Hepatitis B Prevention & Strategies for Increasing Vaccination

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West Virginia Immunization Network- June 9, 2023

Session Description

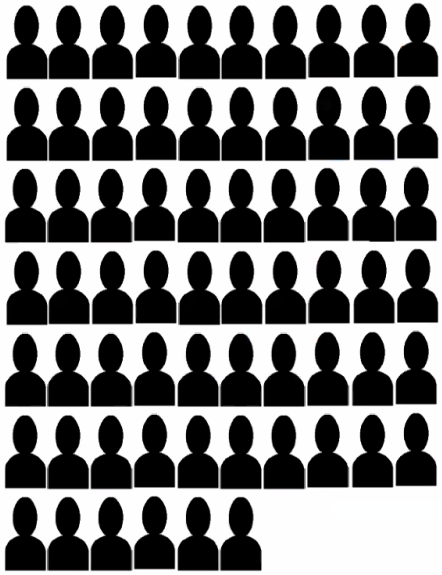
- this session will focus on the high rate of acute hepatitis B in West Virginia and its association with our drug epidemic
- routes of acquisition will be reviewed
- prevention through vaccination will be discussed, including the birth-dose vaccination strategy and the various vaccine formulations available

Objectives

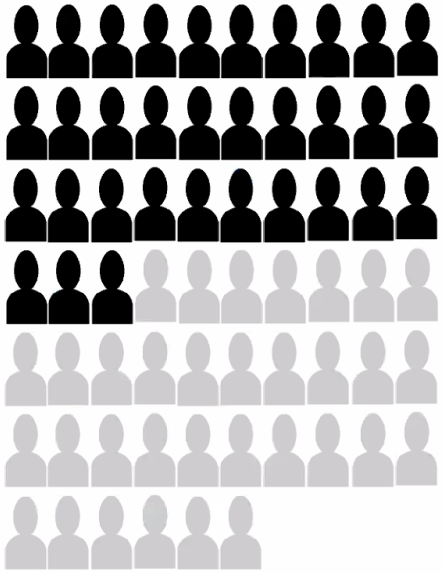
- list the ways that hepatitis B can be acquired
- describe the birth-dose vaccination strategy
- describe a number of approaches that can improve vaccination uptake

HBV Epidemiology in U.S.

- prevalence of chronic HBV infection is 0.35% ~ 1 million people
  - 15-25% those who become chronically ill die prematurely from cirrhosis or hepatocellular carcinoma (HCC)
- 20,000 new infections each year – most will *not* become chronic
- most HBV infections result from:
  - sex, both heterosexual & MSM
  - injection drug use
  - occupational exposure to blood and infectious body fluids
  - household contacts of persons with chronic infection
  - blood-rich environments such as hemodialysis units



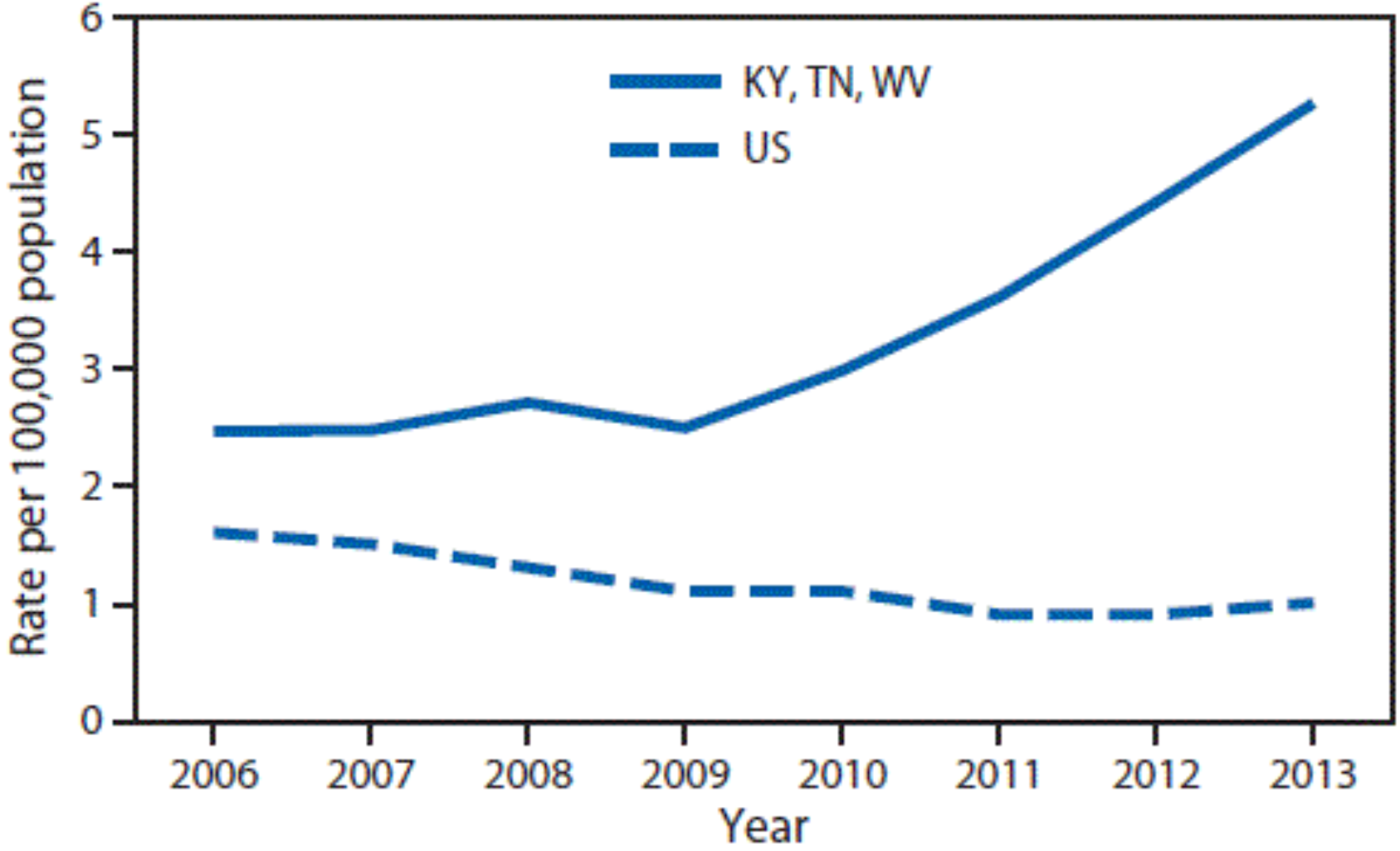
There are **660,000** people with hepatitis B in the U.S.



