Dis. 2007;34(9):663-668; Trantham L, et al. Adherence with and completion of recommended hepatitis vaccination schedules among adults in the United States, Vaccine June 19, 2018, https://doi.org/10.1016/j.vaccine.2018.05.111; Bridges CB, et al. Hepatitis B Vaccine 3-Dose Series Completion in Settings in which a High Proportion of Adults have Hepatitis B-Related Risk Factors — United States 2012-2015. Poster presented at: 48th National Immunization Conference (NIC); May 15-17, 2018; Atlanta, Georgia. Bruxvoort K, et al. IDSA October 2019, Comparing 2-dose and 3-dose Vaccines in KPSC Post-Marketing Study*

Hepatitis B Series Completion Rates Among Dose 1 Recipients

Setting Type (facility)	Number or persons who received dose 1	Number (%) of dose 1 recipients who received dose 3
STD Clinics	11,245	1,928 (17.1)
Department of Corrections	5,150	908 (17.6)
Other	3,447	1,079 (31.3)
Federally Qualified Health Center	2,432	923 (38.0)
Drug Treatment	2,564	349 (13.6)
Healthcare Facility Targeting IDU	2,008	325 (16.2)
HIV Clinics	1,278	379 (29.7)
Local Health Department Clinic	876	531 (60.6)
Healthcare Setting Targeting MSM	457	135 (29.5)
Total	**29,457**	**6,557 (22.3)**

Source: Watson T, Bridges CB, Nelson NP, et al. Hepatitis B Vaccine 3-Dose Series Completion in Settings in which a High Proportion of Adults have Hepatitis B-Related Risk Factors – United States 2012-2015. Poster presented at: The National Immunization Conference; May 15-18, 2018; Atlanta, GA



The Science of Vaccines

Basic Vaccine Immunology

Antigens and Antibodies

- **Antigens** are molecules capable of stimulating an immune response. Each **antigen** has distinct surface features, or epitopes, resulting in specific responses. **Antibodies** (immunoglobulins) are Y-shaped proteins produced by B cells of the immune system in response to exposure to **antigens**.

Passive Immunity

- Immunity that develops after a person receives immune system components, most commonly antibodies, from another person. Immediate, short-term protection. (Examples: Breast milk, Immune globulin such as HBIG)

Active Immunity

- Immunity that develops after exposure to a disease-causing infectious microorganism or other foreign substance, such as following infection or vaccination. Delayed, long-term protection. (Example: 2 dose vaccination)

How Do We Define Protection following Vaccination?

Table 4. Some quantitative correlates of protection after vaccination.

Vaccine	Test	Correlate of protection	Reference(s)
Diphtheria	Toxin neutralization	0.01–0.1 IU/mL	[14]
Hepatitis A	ELISA	10 mIU/mL	[15]
Hepatitis B	ELISA	10 mIU/mL	[16]
Hib polysaccharides	ELISA	1 mcg/mL	[17]
Hib conjugate	ELISA	0.15 mcg/mL	[18]
Influenza	HAI	1/40 dilution	[19]
Lyme	ELISA	1100 EIA U/mL	[20]
Measles	Microneutralization	120 mIU/mL	[7]
Pneumococcus	ELISA; opsonophagocytosis	0.20–0.35 mcg/mL (for children); 1/8 dilution	[21, 22]
Polio	SN	1/4–1/8 dilution	[23]
Rabies	SN	0.5 IU/mL	[24]
Rubella	Immunoprecipitation	10–15 mIU/mL	[25, 26]
Tetanus	Toxin neutralization	0.1 IU/mL	[27]
Varicella	SN; gpELISA	⩾1/64 dilution; ⩾5 IU/mL	[28, 29]

NOTE. gp, glycoprotein; HAI, hemagglutination inhibition; Hib, *Haemophilus influenzae* type b; SN, serum neutralization.

Source: Vaccines, CID, 2008:47 (August 1)

