Chapter

Acute Hepatitis B Infection: U.S. Policy and Guidelines

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Abstract

Hepatitis B virus (HBV) infection can lead to chronic complications and increased mortality, supporting the use of post-exposure prophylaxis (PEP) as an important initiative in public health. Despite positive trends in reducing HBV exposure with effective screening and vaccination, adoption and implementation of US Centers for Disease Prevention and Control (CDC) guidelines reveals gaps in protection for vulnerable populations (e.g., sexual assaulted, IV drug use, incarcerated persons, low socioeconomic status) who remain at risk for infection and viral transmission. This chapter reviews current acute HBV exposure guidelines in the United States (US) and presents opportunities for policy reform to improve equitable access and outcomes across vulnerable populations.

Keywords: HBV, acute infection, sexual assault, ethics, prophylaxis, public health, guidelines, vulnerable populations, immune globulin

1. Introduction

Hepatitis B is a liver infection caused by the hepatitis B virus (HBV) that is spread through blood and bodily fluids from an infected person, with an increased risk of morbidity and mortality as well as public health implications [1]. Evidence-based guidelines and standards of care exist for screening, detection, and prevention of disease. CDC guidelines inform clinical decision-making and public health policy for vaccination and post-exposure prophylactic (PEP) interventions [1]. Despite universal vaccination recommendations and reduction in acute HBV cases, there remain groups of at-risk individuals who are disproportionately affected by hepatitis B within the general population. Further, there are ethical obligations to reduce disparities and risks among vulnerable populations while strengthening public health measures of protection. We review the current state of acute HBV national guidelines and then present opportunities for policy reform to mitigate health disparities among vulnerable populations.

2. Epidemiology of acute hepatitis B infection

New hepatitis B infections in the US have been declining in the general population, with a substantial drop in 2020 from 2019. Since this decrease, the incidence of new hepatitis B infections has remained relatively steady through the CDC's most recent reporting in 2022 [1].

2.1 Acute hepatitis B infection

In 2022, there were 13,800 acute cases of hepatitis B reported in the US, of which 2126 cases were new cases of acute hepatitis B [1]. The rate of reported cases of acute hepatitis B for the US was 0.6 per 100,000 persons. Of the new cases reported, approximately one-quarter had an identified risk factor, but nearly one-half were missing risk data [1]. Rates of reported infections were above the national average in 14 states, with many being in or near the Appalachian region [1]. West Virginia had the highest rate of acute hepatitis B infections in 2022, but the largest increase in infections in 2022 from 2021 was seen in Florida [1]. In 2016 data highlighted that three states in the Appalachian region (Kentucky, Tennessee, and West Virginia) had increased cases of acute HBV infection in individuals that were intravenous (IV) drug users [2]. The increase in prevalence in this population indicates the importance in addressing disparities in groups participating in high-risk behaviors.

When reported cases are categorized further by age group, those in the range of 40 to 49 years of age have the highest rate of acute infection [1]. In 2022, 52% of all acute hepatitis B infections reported were in 40 to 59-year-olds [1]. Rates of reported cases are highest among Black and non-Hispanic persons and have been increasing since 2020 [1]. This rate was 1.7 times higher than non-Hispanic white persons [1].

Acute infection with HBV can progress to chronic hepatitis B (CHB), which is largely underreported with most individuals unaware of infection [1]. It is estimated that up to 2.4 million people in the US have CHB infection [3], with 16,729 new cases reported in 2022, corresponding to a rate of 5.8 cases per 100,000 people [1]. This rate was highest among people of non-Hispanic Asian/Pacific Islander descent at 11.2 times as high as non-Hispanic white people. A majority of new chronic cases are reported in people 30 years of age and older [1]. Foreign-born people living in the US represent a large portion of the population infected with CHB; an estimated 1.47 million persons in this population are living with CHB [4].

2.2 Burden of disease

Acute hepatitis B occurs after an initial infection with HBV. While some people may be asymptomatic with acute infection, others have more severe complications that can result in hospitalization [1]. Those with hepatitis B infections are at an increased risk of hepatocellular carcinoma (HCC), and while spontaneous or treatment-induced clearance of hepatitis B surface antigen (HBsAg) lowers the risk of liver-related complications, there is still a risk of HCC development in people with the hepatitis B virus [5].

Co-infection with other viruses poses a threat to individuals with hepatitis B and can increase the risk for further complications. Approximately 2% of people living with HIV are co-infected with hepatitis B and are at greater risk of complications and death from hepatitis B infection [6]. Co-infection with hepatitis D virus, which has no effective nucleotide/nucleoside analogs, perpetuates additional hepatic damage [7].