50% are aware of their infection

Bixler, et al. Hepatology Communications 2023.

HBV Epidemiology in Central Appalachia



WestVirginiaUniversity.

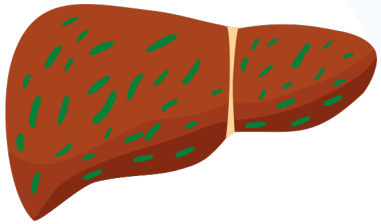
WV has had the highest rate of acute HBV in the U.S. for well over a decade!!

Hepatitis B Virus (HBV) Transmission

- blood and body fluids are the primary transmission vehicles
  - virus is present in **all** body fluids *except stool*
    - saliva, sweat, tears, breast milk, semen, pathologic effusions
  - can remain infectious for 7 days outside of body
- modes of transmission
  - percutaneous or permucosal exposure
  - sexual contact with an infected person
  - perinatal transmission from an infected mother to newborn
  - foodborne
- incubation period
  - ranges from 6 weeks to 6 months

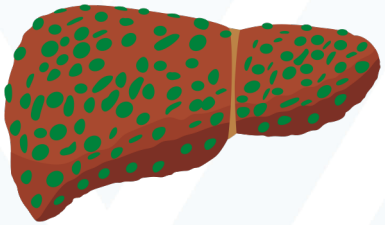
HBV Disease Progression

Chronic Infection



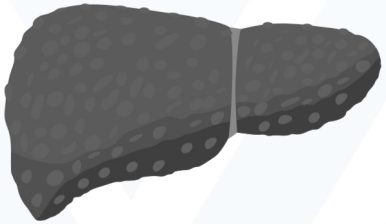
- **300 million** chronically infected worldwide
- **10% diagnosed**
- **<1%** receive **treatment**
- **~1%** of those receiving TX with current options achieve functional cure[1]

Cirrhosis/HCC



- **8% to 20%** of patients progress to cirrhosis and/or hepatocellular carcinoma (HCC)[2]