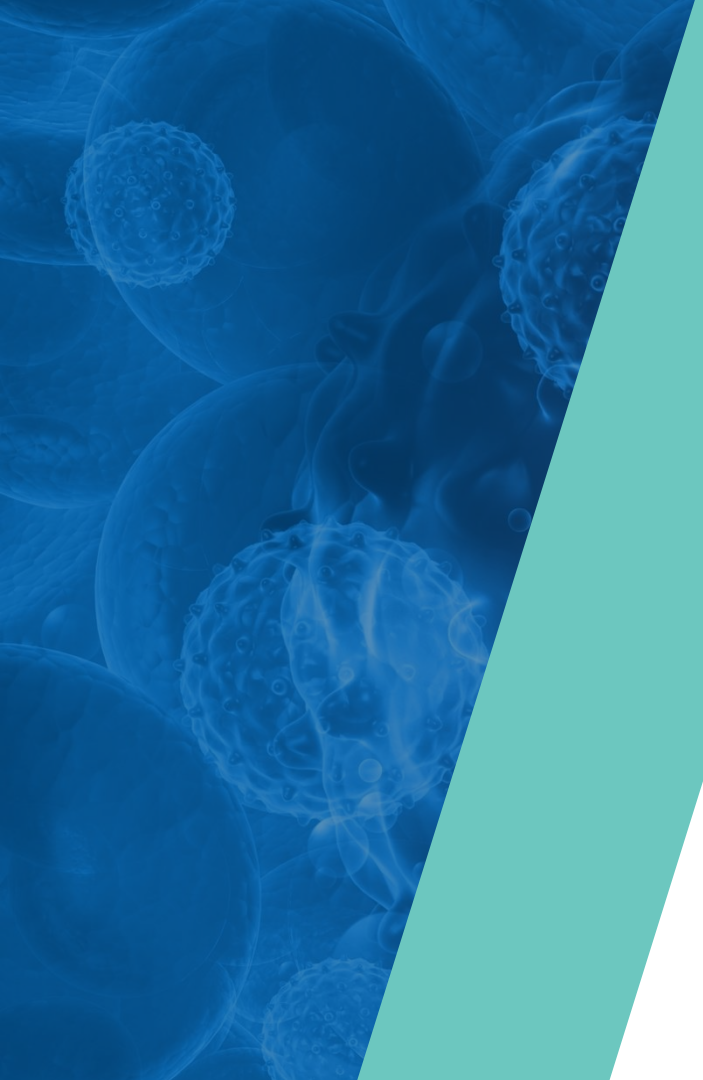
Antibody (anti-HBs) testing following vaccination: Who?

- **Health Care Workers and Public Safety Workers**
- **Chronic Hemodialysis Patients**
- **HIV-infected Persons and other immunocompromised individuals**
- **Sex partners of HBsAg-positive persons**
- **Not recommended following routine adult vaccination**
- **Different in Clinical Trials-EVERYONE was tested**

What is a Challenge Dose?

Challenge Dose of Vaccine

- Individual has a history of vaccination
- Used to determine vaccine-induced immune memory (anamnestic response)
- Single dose used in vaccinated individuals with <10 mIU/mL
- If the response is ≥10 mIU/mL, the individual is considered immune



Hepatitis B Vaccine Adjuvants

Adjuvants Enhance the Immune Response to a Vaccine

- **Immune responses to infection require collaboration between innate immune cells and antigen-specific T lymphocytes generated by the adaptive immune system[1]**
- **Vaccines contain the target Ag for the adaptive immune response and typically an adjuvant to enhance the immune response[1,2]**
- **Clinically, adjuvants are used to[2]**
  - Increase the fraction of subjects that become protectively immunized in a population
  - Increase seroconversion rates in hypo-responsive populations
  - Allow smaller doses of antigen
  - Permit immunization with fewer doses

Ag, antigen; APC, antigen presenting cells; HBsAg, hepatitis B surface antigen; MHC, major histocompatibility complex; Th, T helper.

1. McKee AS, et al. *BMC Biology*. 2010;8:37; 2. Coffman RL, et al. *Immunity*. 2010;33:492-503.

Examples of Commonly Used Adjuvants

Adjuvant	Composition	Vaccines
Aluminum	One or more of the following: amorphous aluminum hydroxyphosphate sulfate (AAHS), aluminum hydroxide, aluminum phosphate, potassium aluminum sulfate (Alum)	Anthrax, DT, DTaP, DTaP, DTaP-IPV, DTaP-IPV, DTaP-HepB-IPV, DTaP –IPV/Hib, Hep A , Hep B, HepA/Hep B, HIB, Japanese encephalitis, MenB, Pneumococcal, Td, Tdap
AS04	Monophosphoryl lipid A (MPL) + aluminum salt	HPV
MF59	Oil in water emulsion composed of squalene	Flu
$AS01_B$	Monophosphoryl lipid A (MPL) and QS-21, a natural compound extracted from the Chilean soapbark tree, combined in a liposomal formulation	Shingles
CpG 1018	Cytosine phosphoguanine (CpG), a synthetic form of DNA that mimics bacterial and viral genetic material	2 dose hepatitis b vaccine
No adjuvant		ActHIB, chickenpox, live zoster, measles, mumps & rubella, meningococcal, rotavirus, seasonal influenza, single antigen polio, yellow fever

First Non-Alum Adjuvanted Vaccine for the Prevention of HBV Infection in Adults-FDA Approved November 2017

Conventional 3-Dose HBV Vaccines

Alum adjuvants activate multiple inflammatory pathways in a broad range of cell types by inducing membrane disruption and cell stress, with no specific cellular receptor for alum[22]