In major US cities, people with CHB and hepatitis C virus (HCV) co-infection were predominantly males, over 40 years of age, and of African American ethnicity [8]. Due to these and other severe implications, receiving care for hepatitis B is critical for management and to prevent further disease progression. However, linkage to care rates for those who screen positive for HBV infection ranges broadly from 36–78% [9].

Recent CDC data report 1797 hepatitis B-related deaths in 2022 [1]. This corresponds to an age-adjusted rate of 0.44 deaths per 100,000 people which remained steady with 2021 rates; however, these rates are higher than the 2018 (0.43) and 2019 (0.42) reported rates [1]. The lack of consistent decline in deaths and national progress to reduce hepatitis B-related deaths indicate the need for additional action to continue to make progress to reduce mortality associated with hepatitis B infection.

People acutely affected by hepatitis B infection experience emotional distress from the initial infection, and they are at risk for developing long-lasting emotional and psychological implications manifested in the progression to CHB. In a survey that investigated health-related quality of life for patients with CHB infection in the US, stressful life events and unemployment were correlated with mental and physical health status of those living with the infection [10]. This reality highlights the importance of social support for individuals who demonstrate lower mental health status [11]. Not surprisingly, hepatitis B infection can have significant social repercussions for individuals affected by the virus, presenting as stigma, discrimination, and challenges with relationships and personal interactions [11].

3. Affected populations

3.1 General population

Hepatitis B transmission within the general population primarily occurs through sexual contact, exposure to infected blood/bodily fluids, and perinatal transmission. Various factors such as socioeconomic status, living conditions, and access to healthcare are important to understanding populations that are disproportionately impacted, addressing disparities and improving health outcomes [3]. While the overall risk within the general population is relatively low and hepatitis B affects individuals across all demographics, specific high-risk groups discussed below are especially vulnerable to hepatitis B transmission.

Although 52% of adults with acute HBV infection reported no risk factors during the six weeks to six months prior to illness onset, the remainder of those infected had at least one risk factor with injection drug use and multiple sex partners being the most common [2].

3.2 Sexual assault survivors

Sexual (heterosexual and men having sex with men [MSM]) contact is a common way for transmission of hepatitis B among adults. Multiple sexual partners (two or more), sexual contact with a known HBV-infected person and men who have sex with men are at increased risk of sexual HBV transmission [2].

One in six US women and one in thirty-three US men reported experiencing completed or attempted rape at some point in their lives [12]. It is estimated that each year, more than 460,000 people aged 12 years and older are raped/sexually assaulted in the US [10]. These individuals are a particularly vulnerable population

at increased risk of hepatitis B transmission through bodily fluids such as semen, vaginal fluids, and blood. This demographic encompasses diverse groups including college students, immigrants, and displaced persons/refugees. Persons who have been sexually assaulted come from all socioeconomic backgrounds and age groups, and they include females (90%), males, and special populations such as the LGBTQ+ community, military personnel, and incarcerated individuals in addition to the elderly and disabled [1].

Sexual assault patients have challenges accessing care and health services. A minority of those who are sexually assaulted present for medical care - typically in emergency department settings. Sexual Assault Nurse Examiners (SANEs) provide comprehensive care to sexual assault patients, medical/forensic examinations, including evidence collection, and courtroom testimony. SANEs, collectively with physicians and advanced practice providers in the acute care settings, address the PEP needs [13].

Sexual assault has physical, emotional, and psychological consequences and may also leave these individuals at risk for sexually transmitted infections. Prophylactic antibiotics for chlamydia, gonorrhea, and trichomoniasis as well as prophylactic measures for hepatitis B and HIV are in the current CDC guidelines for post sexual assault care [13].

Bleeding and tissue injury exacerbate the risk of blood-born infections. Unlike in HIV prophylaxis, where a case-by-case determination for prophylaxis is made when the alleged perpetrator's HIV status is unknown, hepatitis B immune globulin (HBIG) is currently only recommended when the assailant is known to have acute hepatitis B [12]. If the hepatitis B status of the assailant is unknown and the survivor has not been previously vaccinated, post-exposure hepatitis B vaccination is recommended without HBIG. Only if the assailant is known to be HBsAg positive is it recommended that unvaccinated patients receive both hepatitis B vaccine and HBIG. The vaccine and HBIG, if indicated, should be administered to sexual assault survivors at the time of the initial examination, and follow-up doses of vaccine should be administered 1–2 and 4–6 months after the first dose. Individuals who were previously vaccinated but did not receive post-vaccination testing should receive a single vaccine booster dose.