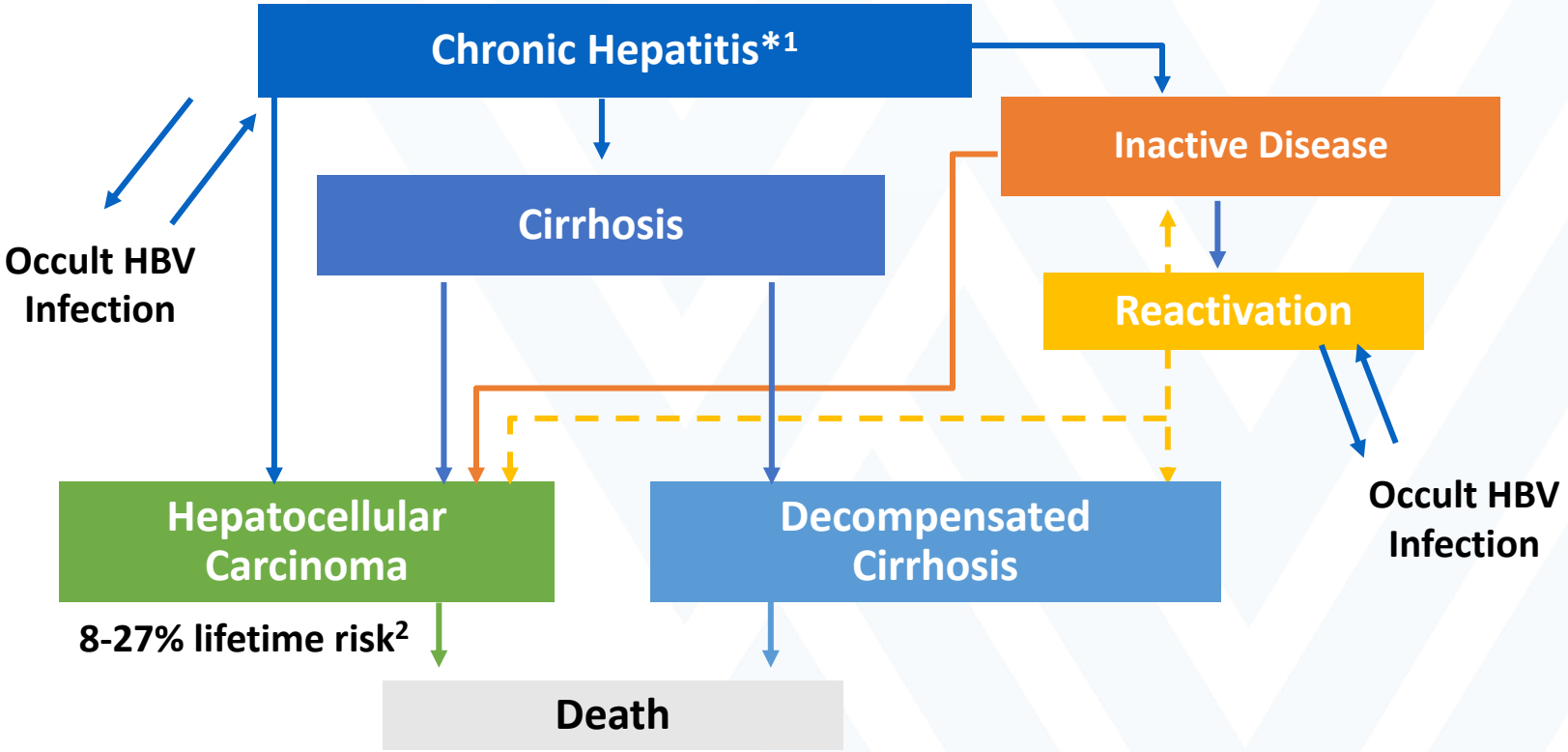
Mortality



- **~1 million** people/yr[3]
- **2** people/minute[4]

1. Hardstock. Patient Prefer Adherence. 2020;14:613. 2. Alqahtani. Hepatoma Res 2020;6:58. 3. Yuen. Nature Medicine. 2021;27:1725. 4. hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/.

HBV Disease Progression and Impact



***failure to clear HBsAg 6 mo after acute infection**

1. Buckley. Eliminating the public health problem of hepatitis B and C in the United States: phase one report. 2016.
2. Huang. JCO. 2011;29:3643.

History of HBV Vaccines

- 1982: first HBV vaccine, derived from the plasma of chronically infected individuals
- 1986: first genetically engineered vaccine based on recombinant HBsAg-- replaced plasma-derived version
  - >95% protection in healthy infants, children, and young adults, but adults >40 y/o are less likely to achieve a seroprotective response
  - response rate drops to 60%–70% in adults ≥60 y/o
  - obesity, smoking, HIV infection, genetic factors, and concomitant chronic disease may also result in poorer responses
- 2017: approval of Heplisav-B, first HBV vaccine with an immune adjuvant to boost response to vaccine (for ≥ 18 y/o)

Pattyn J, et al. The Journal of Infectious Diseases 2021;224(S4):S343–51

History of HBV Vaccination Strategies-1

- strategies were initially focused on vaccination of high-risk groups: HCWs exposed to blood, staff & residents in institutions for the developmentally disabled, & hemodialysis staff and pts[1]
- paradoxically, HBV increased by 37% in decade after 1982 because the limited focus on high-risk groups that received >85% of administered vaccine, yet accounted for only 5-10% of acute cases[2]
  - sources for most cases: IDU (28%), heterosexual contact with infected persons or multiple partners (22%), and MSM (9%)[3]
  - these individuals may be difficult to reach and are often infected before vaccination
  - plus, ≥30% with acute HBV do not have identifiable risk factors and are missed by a high-risk approach

1. Pattyn J, et al. The Journal of Infectious Diseases 2021;224(S4):S343–51. 2. Lawrence MH, Goldstein MA. Hepatitis B Immunization in Adolescents. J Adolesc Health 1995; 17:234-243. 3. MMWR 2/9/90; 39(RR-2);1-2.