2-Dose Vaccine With CpG 1018 Adjuvant[27]

CpG 1018 is highly specific and exerts its actions through a single immune receptor, Toll-like receptor (TLR) 9, which is an important innate immune receptor for sensing the presence of bacterial and viral DNA[22,24]

2-Dose Vaccine utilizes proprietary adjuvant technology that is based on synthetic DNA sequences and is believed to activate the innate immune response by engaging TLR9. This may induce a highly specific, helper T-cell response to generate memory T and B cells.[27]

SELECT IMPORTANT SAFETY INFORMATION

Do not administer 2-Dose Vaccine to individuals with a history of severe allergic reaction (eg, anaphylaxis) after a previous dose of any hepatitis B vaccine or to any component of the 2-Dose Vaccine, including yeast.

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.

CDC Recommended Adult Immunization Schedule for Ages 19 or Older, United States, 2019*

Vaccine	19 – 21 Years	22 – 26 Years	27 – 49 Years	50 – 64 Years	≥65 Years
Haemophilus influenzae type b (Hib)	1 or 3 doses depending on indication				
Hepatitis A	2 or 3 doses depending on vaccine				
Hepatitis B	**2 or 3 doses depending on vaccine**				
Influenza inactivated or Influenza recombinant	1 dose annually				
Pneumococcal polysaccharide	1 or 2 doses depending on indication				1 dose
Varicella	2 doses (if born 1980 or later)				
Zoster recombinant				2 doses	

***List shown does not include all recommended adult vaccines.**

United States Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html.Accessed: March 14, 2019.

Real world efficacy = “eSPR”

Effective Seroprotection as a Measure of Real-world Efficacy

- The effective (“real world”) seroprotection rate (eSPR) = clinical study derived SPR by dose adjusted by compliance rates by dose over a given period of time

- The effective SPR also includes patients who achieved seroprotection despite not completing the entire regimen.

Estimate of Effective SPR in Adults

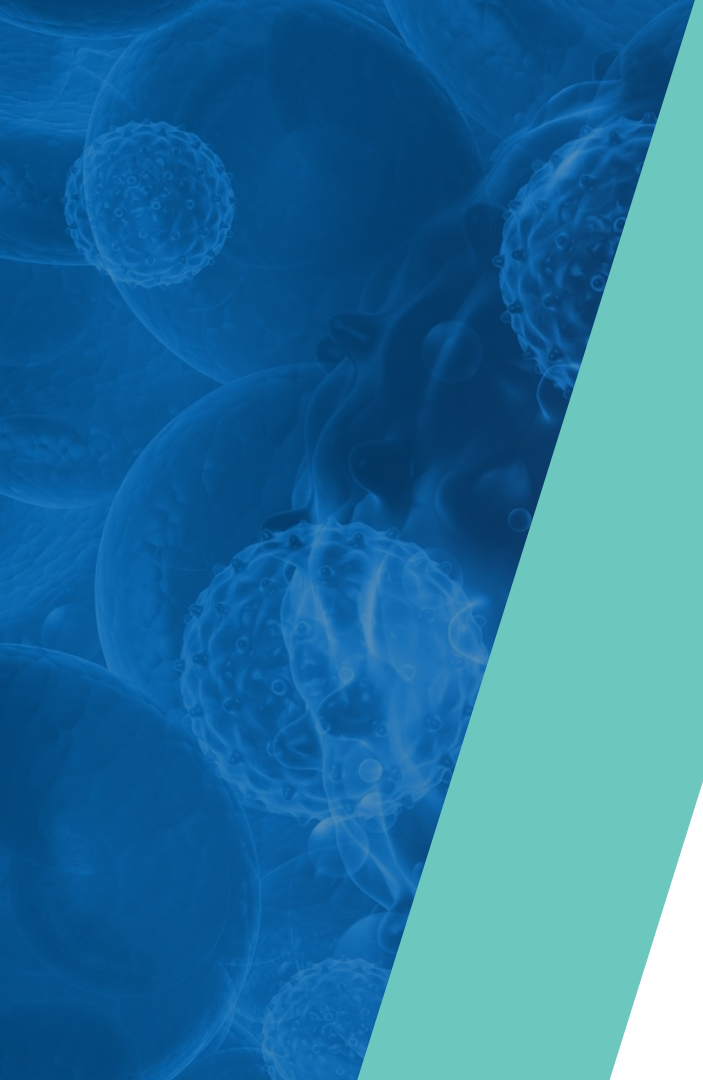
SPR vs. Estimate of Effective Seroprotection Rates in Adults After Receiving 1, 2, or 3 Doses of HepB Vaccine Using Compliance Data from Range of Sources

	2-Dose SPR[17]	3-Dose SPR[17]	Difference in SPR
	95.7%	79.5%	16.2%
Compliance Data Source	**2-Dose Effective SPR[13]**	**3-Dose Effective SPR[13]**	**Difference in Effective SPR**
Nelson[14]	81.3%	49.9%	31.4%
Bruxvoort[15]	68.1%	36.0%	32.1%
Bridges[16]	45.0%	17.0%	28.0%

SELECT IMPORTANT SAFETY INFORMATION

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of 2-Dose vaccine.