A particular challenge with this guideline is that it is not uncommon for individuals who have been sexually assaulted to not know the hepatitis status of their assailant. In addition, after such a traumatic event, patients may not recall their hepatitis B vaccination status or if they received post vaccination testing.

After hepatitis B vaccination, protective antibody levels are not present for fourteen days, whereas HBIG may provide immediate protective serum concentrations and contribute to protection until protective antibody levels from the vaccine are achieved [14]. In addition, HBIG can offer passive immunity and protection for 3-6 months in patients who do not respond to vaccination. Follow-up rates are low in patients who have experienced a sexual assault [14]. Knowing that hepatitis B is even 50-100 times more infectious than HIV, HBV prophylaxis is thus essential for preventing new infections following sexual assault [15].

3.3 Injection drug use/homeless

Individuals engaged in injection drug use face disproportionate risks of hepatitis B transmission due to high-risk behaviors and living conditions. Sharing needles and syringes poses a significant risk for blood-borne infections. Individuals may lack access to safe injection equipment, harm reduction services, and healthcare

facilities—all of which further increases susceptibility to hepatitis B and other infectious diseases. Injection drug use has been reported as a risk factor in up to 30% of people who reported a new hepatitis B infection [2]. Hepatitis B vaccination and testing is recommended in persons who are injecting drugs or who have a history of injection drug use.

The prevalence of hepatitis B in persons experiencing homelessness is underestimated. Data show prevalence in persons experiencing homelessness was seven to ten times higher than in the US general population [16]. These statistics highlight the urgent need for targeted interventions and implementation strategies to help lower the risk of hepatitis B transmission in individuals who are experiencing homelessness. Currently, CDC does not recommend routine hepatitis B testing and vaccination in homeless individuals.

3.4 Incarcerated persons

Incarcerated individuals represent another population at increased risk of hepatitis B transmission because of overcrowded living conditions, decreased access to healthcare, and high rates of injection drug use. HBV prevalence has been estimated at three to 38 times higher in correctional settings than in the general population [17].

Comprehensive screening, vaccination, and treatment programs are essential components of hepatitis B prevention and control within this population. Recent guidelines recommend routine testing for HBV infection among persons incarcerated or formerly incarcerated [18]. Facilities should consider offering all the following: 1) testing at intake, 2) periodic testing for persons serving long term sentences who are susceptible to infection, and 3) vaccination for susceptible individuals. Routine testing for hepatitis B surface antigen (HBsAg) of susceptible individuals can help identify cases of acute and chronic HBV infection, and vaccination can help prevent further transmission among incarcerated individuals. Additionally, access to medical care, substance use disorder treatment, and harm reduction services can help reduce hepatitis B transmission and improve overall health outcomes among incarcerated persons.

3.5 Persons with low socioeconomic status

Individuals with low socioeconomic status face multiple barriers to accessing healthcare, including financial constraints, limited health literacy, and inadequate or no insurance coverage. These disparities contribute to elevated risks of preventable diseases, such as hepatitis B and poorer health outcomes. Social determinants of health, such as poverty, unemployment, and lack of/low education all play a significant role in the outcomes of patients with hepatitis B, including greater HCC incidence, delayed hepatitis B diagnosis, and lower survival rates [19].

Addressing the root causes of health inequities is essential for reducing the burden of hepatitis B within disadvantaged communities. Policies aimed at improving access to healthcare and addressing social determinants of health along with targeted outreach and education efforts can help mitigate disparities in hepatitis B prevalence and improve health outcomes among individuals with low socioeconomic status [19].

3.6 Other populations

Other populations at risk for HBV infection include household contact, developmentally disabled persons in long term facilities, hemodialysis patients, persons with

HCV infection or HIV infection or diabetes, persons with chronic liver disease, and travelers to countries where HBV is endemic [1].

Refugees and displaced persons are also at increased risk with a wide variation between countries and regions. By some estimates, 23 million individuals meet this population criteria, of which the most-reported region is the US. Given their poor access to health care and compromising conditions, this population bears a greater burden of carrying and transmitting communicable diseases [20].

HBV transmission can also occur within the healthcare setting. The CDC approximates that hospitals witness approximately 385,000 sharps-related injuries among healthcare personnel annually, placing such personnel at risk of hepatitis B infection [21].

3.7 Disparities among vulnerable populations

Current US guidelines reveal gaps in protection for those exposed to hepatitis B. In patients who are survivors of sexual assault, the guidelines rest upon the vaccination status of the survivor as well as the status of the assailant to determine if the survivor will get vaccination alone or vaccination combined with HBIG [13].