History of HBV Vaccination Strategies-2

- plus, ≥30% with acute HBV do not have identifiable risk factors and are therefore missed by a high-risk approach
- in 1990, ACIP also recommended vaccination for those with occupational, travel, sexual, IDU risks[3]
- public health experts started to discuss a strategy of universal hepatitis B immunization worldwide
- Nov. 1991- ACIP recommended the "birth dose" strategy for all infants starting at birth (universal vaccination) because perinatal/early postnatal transmission are major causes of chronic HBV worldwide & in persons from endemic areas
  - also recommended 'catch-up vaccination' for adolescents who did not receive the hepatitis B vaccine during infancy

1. Pattyn J, et al. The Journal of Infectious Diseases 2021;224(S4):S343–51. 2. Lawrence MH, Goldstein MA. Hepatitis B Immunization in Adolescents. J Adolesc Health 1995; 17:234-243. 3. MMWR 2/9/90; 39(RR-2);1-2.

HBV Birth Dose Vaccination Strategy

- in 1991, U.S. Advisory Committee on Immunization Practices (ACIP) recommended starting HBV vaccination for all infants at birth before hospital discharge *or* at age 1-2 months
- this was primary focus of a strategy to eliminate HBV transmission in the U.S.
- recommended timing of 1st dose administration to infants has evolved since then
  - in 2002, ACIP indicated a preference for 1st dose to be given to newborns *before* hospital discharge
  - in Dec. 2005, ACIP revised its recommendation to specify that all medically stable newborns who weigh ≥2,000 g (4.4 lbs) receive their 1st dose before hospital discharge

Why should my baby get the hepatitis B shot?

- Protects your child from against hepatitis B, a potentially serious disease.
- Protects other people from the disease because children with hepatitis B usually don't have symptoms, but they may pass the disease to others without anyone knowing they were infected.
- Prevents your child from developing liver disease and cancer from hepatitis B.
- Keeps your child from missing school or child care and you from missing work.

When should my child get the shot?

One dose at each of the following ages:

1st Dose	Shortly after birth
2nd Dose	1 – 2 months
3rd Dose	6 – 18 months

Recent Updates to Birth Dose Strategy

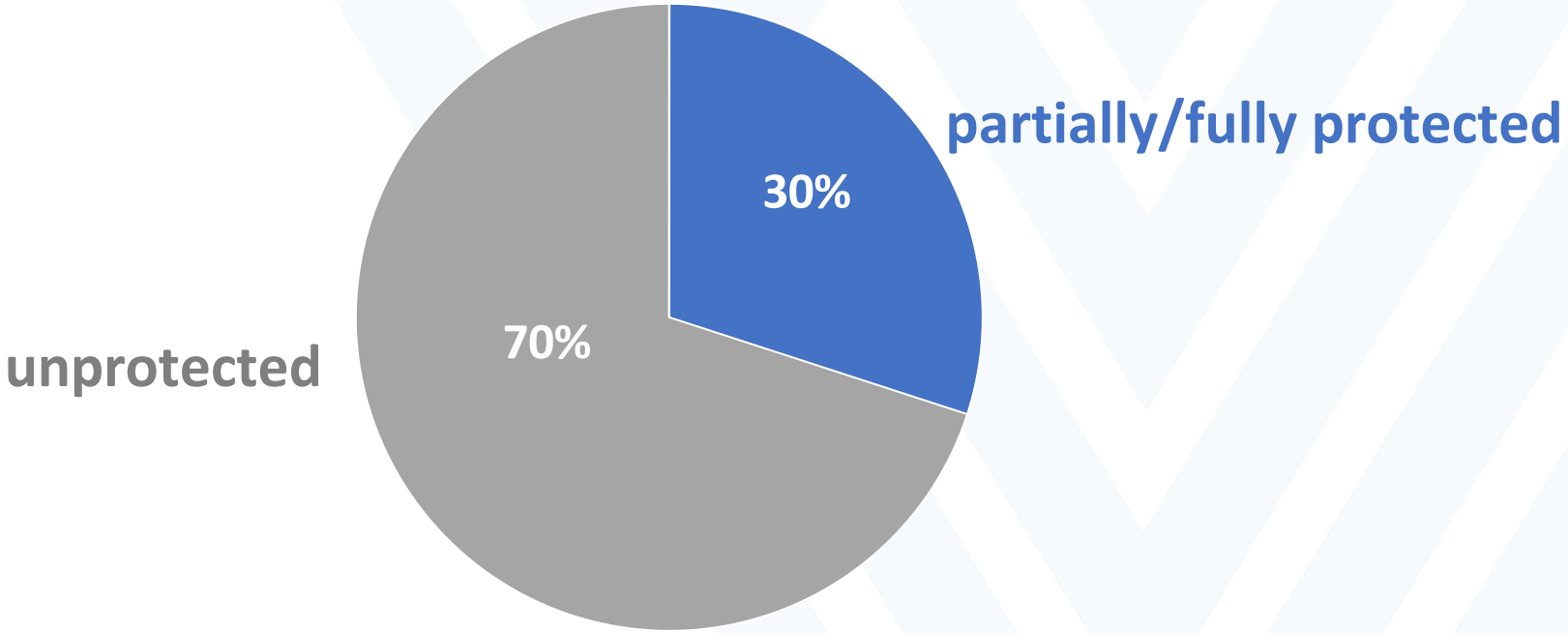
- Aug. 1995: ACIP recommended ‘catch-up’ vaccination for all 11-12 y/o not previously vaccinated
- Jan. 1999: ACIP recommended vaccination all children 0-18 y/o not previously vaccinated
- Jan. 2002: birth dose strategy preferred by ACIP

1. Lawrence MH, Goldstein MA. Hepatitis B Immunization in Adolescents. J Adolesc Health 1995; 17:234-243.

So where does that leave us?