Please see additional Important Safety Information throughout this presentation and accompanying full Prescribing Information.



Special Populations: HIV & HCV

HIV and Hepatitis B- The Compounding Effect [18]

- 1 in 10 people living with HIV are coinfected with hepatitis B virus (HBV)
- HBV progresses faster and causes more liver-related health problems
- HBV infection less likely to spontaneously cure.
- HBV infection has increased rates of cirrhosis (10–20%),
- Higher risk of hepatocellular carcinoma and liver-related death.
- Hepatotoxic side effects of highly active antiretroviral therapy (HAART) are increased with HBV coinfection

Maine Medical Center Retrospective Study

Maine Medical Center
MaineHealth

EFFECTIVENESS OF THE NOVEL, ADJUVANTED HEPATITIS B VACCINE AMONG HIV AND HCV PATIENTS

0605

Brooke M Kimball[1], Katy L Garrett[1]
[1]Maine Medical Center, Portland, Maine

BACKGROUND

- People living with HIV or chronic hepatitis C virus (HCV) have diminished immune responses to hepatitis B virus (HBV) vaccination.
- The 3-dose HBV vaccine series has a positive response rate upwards of 85%[1] in the general population, but that same series only provides immunity for 20-70%[2] of people living with HIV and 40-60%[3] for the HCV population, emphasizing the need for advancement.
- A new, adjuvanted, 2-dose HBV vaccine series (HepB-CpG) demonstrated an improved immune response (>90%)[1] in non-HIV and non-HCV cohorts, yet the effectiveness in HIV and HCV patients is unknown.
- This study evaluated the immune response to HepB-CpG among HIV and HCV patients at an outpatient virology clinic.

METHODS

- HIV and HCV patients who received at least one dose of HepB-CpG between October 1, 2018 and September 30, 2019 were included for analysis.
- HBV vaccinations were given a minimum of 4 weeks apart and timed with routine clinical appointments. HBV surface antibody was tested at least 4 weeks after last immunization with a result ≥10mIU/mL deemed immune.
- Population characteristics and overall effectiveness were evaluated using descriptive statistics and represented as n(%) or median[IQR] as appropriate.

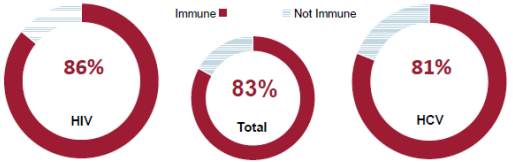
	HIV (n=41)	HCV (n=96)	TOTAL (n=137)
MALE	24 (59)	66 (69)	90 (66)
WHITE	23 (56)	93 (97)	116 (85)
AGE	50 [46-60]	54 [37-60]	53 [38-61]
WEIGHT, kg	81 [71-96]	85 [74-100]	83 [74-100]
DIABETIC	5 (12)	15 (15)	20 (15)
SMOKER	7 (17)	51 (53)	58 (43)
HIV VIRAL LOAD <20	26 (63)	-	26 (63)
ABSOLUTE CD4 COUNT	581 [376-798]	-	581 [376-798]

Novel, **two-dose Hepatitis B vaccine** *confers robust immune response* in **HIV** and **HCV** patients

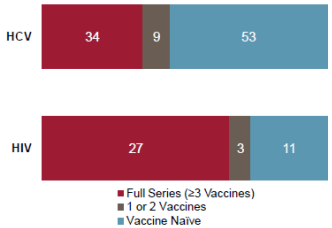
RESULTS

- Currently, 29 (71%) of the HIV cohort have been tested for immunity and 25 (86%) are immune. Another 42 (44%) have been tested in the HCV cohort and 34 (81%) are immune.
- Of the 71 (52%) that were tested for immunity, 16 (23%) were found to be immune after just one dose, and a total positive immune response in 59 (83%).
- Of the 25 immune patients with HIV, 17 (68%) were non-responders to a full, prior HBV vaccination series.
- No adverse events reported. From the HCV cohort 3 patients have died due to unrelated causes.