Of note, the assailant's unknown hepatitis B status does not result in the sexual assault survivor receiving HBIG as well as vaccination, treating the unknown status as potentially negative versus potentially positive [13]. Regarding an unknown status as negative contradicts the recommendation within occupational exposure guidelines. The high comorbid implications of having hepatitis B transmitted via a sexual assault, added to the psychological repercussions of being assaulted, should justify treating an unknown status as a potentially positive one.

The most thoroughly studied population for PEP is infants born to hepatitis B positive mothers. To bridge the gap between exposure to HBV and active production of anti-HBs induced by the hepatitis B vaccine, HBIG is given as soon as possible in these newborns no later than 24 hours after birth. This combination is 85–95% effective in preventing CHB infection, whereas sole vaccination within 24 hours after birth is 70–95% effective in preventing perinatal HBV infection [22].

Given this gap between exposure and vaccination-elicited protective titers, HBIG should also be universally given to sexual assault survivors. Likewise, similar considerations apply to IV drug use populations who may not be aware of HBV status when sharing needles.

The coverage gap found in the guidelines for PEP of persons with nonoccupational exposure to blood or body fluids that contain blood is inconsistent with the guidelines to prevent HIV transmission post sexual assault [13]. For HIV prevention in sexual assault survivors, nonoccupational PEP (nPEP) is recommended when the source of the body fluids is known to be HIV-positive and the reported exposure presents a substantial risk for transmission. If the risk associated with the exposure is high, guidelines recommend starting nPEP and then making a decision whether to continue nPEP after the source's HIV status is determined [23].

4. Therapeutic strategies in acute HBV infection

4.1 Goal

Preventive measures are the primary methods to reduce the burden of hepatitis B on public health. Public health initiatives look to reduce transmission of hepatitis B

through screening, vaccination, and PEP. The current goal of PEP is to decrease the transmission of hepatitis B after exposure [2].

4.2 Vaccination

In the United States, according to data from the National Notifiable Diseases Surveillance System (NNDSS), cases of acute hepatitis B declined by 87%, from a high of 26,654 in 1985 to 3350 in 2010, after implementation of national vaccination strategies [24].

Currently, the CDC recommends routine hepatitis B vaccination at birth. In adults, the CDC recommends universal vaccination for those 19 to 59 years old and in those 60 years and old with risk factors. Universal vaccination in adults 19 to 59 years old was implemented in 2022 due to the higher rates of acute infection in the adult population and to address suboptimal vaccine coverage in the adult population. Additionally, removing the need for risk assessments decreases the need for disclosure of stigmatizing behavior in order to protect vulnerable groups [25].

Assessing postvaccination immunity via serologic testing is not routinely recommended, except possibly for persons that need to know their immune status for their subsequent management, and for immunocompromised patients in which titers should be checked annually. The lack of serologic testing post vaccination might impede the success of the universal vaccination campaign by not confirming the presence of protective titers [22].

Also limiting the impact of the vaccination initiative in eradicating hepatitis B are vaccination non-responders, with 5–10% of people who receive vaccination not developing serological protection [26]. About 95% of individuals who received all doses of HepB vaccine, at the appropriate schedule, will develop detectable anti-HBs antibody and approximately 5–10% of immunized individuals fail to develop a protective antibody response (HBsAb level higher than 10 mIU/mL), despite completing their hepatitis B vaccine series. For persons who fail to generate adequate antibody levels in response to a primary hepatitis B vaccine series, revaccination can achieve a protective response at least half of the time [2, 27–29].

It is also possible that a person who does not respond to the vaccine may already be infected with hepatitis B. Therefore, testing for the presence of the hepatitis B virus (hepatitis B surface antigen or HBsAg) is recommended before diagnosing a person as a "vaccine non-responder" [2].

Prior to the 2022 recommendation of universal vaccination of adults, in 2017, 25.8% of adults (19 years of age or older) were immunized with at least three doses of hepatitis B vaccine. Among healthcare providers who interact directly with patients, 70% had received at least three doses of hepatitis B vaccine [22]. Even populations deemed to have an increased risk such as MSM have demonstrated low vaccination rates despite having access [30].

Non-adherence to intervention further limits the impact of vaccination, with people not completing the prescribed full series of vaccine. Even with an option of two visits versus three, the time gap, missed appointments, nihilism, apathy, fear, miseducation, access and life changes can all prove to be barriers to adherence. A study investigating completion rates of various vaccines found that the 3-dose series had a much lower completion rate compared to the 2-dose series. In addition, lower completion rates were associated with male gender, younger age, Black or Hispanic race/ethnicity, lower educational or household income attainment, and more comorbidities [31]. The failure to complete their vaccination series can leave people vulnerable to infection.