Adult HBV Vaccination: Where Are We Now?

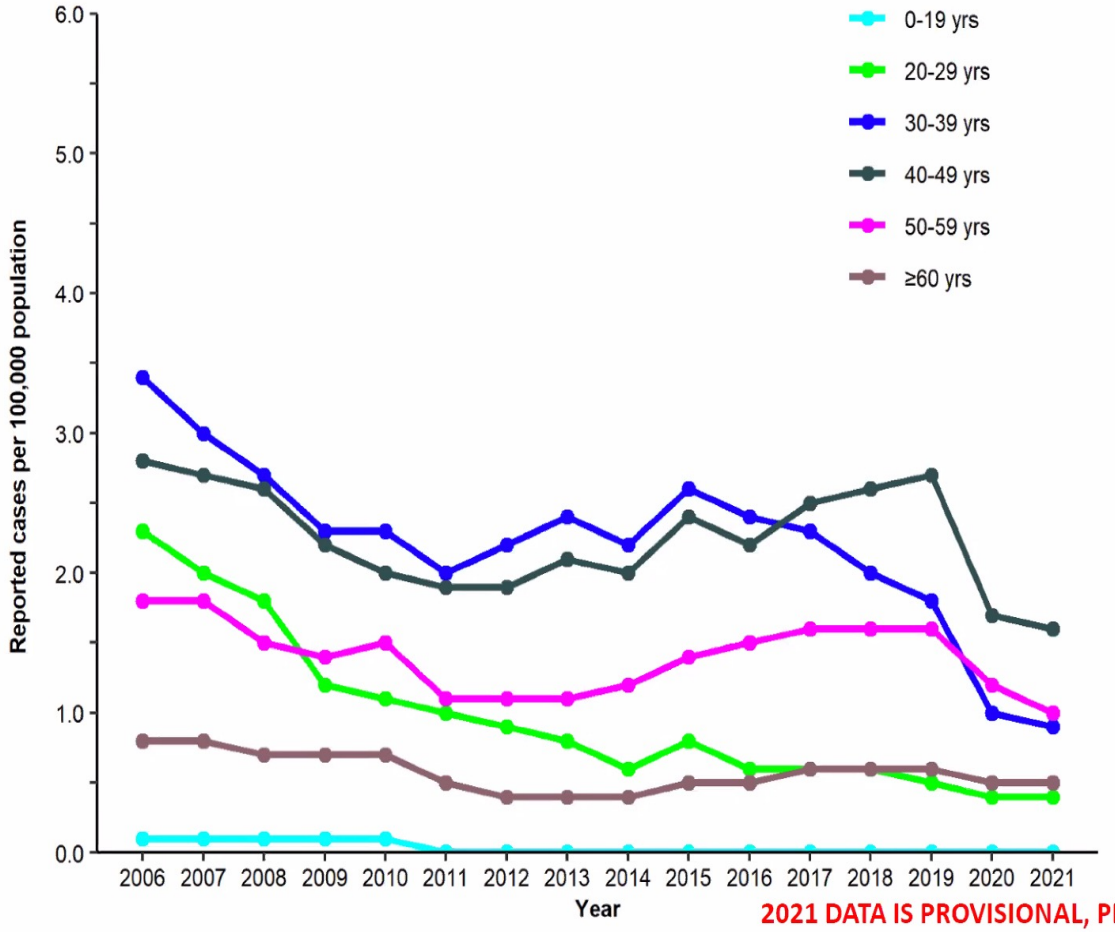
- 70% of US adults are **unprotected** against HBV[1,2]
- **the greatest remaining challenge to HBV prevention is vaccination of high-risk adults**



1. nfid.org/wp-content/uploads/2019/08/cta-hep-b-at-risk-adults.pdf.
2. Lu. MMWR Surveill Summ. 2021;70:1.