IMMUNE RESPONSE



NUMBER OF PATIENTS PREVIOUSLY VACCINATED



CONCLUSIONS

- Analysis shows an overall immune response to HepB-CpG of 83% with 52% of the patient population being tested for immunity thus far.
- The immune response is considerably higher than historical data using the three-dose vaccine, and is demonstrating a response in previous non-responders.
- As part of a robust immunization program to protect HIV and HCV patients, HepB-CpG should be considered as an alternative to the traditional HBV vaccination series.
- A larger, prospective study is needed to determine generalizability of results.

ACKNOWLEDGEMENTS

We wish to thank the patients in this study without whom these data would not be possible as well as all the staff at Gilman Clinic for their assistance and encouragement.

REFERENCES

1. Halperin SA, et al. *Vaccine* 2012;30:2556-63
2. Van den Berg R, et al. *AIDS Rev*. 2009;11:157-64
3. Moorman JP, et al. *Vaccine*. 2011;29(17):3169-3176

ADDITIONAL KEY INFORMATION

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INDICATION: HEPLISAV-B [Hepatitis B Vaccine (Recombinant), Adjuvanted] is indicated for the prevention of infection caused by all known subtypes of hepatitis B virus in adults 18 years of age and older

Methods

The dosing regimen described in this study has not been approved or cleared by the FDA.

41 HIV and 96 HCV patients who received at least one dose* of HepB-CpG between October 1, 2018 and September 30, 2019 were included for analysis.

For those who received two doses, HBV vaccinations were given a minimum of 4 weeks apart and timed with routine clinical appointments. HBV surface antibody was tested at least 4 weeks after last immunization with a result ≥10mIU/mL deemed seroprotected.

Population characteristics and overall effectiveness were evaluated using descriptive statistics and represented as n(%) or median[IQR] as appropriate.

	HIV (n=41)	HCV (n=96)	TOTAL (N=137)
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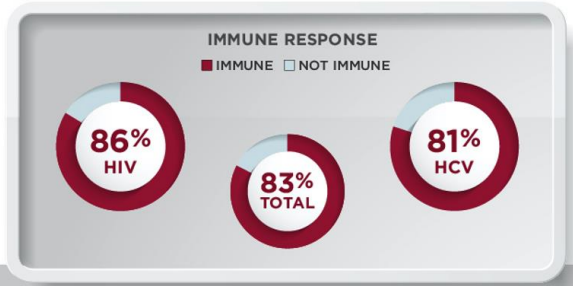
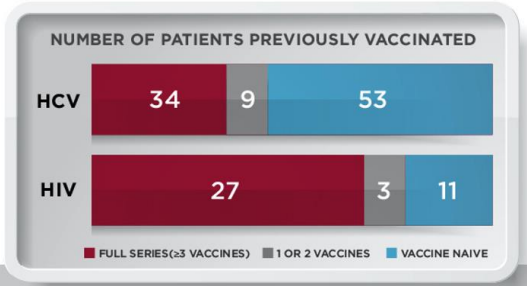
SMOKER	7 (17)	51 (53)	58 (43)
HIV VIRAL LOAD <20	26 (63)	—	26 (63)
ABSOLUTE CD4 COUNT	581 [376-798]	—	581 [376-798]

* The FDA approved dosing regimen for the 2-dose vaccine is 2 doses at least one month apart. Immune response data in this study represent a collective response from patients who received the correct dosing regimen, as well as from patients who only received one dose. All patients should receive 2 doses of the 2-dose vaccine.

Results

- Currently, 29 (71%) of HIV cohort have been tested for immunity and 25 (86%) were found to be immune. Another 42 (44%) have been tested in the HCV cohort and 34 (81%) were found to be seroprotected.
- Of the 71 (52%) that were tested for immunity, 59 (83%) were found to have a total positive immune response, and 16 (23%) were seroprotected after just one dose.
- Of the 25 immune patients with HIV, 17 (68%) were non-responders to a full, prior HBV vaccination series.*
- No adverse events reported. From the HCV cohort 3 patients have died due to unrelated causes. 2-Dose vaccine clinical trials, the most common local reaction was injection site pain (23% - 39%). The most common systemic reactions were fatigue (11% - 17%) and headache (8% - 17%).





*The data in this study does not include the baseline SPR of patients who were previously vaccinated with a partial or complete regimen of a 3-dose vaccine.

UCSF Single Center Study [20]

BRIEF REPORT: CLINICAL SCIENCE: PDF ONLY

2-Dose Vaccine Seroprotection in People with HIV

A Single-Center Experience

Schnittman, Samuel R. MD[1]; Zepf, Roland PhD, RN[2,3]; Cocohoba, Jennifer PharmD[4]; Sears, David MD[2]

Author Information

JAIDS Journal of Acquired Immune Deficiency Syndromes: November 09, 2020 - Volume Publish Ahead of Print - Issue -
doi: 10.1097/QAI.0000000000002573

- University of California, San Francisco, San Francisco, CA, USA
- Quaternary care center HIV clinic
- Retrospective cohort study evaluated PWH aged >18 years without current HBV seroprotection who were administered 2-Dose Vaccine
- 64 participants in total

Schnittman SR, et al. *J Acquir Immune Defic Syndr.* 2020 Nov 9. Online ahead of print.