4.3 Immune globulin and vaccination

Earlier studies established the relative efficacies of HBIG and/or hepatitis B vaccine in different exposure situations. For an infant with perinatal exposure to an HBsAg-positive and HBeAg-positive mother, a regimen combining one dose of HBIG at birth with the hepatitis B vaccine series administered perinatally is 85%-95% effective in preventing transmission state. Regimens involving either multiple doses of HBIG alone or the vaccine series alone have 70%-90% efficacy [32].

In 2022, one study demonstrated that mother-to-child-transmission (MTCT) rates were not statistically different between children who had received the vaccine alone and those who had received both HBIG and the vaccine [33]. A meta-analysis study also conducted in 2022 showed that the combination of hepatitis B vaccination and HBIG in infants significantly reduced transmission risk compared with vaccination alone, with a risk ratio of 0.52 (95% confidence interval; 0.30-0.91). With the high burden of disease for MTCT transmissions, the fact that two of the fifty-eight (3.4%) newborns from positive mothers receiving vaccine alone became chronically infected with HBV, while all infants administered the vaccine and HBIG were protected, can offer a rationale for the addition of HBIG to perinatal vaccination [33].

Widespread pediatric vaccination and the use of HBIG have made vertical transmission a rare occurrence in the United States (only 10 reported cases from 2005 to 2020), and with PEP (perinatal HepB vaccine and HBIG, followed by completion of the HepB vaccine series) only 0.7% through 1.1% of infants develop infection [34].

4.4 Guidelines for populations

4.4.1 Occupational exposure

After exposure to HBV, appropriate and timely prophylaxis can prevent infection and subsequent development of chronic infection or liver disease. The mainstay of PEP intervention is hepatitis B vaccination, but in certain circumstances HBIG is recommended in addition to vaccine for enhanced seroprotection [2].

Table 1 outlines the guidelines for post-exposure hepatitis B testing and PEP measures of persons with occupational exposure to blood or body fluids that contain blood by source patient status and HCP vaccination status. For responders who completed the full vaccine series, no measures need to be taken, regardless of the source's hepatitis B status. For documented non-responders who received six doses of vaccines, no measures need to be taken if the source is negative and if the source is positive; the HCP will get tested at baseline and receive HBIG (two doses separated by a month) [35].

When the vaccination response is unknown after three doses, a baseline test is required that will instruct the following measures: If the test shows the titer is below the protection level (<10 mIU/mL) and the source is either positive or unknown, vaccination will be initiated and one dose of HBIG will be administered. If the source is negative, then no measures are recommended. If the test shows a titer that is greater than the cutoff for achieving protection level (≥10 mIU/mL), no measures are recommended. For unvaccinated, or incompletely vaccinated or vaccine refusers, if the source is negative no measures are recommended. However, if the source is positive or unknown, the vaccination series is recommended as initiated with one does of HBIG administered [35].

Health Care personnel status	Post exposure testing		Post exposure prophylaxis		Post vaccination serologic testing
	Source patient status	HCP testing	HBIG	Vaccination	
Documented responder after complete series (≥3 doses)	No action needed				
Documented nonresponder after 6 doses	Positive/ unknown	Baseline testing for hepatitis B virus infection as soon as possible after exposure	2 doses separated by one month	No	No
	Negative	No action needed			
Response unknown after 3 doses	Positive/ unknown	<10 mIU/mL	One dose	Initiate revaccination	Yes
	Negative	<10 mIU/mL	None		
	Any result	≥10 mIU/mL	No action needed		
Unvaccinated or incompletely vaccinated or vaccine refusers	Positive/ unknown	Baseline testing for hepatitis B virus infection as soon as possible after exposure	One dose	Complete vaccination series	Yes
	Negative	No	None		

Table 1.
Guidelines for post exposure hepatitis B testing and PEP measures of persons with occupational exposure to blood or body fluids that contain blood by source patient status and HCP vaccination status [35].

4.4.2 Non-occupational exposure

Table 2 outlines the guidelines for PEP of persons with nonoccupational exposure to blood or body fluids that contain blood by exposure type and vaccination status. For persons with documented completion of the HBV vaccine series without postvaccination testing who are exposed to a positive HBV source, the CDC recommends a single dose of the HBV vaccine. Those who are in the process of being vaccinated and are exposed to an HBV positive source are recommended to complete the vaccination series. In vaccinated persons exposed to an unknown HBV source, only persons who are not fully vaccinated should complete the vaccine series. Fully vaccinated persons should not receive any additional measures [13].