Approximately 73% of all acute hepatitis B cases reported to CDC in 2021 occurred among persons aged 39-59 years

Rates of reported cases of acute hepatitis B virus infection, by age group — United States, 2006-2021



2021 DATA IS PROVISIONAL, PRE-PUBLICATION -- DO NOT SHARE

Paradigm Shift in Screening & Vaccination Recommendations

- universal opt-out screening at least once in lifetime for everyone ≥ 18 y/o **NEW**
- screening in pregnancy
  - 1st trimester of each pregnancy, regardless of vaccination status or testing history
  - for ≥ 18 y/o, order 3-test panel (HBsAg, HBsAB, HBcAB) unless they have been screened with 3-test panel in past **NEW**
  - check HBsAg only in adults screened with prior 3-test panel and no subsequent risk
- risk-based testing
  - all individuals of any age with h/o incarceration, hepatitis C, STIs or multiple sex partners **NEW**

The following persons have an increased risk for HBV infection:

- **People currently or formerly incarcerated in a jail, prison, or other detention setting [*New recommendation*]**
- **People with a history of sexually transmitted infections or multiple sex partners [*New recommendation*]**
- **People with current or past hepatitis C virus infection [*New recommendation*]**
- **Anyone who requests hepatitis B testing [*New recommendation*]**
- People born in regions with HBV prevalence ≥2%
- U.S.-born people not vaccinated as infants whose parents were born in regions with HBV prevalence ≥8%
- People with HIV infection
- People with current or past injection drug use
- Men who have sex with men
- Infants born to HBsAg positive persons
- Household, needle-sharing, or sexual contacts of people with known HBV infection
- Patients receiving predialysis, hemodialysis, peritoneal dialysis, or home dialysis
- People with elevated alanine aminotransferase or aspartate aminotransferase levels of unknown origin

2023 Updated CDC Vaccination Recommendations

- **should** receive HBV vaccine:
  - adults 19-59 y/o
  - adults ≥60 y/o **with risk factors** for HBV infection

- **may** receive HBV vaccine:
  - adults ≥60 y/o **without** risk factors for HBV infection

Risk Factors

- chronic liver disease
- infection with HIV
- sexual exposure risk
- blood exposure risk:
  - percutaneous or mucosal
- current/recent IDU
- incarcerated persons
- travel to countries where HBV is endemic (high or intermediate)

cdc.gov/vaccines/schedules/hcp/imz/adult.html#note-hepb

2022 ACIP Recommendations
Adult HepB Vaccination

- **The following groups *should* receive hepatitis B vaccines:**
  - Adults aged 19 - 59 years
  - Adults aged ≥ 60 years with risk factors for hepatitis B
- **The following groups *may* receive hepatitis B vaccines:**
  - Adults aged ≥ 60 years without known risk factors for hepatitis B

Viewpoint

March 10, 2023

Universal Adult Hepatitis B Screening and Vaccination as the Path to Elimination

Samuel So, MBBS[1]; Norah Terrault, MD, MPH[2]; Erin E. Conners, PhD, MPH[3]

» Author Affiliations

JAMA. 2023;329(19):1639-1640. doi:10.1001/jama.2023.2806

Current Adult HBV Vaccines

VACCINE	HBV Antigen
Standard Adult Regimen: 3 Doses (at 0, 1, and 6 Mo)	
Recombivax HB[1]	HBsAg
Engerix-B[2]	HBsAg
Twinrix[3]	HBsAg (also contains HAV antigen)
PreHevbrio[4]	**Trivalent:** S, pre-S1, and pre-S2 HBsAg
Standard Adult Regimen: 2 Doses (at 0 and 1 Mo)	
Heplisav-B[5]	HBsAg (also contains immune adjuvant CpG 1018)

1. Recombivax HB PI. 2. Engerix-B PI. 3. Twinrix PI. 4. PreHevbrio PI. 5. Heplisav-B PI.

Measuring Vaccine Response

- IgG antibodies to HBsAg (anti-HBs) after completion of vaccination are used as a marker of immunity
- an anti-HBs (HBsAB) concentration of $\geq$10 mIU/mL or more measured 1-3 months after the last dose is considered a reliable marker of protection
  - protection in immunocompetent individuals documented up to 30 years so far
  - even if, over time, anti-HBs concentrations decline to $\leq$10 mIU/mL, vaccinees are still protected..
  - because protective vaccine efficacy is not only related to induction of anti-HBs antibodies, but also involves the induction of memory B and T cells

Nonresponse to HBV Vaccination

- HBV vaccination is **recommended** and **effective** in most individuals

- however, 5%-15% **may not respond** because of smoking, age, obesity, or chronic illness
- consider assessing patients for nonresponse

- nonresponders = people who do not develop sAB after completing vaccine series

www.hepb.org/prevention-and-diagnosis/vaccination/vaccine-non-responders/.

www.hepb.org/prevention-and-diagnosis/vaccination/vaccine-non-responders/

Suggestions for Addressing Vaccine Non-Response

- if inadequate response to 3-dose series:
  - revaccinate at double dose
  - vaccinate with 2-dose series that has immune adjuvant

Does HBV Vaccination Need To Be Boosted?