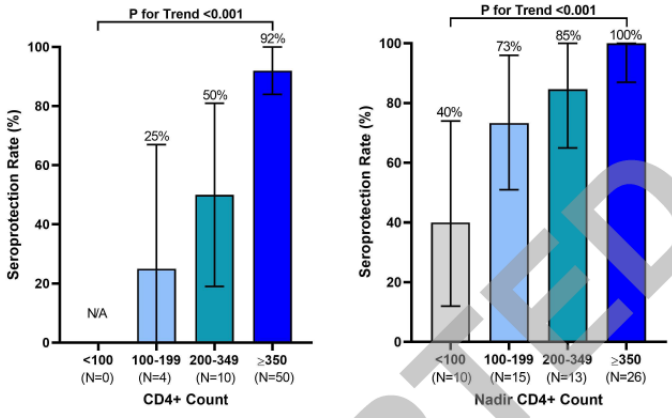
NOTE: The dosing regimen used in this study has not been approved by the FDA.

UCSF Single Center Study [20]

2-Dose Vaccine Seroprotection Rates by Subgroups

Subgroup	Responders	Percent (95% CI)	P Value
Demographics and Comorbidities			
Age			
<65 years	40/49	82% (71-92%)	1.00
≥65 years	12/15	80% (60-100%)	
Gender			
Male	43/52	83% (72-94%)	0.68
Female	9/12	75% (51-100%)	
BMI			
BMI <25	15/21	71% (52-91%)	0.19
BMI ≥25	37/43	86% (76-96%)	
Diabetes Mellitus			
No	42/52	81% (70-91%)	1.00
Yes	10/12	83% (62-100%)	
CKD III-IV			
No	49/61	80% (70-90%)	1.00
Yes	3/3	100% (29-100%)	
Current Smoking			
No	42/51	82% (72-93%)	0.70
Yes	10/13	77% (54-100%)	
HIV Viral Load (cells/mm^3)			
<40	46/58	79% (69-90%)	0.58
≥40	6/6	100% (54-100%)	
Non-HIV immunosuppression			
No	48/56	86% (77-95%)	0.03
Yes	4/8	50% (15-85%)	
HBV Vaccination Status and Serologies			
Prior HBV vaccine	35/43	81% (70-93%)	*
Prior anti-HBs	4/6	67% (22-96%)	0.31
No prior anti-HBs	31/37	84% (72-96%)	
No prior HBV vaccine	17/21	81% (64-98%)	*
Prior anti-HBc	6/7	86% (60-100%)	1.00
No prior anti-HBc	11/14	79% (57-100%)	

Seroprotection Rate by Current and Nadir CD4+ Count



Schnittman SR, et al. *J Acquir Immune Defic Syndr.* 2020 Nov 9. Online ahead of print.