Unvaccinated persons who are exposed to an HBV positive source are recommended to receive HBIG in addition to HBV vaccination as soon as possible after exposure. However, when the HBV source status is unknown, unvaccinated persons are recommended to receive their HBV vaccination only [13]. There is limited information on the maximum interval for PEP to be effective, but it is generally accepted that the interval should not exceed 7 days for percutaneous exposure and 14 days for sexual exposure [2, 13].

Source of exposure	Unvaccinated person	Previously vaccinated person
HBsAg-positive source Percutaneous (e.g., bite or needlestick) or mucosal exposure to HBsAg-positive blood or body fluids or Sex or needle-sharing contact with an HBsAg-positive person or Victim of sexual assault or abuse by an assailant who is HBsAg positive	Administer hepatitis B vaccine series and HBIG	Complete hepatitis B vaccine series and HBIG, if vaccine series not completed or Administer hepatitis B vaccine booster dose, if previous vaccination without serologic testing*
Source with unknown HBsAg status Percutaneous (e.g., bite or needlestick) or mucosal exposure to potentially infectious blood or body fluids from a source with unknown HBsAg status or Sex or needle-sharing contact with person with unknown HBsAg status or Victim of sexual assault or abuse by a perpetrator with unknown HBsAg status	Administer hepatitis B vaccine series	Complete hepatitis B vaccine series

**A booster dose is recommended for persons who have written documentation of hepatitis B vaccine series with serologic response.*

Table 2.
Guidelines for postexposure prophylaxis of persons with non-occupational exposure to blood or body fluids that contain blood by exposure type and vaccination status [13].

5. Ethical considerations in suspected acute HBV infection

5.1 General principles

The ethical implications surrounding HBV treatment are rooted in principles assigned to any range of communicable diseases of bacterial or viral nature. These principles are anchored in societal and provider-level duties to mitigate harm for the at-risk individual while also promoting the welfare and protection of others who may be at risk from transmission. The ethical argument proposed here is two-prong: providing duty for the individual and for public health.

These clinical-applied principles are neither novel nor recent. Early variants of formal codes of medical ethics can be traced to the Nuremberg Code in 1947 and subsequently expanded over the course of subsequent decades through the Guiding Principles of the Declaration of Helsinki by the World Medical Association in 1964. Today, variations of medical ethics have been expanded and exist to protect research subjects in the codification of the *Belmont Report*, developed in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Regardless of its clinical or research origins, the cannon of biomedical ethics illuminates a consistent trajectory and evolution that positions respect, autonomy, beneficence, non-maleficence, and health justice at the core and further emulated in public health codes of ethics [36]. The more recent pandemic of COVID-19 further brought to life similar ethical implications of individual and societal duties, of which bioethical experts likewise have reported the need for adherence to values of honesty, trust, human dignity, accountability, transparency, and justice [37].

5.2 Ethical application to vulnerable populations

Populations with limited rights and compromised decision-making capacity are unique in their inability to express competent decisions or act in their self-interest. Such "vulnerable" populations are deemed susceptible to duress and coercion by dominant forces, and they are disadvantaged by existing power dynamics and institutional policies. Given their diminished capacity of voluntariness these groups are afforded special attention as to the health rights owed to them. As noted above, such at-risk populations exposed to conditions of HBV infection are statutorily defined as vulnerable (i.e., prisoners) or regarded as susceptible due to compromised decision-making capacity. These groups comprise subsets of individuals who are afforded even less protection and limited means of advocacy compared to the general population.

Incarcerated persons may *prima facie* have the capacity for uncoerced voluntariness and decision-making capacity, yet their right to self-determination is limited by law, as they are bound by prison policies and subject to regulations that are otherwise unrestricted in the general population. Despite their protection under constitutional rights, prisoners are defined by the constraints of incarceration that can affect their ability to make voluntary decisions regarding health and wellness.

Other groups as noted above have unique factors that contribute to limited decision-making capacity. Survivors of sexual assault, despite being of sound mind and mentally competent, may be impaired by the acute stress of trauma, rape, and battery—all of which can have profound impact on one's ability to act rationally and in their best interests. IV drug users, although not necessarily subject to emotional or physical trauma across the affected population, nevertheless suffer from psychologic disorders and behavioral conditions that present with altered mentation that compromises rational thinking and competent decision-making, leading to a pattern of self-harm.