- 15%-50% of children who respond to a primary 3-dose vaccination series have low or undetectable HBsAB concentrations 5 to 15 years after vaccination
  - typically see this when college entry requires proof of vaccination– do they need to be revaccinated?
  - the majority of vaccinated people with HBsAB concentration ≤10 mIU/mL or less will mount an anamnestic response when they receive a booster dose or are exposed to HBV, indicating that they were protected by memory B and T cells
- so, vaccine protective effect outlasts the presence of vaccine-induced antibodies, conferring long-term protection

Hepatitis B Screening Tests

HBsAg

Anti-HBs

Total anti-HBc

Vaccine 37 (2019) 5111–5120

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Challenges with hepatitis B vaccination of high risk adults – A pilot program ☆

Carolyn B. Bridges [a,*,1], Tureka L. Watson [b], Noele P. Nelson [c], Maribel Chavez-Torres [d], Patric
Boatemaa Ntiri-Reid [f], Edward Wake [g], Judith M. Leahy [h], Anita K. Kurian [i], Mary Ann K. Hall
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San Antonio Metropolitan Health District, San Antonio, TX, United States
Cherokee Nation Assurance, Atlanta, GA, United States

CDC Hepatitis B Vaccination of High-Risk Adults Pilot Project, 2012-2015

Purpose

- Reduce incidence of acute HBV infection through targeted hepatitis B vaccination of adults who presented for medical care in
  - Universal settings (ie, where all patients are likely to be at high risk)
  - Non-universal settings (adults at increased risk based on screening)

Study was conducted in 14 states, incl WV

Methods

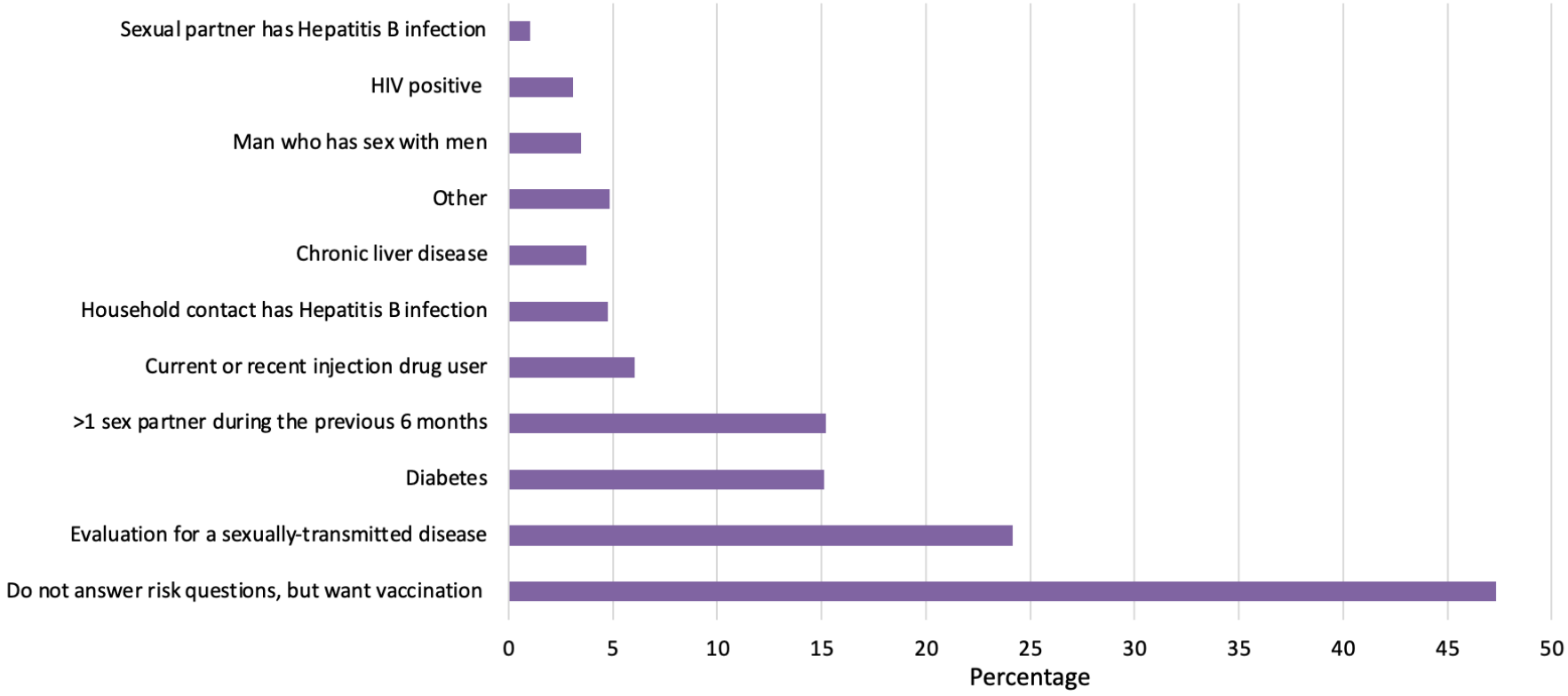
- Awardees could target pilot program vaccines for certain high-risk persons
  - Did not include hepatitis B vaccination for health care personnel, persons with end-stage renal disease, or international travelers during the 2-year project period