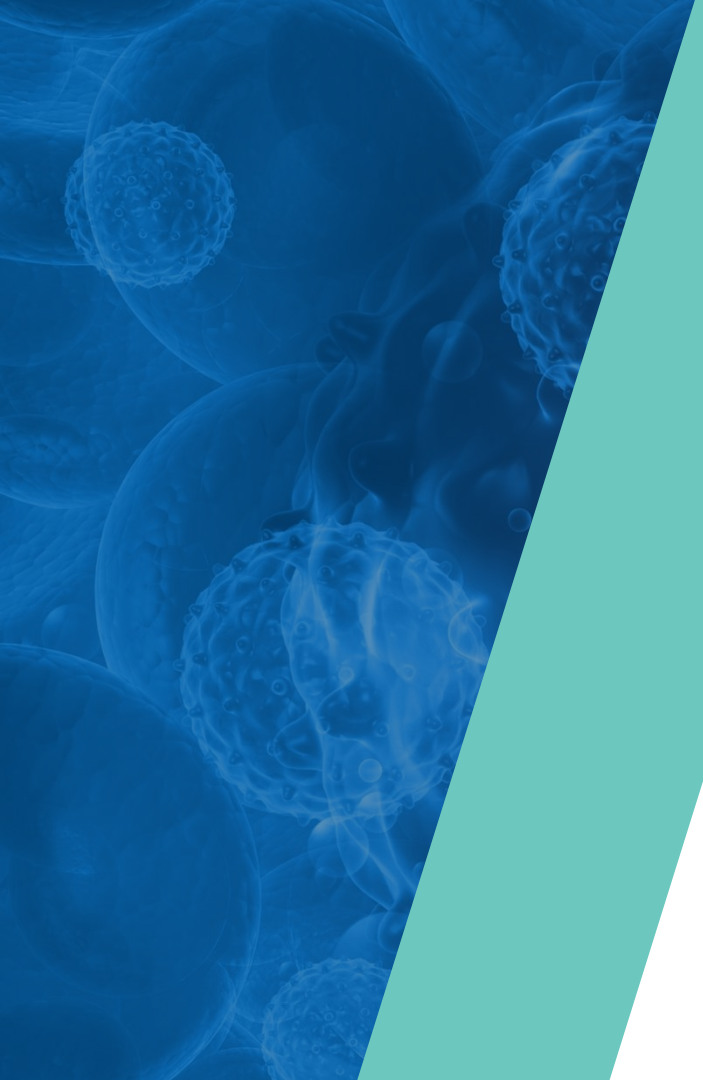
HIV Data - Putting it all together

- **Two recent separate studies across the US have shown an increased SPR rate in the HIV population with the 2-dose vaccine versus historical SPRs with 3-dose vaccine**

- **Due to the low # of patients in each of these HIV studies (29 & 64 respectively), more data is needed in this difficult to vaccinate population to further corroborate these results**

2-Dose Vaccine Important Safety Information:

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the 2-Dose Vaccine.



Chronic Liver Disease

Digestive Diseases and Sciences
https://doi.org/10.1007/s10620-020-06437-6

ORIGINAL ARTICLE

Check for updates

Two-Dose Hepatitis B Vaccine Results in Better Seroconversion Than Three-Dose Vaccine in Chronic Liver Disease

Waseem Amjad[1] · Joseph Alukal[1] · Talan Zhang[1] · Anurag Maheshwari[1,2] · Paul J. Thuluvath[1,2]

Received: 25 March 2020 / Accepted: 21 June 2020

Abstract

Background The efficacy of the two-dose hepatitis B virus (HBV) vaccine in patients with chronic liver disease (CLD) is unknown.

Aims To compare the immunogenicity achieved with the 2-dose vaccine and the conventional 3-dose vaccine in patients with CLD, and to identify factors that predict seroconversion.

Methods We retrospectively identified all adults who completed the 2-dose or 3-dose vaccine regimens from August 1, 2015, to January 31, 2019. Post-vaccination immunity was assessed by quantitative HBV surface antibody (HBsAb) measurement.

Results We identified 166 patients (106 3-dose and 60 2-dose) with chronic liver disease (mean age 59.0 ± 11.3 years, 52% male, 34% cirrhosis, mean MELD score of those with cirrhosis 10.1 ± 5.4) who had completed the vaccinations and had data available on post-vaccination HBsAb levels at least 2 months after completion of the vaccine regimen. Seroprotective HBsAb levels (> 10 mIU/ml) were achieved in 63% with 2-dose and in 45% with 3-dose ($p = 0.03$). Univariable analysis showed that age ($p = 0.01$), insurance ($p = 0.02$), renal failure ($p = 0.02$), COPD ($p = 0.05$), and cirrhosis ($p < 0.01$) had a significant effect on achieving immunogenicity. On multivariable analysis, patients with cirrhosis (adjusted odds ratio [aOR]: 0.27, 95% CI 0.13–0.55), COPD (aOR: 0.06, 95% CI 0.01–0.56), or renal failure (aOR 0.36, 95% CI 0.14–0.93) had a lower likelihood of achieving immunity, and patients who received the 2-dose vaccine had a 2.7-fold greater likelihood of achieving immunity than those who received the 3-dose vaccine (aOR: 2.74, 95% CI 1.31–5.71).

Conclusion The 2-dose recombinant hepatitis B vaccine resulted in better seroconversion than the 3-dose vaccine. Cirrhosis, COPD, and renal failure were associated with a lower likelihood of achieving immunogenicity.

- **60 2-Dose Vaccine patients & 106 3-Dose Vaccine patients were analyzed**
  - 63% of the HEP patients achieved seroprotection (p=0.03)
  - 45% of the ENG patients achieved seroprotection (p=0.03)

- **Patients who received 2-Dose Vaccine had a 2.7-fold greater likelihood of achieving immunity than those who received 3-Dose Vaccine. (aOR: 2.74, 95% CI 1.31 – 5.71)**

Important Safety Information:

Hepatitis B has a long incubation period. The 2-Dose Vaccine may not prevent hepatitis B infection in individuals who have an unrecognized hepatitis B infection at the time of vaccine administration.