Principles that guide the clinician's duty to prevent unnecessary harm are predicated on a normative foundation that recognizes the limited rights and decision-making capacity of such populations. Traditional models list four such principles of bioethics: beneficence, non-maleficence, autonomy, and justice [38]. Two of these principles—beneficence and non-maleficence—can be applied as a guide toward the obligation for physicians to individuals suspected of exposure to HBV infection. For survivors of sexual assault suspected of HBV exposure, for example —regardless of known status of the perpetrator — the duty to rescue the individual and the duty to protect the community aligns with promotion of welfare while preventing harm to the public.

5.2.1 Principle one: duty to rescue

The widely accepted foundation of biomedical principles serves as a model for a top-down approach to ethical principles in addressing suspected HBV infection in vulnerable populations. The first set of principles is the provider-level duty to his or her patient. Consider one's professional duty to rescue, defined as preventing serious harm to another at minimal cost to oneself. This obligation implies a level of duty greater than ordinary sacrifice by the layperson. This duty is far greater for clinicians and healthcare professionals who are trained within their scope of practice with the requisite knowledge and tools to engage in high-risk situations whose severity and likelihood of harm can be minimized with appropriate intervention.

One's duty to rescue need not present significant risks, costs, or burden to the agent to be enacted. In patients suspected of HBV exposure, the risk to the clinician is low, whereas the risk level for the patient may be comparably high. These patients may include those who are young, poor, living in social housing, suffering from poor health, and have poor access to support systems.

In the ER setting, clinicians are obligated to take on a greater than minimal duty to rescue through a duty to warn others. The ER clinician who suspects a patient is at risk for infection is thus obligated to warn the patient of health risks and the consequences of both intervention and lack thereof due to gaps in the current guidelines. Moreover, failure to provide the patient with options for evidence-based interventions strips the patient of autonomy to make an informed decision of their health.

Prophylactic strategies for intervention provide clinicians with a tool by which to effectively rescue patients from the risk of infection and sequelae of organ damage and disease associated with hepatitis B. The duty to rescue is inherent to the nature of the ER setting with minimal risk to agents who act as rescuers. Administration of hyperimmune immune globulin to these patients is one example that may provide immediate protection with minimal harm or burden to the medical community.

5.2.2 Principle two: duty to protect

The second principle, duty to protect, is predicated on the obligation of clinicians to promote the welfare of patient as well as society. As an example, this principle has been applied as a public health mandate with the general acceptance of immunization. Beyond the clinical value of providing their patients with active immunity to potentially harmful pathogens, physicians apply evidence-based medicine of community vaccination to extend protective measures to the larger community. The public's trust in the medical profession is rooted in a belief that clinicians serve the greater good of society.

Patients suspected of HBV infection who are subsequently discharged without protective measures remain infectious and carry the risk of transmission to others via various routes of sexual and non-sexual exposure. The duty to protect a patient from further harm thus extends beyond their own person to others with whom they may come into contact. These possibilities include risks across social settings, the workplace, healthcare facilities, educational institutions, and family-home environment.

5.3 Ethical application to public health

In its *Code of Ethics*, the American Public Health Association supports fundamental values inherent in obligations to the public. Germane to HBV and prevention of viral transmission, several of these categories are warranted here: Professionalism and trust, health and safety, health justice and equity, and inclusivity and engagement. Trust requires adoption and acceptance of policies developed through the "highest ethical, scientific, and professional standards" and informed by evidence [39].

Next, public heath principles demand an "ethical responsibility to prevent, minimize, and mitigate health harms and to promote and protect public safety, health, and well-being" [39]. Health justice and equity have broad implications for vulnerable populations, particularly those susceptible to HBV infection, thus requiring the medical community to ensure appropriate access to resources that afford equal access and the opportunity to achieve and maintain health. In limited-rights settings such as prisons and homeless shelters, such equity is of vital importance to realize equal

allocation of scarce medical resources such as vaccines and prophylactic therapeutic interventions, but to also help navigate the power dynamics and structural inequities that may limit decision-making capacity for these individuals.

The *Code* advocates for the inclusiveness of public health stakeholders in the effort to prevent poor health outcomes on a community level. Providers and medical institutions thus bear a duty beyond the individual with suspected viral exposure, to extend accountability with the public.

Other public health experts articulate similar goals, recommending that stakeholders assume a leadership role to sustain protection against public health threats and to reduce gaps in health inequity [40]. These goals can be realized by prioritizing population health, health of populations, shifting strategies to multi-sectorial public health, and by adopting the Universal Declaration of Human Rights as the *de facto* code of public health ethics [40].