- Funds were not provided for hepatitis B virus (HBV) serologic testing

Results

- Wide variety of vaccination sites selected
- Vaccine uptake overall slower than initially anticipated by awardees
- Tracking of 3 dose-series completion very challenging
  - Some awardees without mature IIS, difficulty accessing IIS at vaccination site, some locations not able to/motivated to use IIS
  - Mobile populations (eg, movement of incarcerated persons, homeless vaccinees) not returning for follow-up to clinics for high risk (eg, STD clinics)
  - Many different vaccination partners/clinics involved
  - Awardee project staffing challenges

Percentages of Hepatitis B Vaccinees Reporting One or More Risk Factors (N = 44,355), 2012-2015



Six of 14 Awardees Reported Dose-series Completion

Setting Type	Number of persons who received dose 1	Number (%) of dose 1 recipients who received dose 2	Number (%) of dose 1 recipients who received dose 3	Total number of doses 1–3 administered by setting type
STD clinic	11,245	4,000 (35.6)	1,928 (17.1)	17,173
Corrections	5,150	2,058 (40.0)	908 (17.6)	8,116
Other	3,447	1,552 (45.0)	1,079 (31.3)	6,078
FQHC	2,432	1,359 (55.9)	923 (38.0)	4,714
Drug treatment facility	2,564	791 (30.9)	349 (13.6)	3,704
Health care facility - IDU	2,008	674 (33.6)	325 (16.2)	3,007
HIV clinic	1,278	551 (43.1)	379 (29.7)	2,208
Local health department	876	585 (66.8)	531 (60.6)	1,992
Health care setting - MSM	457	327 (71.6)	135 (29.5)	919
Total	29,457	11,897 (40.4)	6,557 (22.3)	47,911

Conclusions

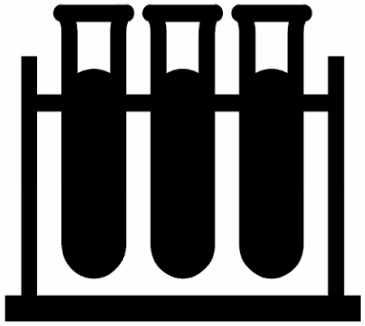
- Study illustrates the many challenges with reaching and vaccinating high risk adults, including vaccine dose tracking, and two and three vaccine-dose series completion
  - Highest 2-dose completion in FQHC, health depts, clinics with focus on MSM communities
- Many lessons learned that may be applicable for hepatitis B vaccination programs
  - Over-estimation of vaccine utilization – much less wastage in providers ordering more frequently and in smaller quantities from prior studies
  - Challenges with IIS use and reporting and follow-up for missed doses
  - Many high-risk persons changed phone numbers and addresses
  - Partners vaccination capacity for administering and reporting vaccines over estimated
  - Completion rates may be most difficult in settings where high risk adults may be less likely to return to that specific setting for follow-up

Strategies to Boost HBV Vaccine Uptake in Adults

- ‘meet people where they are at’ = offer vaccine in a range of healthcare & healthcare-adjacent venues
  - as key part of hepatitis C treatment
  - harm reduction/syringe services programs
  - treatment programs for Substance Use Disorder, both residential & outpatient
  - STI clinics
  - carceral settings
  - **via universal screening thru routine primary care**
- if concerned about follow-through or pt would benefit from immune adjuvant, offer 2-dose vaccine so that vaccination is completed in 1 month

New screening & vaccination recommendations in summary…

New Recommendations Support Co-located, Comprehensive Hepatitis B Vaccination and Screening Services



- Collect blood
- Offer vaccine per ACIP
- No need to wait for results
- Screening should not be a barrier to vaccination

Prevention of Mother-to-Child Transmission (MTCT)

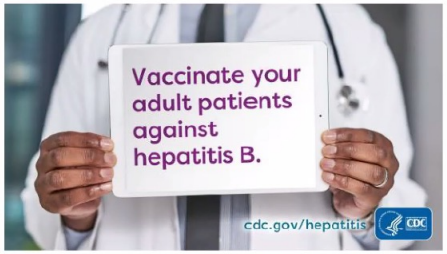
- antiviral therapy for pregnant woman with chronic HBV begun in 3rd trimester if mother's DNA quant (HBV viral load) is >50,000,000 (10^7), or unless otherwise indicated for mom's health
- treatment given to newborn ***within 12 hours of birth:***
  - HBV immune globulin
  - 1st dose of HBV vaccine series

Hepatitis B Treatment

- *acute* hepatitis B in adults usually resolves on its own
  - does not require specific medical treatment
  - supportive care for severe vomiting or diarrhea to restore fluids and electrolytes
  - no Rx can prevent acute hepatitis B from becoming chronic
- chronic hepatitis B
  - many treatment options available, but current TX algorithms are not simple
  - however, HBV therapeutics are in stage of rapid advancement with great potential promise

CDC Resources

- [CDC hepatitis C screening and testing recommendations among adults]
- [CDC universal hepatitis B vaccination recommendations for adults]
- [CDC hepatitis B screening and testing recommendations]



Thank you!