Cost Considerations and Health Outcomes

2-DOSE VACCINE IS COST-EFFECTIVE VERSUS 3-DOSE VACCINE

An independent cost-effectiveness analysis by the Division of Viral Hepatitis at the CDC showed that the 2-Dose Vaccine is dominant versus the 3-Dose Vaccine across the majority of ACIP Risk Groups[21]

	Costs/person			QALYs/person			ICER ($/QALY)
	2-Dose Vaccine	3-Dose Vaccine	Difference	2-Dose Vaccine	3-Dose Vaccine	Difference	
Diabetics	$416.74	$421.38	-$4.64	15.0832	15.0827	-0.0005	Dominant
CKD patients	$631.62	$679.90	-$48.28	10.2971	10.2952	-0.0019	Dominant
Older adults	$409.01	$409.03	-$0.02	10.6495	10.6495	0.0000	Dominant
Obese patients	$421.08	$430.21	-$9.13	18.9796	18.9786	-0.0010	Dominant
Non-responders	$512.11	$497.95	$14.16	16.5831	16.5826	-0.0005	$27,470
HIV patients	$891.62	$1,368.08	-$476.46	16.8959	16.8496	-0.0463	Dominant
People who inject drugs (PWID)	$3,657.15	$8,403.93	-$4,746.78	23.9608	23.2534	-0.7074	Dominant

In Conclusion

HEPLISAV-B®
Hepatitis B Vaccine (Recombinant), Adjuvanted

Real-World Considerations Associated With HBV Vaccination

Successfully vaccinating adults at risk for HBV is an ongoing challenge[12]

- The purpose of HBV vaccination is to maximize seroprotection in a susceptible population[12]
- Achieving this goal is influenced by 3 factors[12]:

Compliance with dosing regimen

Speed at which a vaccine generates seroprotection in individuals

Immunogenicity in populations with known reduced SPRs

- Conventional 3-dose HBV vaccines may be limited by poor adherence to the 6-month vaccination schedule[14]

ONLY ABOUT 25% OF ADULTS AGED 19 AND OLDER ARE FULLY VACCINATED AGAINST HEPATITIS B[22]

Thank You!

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HEPLISAV-B®
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Appendix

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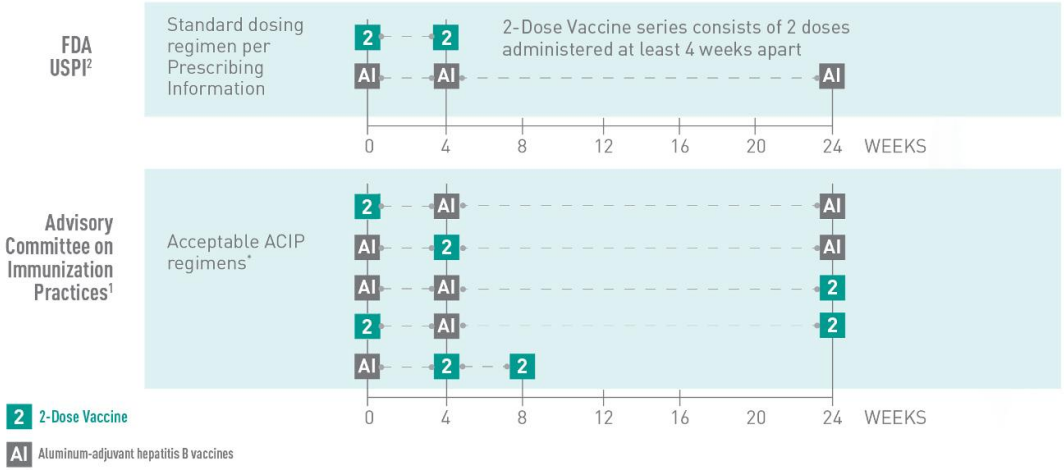
Interchangeability and Dosing Schedule

ACIP RECOMMENDATIONS FOR INTERCHANGEABILITY AND DOSING SCHEDULE SCENARIOS FOR THE 2-DOSE VACCINE WITH AN ALUMINUM ADJUVANT HEPATITIS B VACCINE FROM OTHER MANUFACTURERS TO COMPLETE A DOSING REGIMEN



Data are limited on the safety and immunogenicity effects when the 2-Dose Vaccine is interchanged with hepatitis B vaccines from other manufacturers. The CDC's ACIP guidance for interchangeability indicates that when feasible, the same manufacturer's vaccines should be used to complete a hepatitis B series. A 2-Dose Vaccine series only applies when both doses in the series consist of the 2-Dose Vaccine. A dosing regimen consisting of 2 different vaccine products should consist of a total of 3 doses in the possible combinations shown above. Adhere to minimum windows: 4 weeks between dose 1 and 2; 8 weeks between dose 2 and 3; 16 weeks between dose 1 and 3. Doses administered at less than the minimal interval should be repeated. However, a series containing 2 doses of the 2-Dose Vaccine administered at least 4 weeks apart is valid, even if the patient received a single earlier dose from another manufacturer.

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