6. Recommendations for reform

Gaps in the formal CDC guidelines for PEP of sexual assault survivors suspected of HBV exposure reveal a clinical and ethical need to address the risk of infection and transmission across all populations. To address this challenge, public health stakeholders have argued and presented a number of viable recommendations for implementing reform of policy.

6.1 General considerations

The following represent recommendations for reform of the highest priority and viability, with the greatest impact on ensuring equitable and cost-effective delivery of public health intervention for populations at-risk of HBV exposure. These can be categorized as follows:

- Recognition of populations with limited decision-making capacity
- Inclusion of vulnerable populations in guidelines and affording their protection under guidelines consistent with statutory definitions
- Adoption of public health code of ethics in treatment and clinical decision- making for preventative measures
- Reinforcement of a clinician's duty to protect and promote welfare of persons even suspected of HBV exposure
- Integration and/or harmonization with international guidelines that afford protection to vulnerable populations (e.g., Canadian 2018 Guidelines from the Canadian Association for the Study of Liver Disease and Association of Medical Microbiology and Infectious Disease Canada) [41, 42]

6.2 Guidelines revision

The evaluation and reform of CDC PEP guidelines for acute HBV presents an opportunity to align intervention with ethical principles, particularly for inclusion of vulnerable populations. At minimum, adapting the existing HIV nPEP guidelines—where decisions for unknown assailants are made on a "case-by-case

determination"— can help to inform modification of HBV PEP guidance for sexual assault survivors.

For patients at greater risk of infection and with limited decision-making capacity, prompt prophylactic therapeutic intervention with HBIG may not only protect them from risk of infection but may also mitigate the effects of PTSD by providing them with psychological and emotional reassurance that all the available medical interventions are being utilized for their short- and long-term care. Equally important, a preventative model with access available across all populations provides a greater level of certainty in producing immediate seroprotection with adequate levels of HBIG antibodies.

Table 3 outlines a summary of adoptions for revising acute HBV infection guidelines to integrate HBIG as part of the intervention regimen. These recommendations incorporate ethical principles and public health protection measures across the general population and vulnerable groups. Policy and guideline reform should account for the practical challenges of determining vaccination status of non-HCPs as well as the limitations to verifying source HBV status in non-occupational settings. Likewise, the multiple-doses series of vaccination and associated poor compliance offer a strong rationale for the addition of HBIG to any regimen.

Affected population	**Source HBV status**	**Current HBIG intervention guideline with vaccination**	**Recommended revision**
		Occupational exposure	
HCP vaccine responder	Any	No HBIG	No change
HCP vaccine non-responder	Positive/Unknown	HBIG	No change
	Negative	No HBIG	No change
HCP vaccine response unknown	Positive/Unknown	HBIG if required by serologic testing	No change
	Negative	No HBIG	No change
HCP incomplete vaccination or unvaccinated	Positive/Unknown	HBIG	No change
	Negative	No HBIG	No change
		Non-occupational exposure	
Percutaneous or mucosal exposure, sex or needle sharing, victim of sexual assault or abuse	Positive	HBIG if unvaccinated or incomplete series	No change
	Unknown	No HBIG	Administer HBIG/vaccine for seroprotection
Homeless/displaced persons	—	Not explicit in guidelines	Administer HBIG/vaccine for seroprotection and integrate population
Incarcerated persons	—	Not explicit in guidelines	Administer HBIG/vaccine for seroprotection and integrate population
Persons with low socioeconomic status	—	Not explicit in guidelines	Administer HBIG/vaccine for seroprotection and integrate population

Table 3.
Summary of guidelines revisions for patients with exposure to blood or body fluids that contain blood.

7. Conclusion

The success of current US guidelines for managing risk and transmission of HBV infection has yielded significant advances across the general population, including improved screening rates, reducing the level of reported incidence of new infection and antigen detection rates. The impact of such measures has strengthened the nation's fight to eradicate HBV. Despite the realization of these milestones, vulnerable populations remain at-risk of infection and transmission, posing threats to individual welfare and public health.

Recognition and adoption of ethical principles that promote benefit, reduce harm, and afford justice and equity can help to further provide obligated protections for the individual and the public. Reform of guidelines and equitable implementation across the medical community can have a measurable and profound effect toward realizing a just and healthy society.

Conflict of interest

Sally Henin is a paid consultant for ADMA Biologics. Jeffrey Gruenglas, Miranda Anaya, and Marie-Chantale Simard are paid employees of ADMA Biologics.

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