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Universal Hepatitis B Vaccination at Birth

Safety, Effectiveness, and Public Health Impact

An independent evidence review of the safety, effectiveness, and public health impact of universal hepatitis B vaccination at birth to compare current recommendations with a delayed first hepatitis vaccine dose at one month or more after birth.

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Executive Summary

Background

The US recommendation for routine screening for hepatitis B virus (HBV) infection in pregnancy and universal hepatitis B vaccination of all medically stable infants at birth has been in place since 1991, serving as a core strategy for preventing pediatric HBV infection and elimination of hepatitis B nationwide. The hepatitis B vaccine birth dose recommendation was developed as a safety net to protect infants born to HBV-infected mothers who may not be detected at birth, such as those infected after testing or due to errors or delays in communication of test results. The Vaccine Integrity Project conducted a review of the evidence related to the safety, effectiveness, and public health impact of the hepatitis B vaccine birth dose, reviewing four decades of research to compare current recommendations with delayed administration of the first vaccine dose.

Key Findings

Historical trends in vaccine policy and public health impact

For more than 30 years, the Advisory Committee on Immunization Practices (ACIP) has systematically reviewed data on hepatitis B vaccination in newborns. Recommendations shifted from risk-based vaccination to a universal birth-dose strategy; each review refined recommendations to address specific gaps. As a result, pediatric HBV incidence declined by 99% since 1991. Given the long-term protection provided by the hepatitis B vaccine, the birth dose was also key in reducing HBV transmission, disease, and death in the US overall.

Safety of the hepatitis B birth dose

Results of randomized trials, large national safety monitoring programs, and long-term follow-up studies consistently demonstrate that the hepatitis B vaccine is safe regardless of vaccine timing. No safety benefits were identified for a delayed first dose versus vaccination at birth.

Effective, long-lasting protection

Vaccination in infancy provides documented protection against HBV infection for 35 years. Vaccination at birth and delayed vaccination confer similar long-lasting protective immunity.

Critical safety net

More than 17,000 infants are born annually to women with HBV, yet 18% of pregnant women do not receive hepatitis B testing, and only 35% of women who test positive receive all recommended follow-up care. Delaying the first dose leaves infants vulnerable to both undiagnosed maternal infection and HBV exposure after birth.

Conclusion

This review found no benefit related to vaccine safety or protection of a delayed first dose compared with vaccination at birth, but identified critical risks of changing current US recommendations.

Introduction and objectives

The recommendation for routine screening for hepatitis B virus (HBV) infection in pregnancy and universal hepatitis B vaccination of all medically stable infants at birth has been in place in the United States since 1991, serving as a core strategy for the prevention of HBV infection, disease, and death in children, and a cornerstone of the US national strategy for the elimination of hepatitis B (CDC 1991, HHS 2025). In the meeting of the Advisory Committee on Immunization Practices (ACIP) on September 18-19, 2025 (CDC 2025a), the newly formed committee raised questions about the standing guidelines for the universal hepatitis B vaccine birth dose and proposed a vote to recommend delaying newborn vaccination for one month or more for infants born to mothers who test negative for hepatitis B surface antigen (HBsAg). Although the vote was deferred, the committee raised concerns that the data on safety, efficacy, and impact on individuals and public health had not previously been adequately assessed. Review of the hepatitis B vaccine is again on the agenda for the upcoming ACIP meeting scheduled for December 4-5, 2025 (CDC 2025b).

The Vaccine Integrity Project was launched in April 2025 by the Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota, an initiative dedicated to providing evidence-based information related to vaccine policies and programs to optimize protection of individuals and the public from vaccine-preventable diseases (CIDRAP 2025). In light of recent events, the Vaccine Integrity Project conducted an independent review and assessment of information related to the safety, effectiveness, and public health impact of universal hepatitis B vaccination at birth in the United States. This report does not reflect a comprehensive systematic review, but rather an overview of information and recommendations of the past 40 years related to epidemiologic trends in HBV incidence and prevalence, vaccine coverage, changes in recommendations to address gaps, clinical trials, safety data from post-licensure surveillance and clinical studies, prior systematic reviews, meta-analyses, and risk-of-bias analyses. Sources of information included data reviewed in previous ACIP reports and searches of the peer-reviewed medical literature on PubMed and Google Scholar. Assessment of hepatitis B vaccine safety included a review of studies (randomized clinical trials, cohort studies, case series, and non-randomized trials) using US-licensed products and US populations. US and European data were reviewed to evaluate public health practices and population-level impact of the birth dose versus delayed hepatitis B vaccination, irrespective of the vaccine product. Studies of pre- and post-1999 vaccine formulations, before and after the 1999 recommendation to remove thimerosal from vaccines, were included in the review. No artificial intelligence (AI) tools or support were used in any part of the literature search, review of studies, or writing of this report.

Background

HBV infection in children occurs predominantly through maternal-infant transmission during pregnancy, labor, and delivery and, to a lesser extent, through postnatal transmission primarily through household contacts and caretakers. Maternal-infant transmission is one of the leading routes of HBV transmission worldwide (AAP 2017, Dionne-Odom 2022, de Villiers 2021). HBV-infected infants have a much greater risk of developing chronic hepatitis and have a more aggressive clinical course compared with those infected as adults (Li 2024, Edmunds 1993).

Without prophylaxis at birth, approximately 90% of newborns infected perinatally will develop chronic hepatitis B infection, and 25% of those with chronic infection will die prematurely from chronic liver disease, including cirrhosis and hepatocellular carcinoma (Schillie 2015, Beasley 1983, Nelson 2014, Margolis 1995, Kimberlin 2021). In comparison, approximately 5% of persons infected with HBV as adults develop chronic hepatitis (Haber 2024). Although beyond the scope of this review, antivirals may be used in the management of hepatitis B disease, though not curative and generally require lifelong use once initiated, underscoring the importance of primary prevention.

For decades, prevention of perinatal transmission of HBV in the United States has relied on routine testing for HBsAg during pregnancy and providing appropriate and timely interventions to both pregnant women and newborns (Schillie 2018, Kimberlin 2021, AAP 2017, Drutz 2025). For infants born to mothers who test positive for HBsAg, effective postexposure prophylaxis includes both hepatitis B immune globulin (HBIG) and vaccination of the newborn within 12 hours of birth. If maternal HBsAg results are unknown or missing, newborn vaccination is recommended within 12 hours of birth. Routine universal vaccination is recommended for all medically stable newborns weighing 2,000 grams (~4 pounds, 4 ounces) or more within the first 24 hours of birth. The routine administration of hepatitis B vaccine at birth was implemented to serve as a safety net to protect infants from early postnatal and perinatal transmission, particularly those born to infected mothers who are not identified at birth, including maternal infections that occur after prenatal screening, or when HBsAg results are not accurately recorded or transmitted between laboratory, prenatal, hospital, and pediatric care teams (AAP 2017).

The recommendation for universal prenatal screening and newborn vaccination was developed to protect infants and children from HBV infection and disease and has served as an important pillar of the national strategy for the elimination of hepatitis B in the United States (CDC 2002a, CDC 1991, Bixler 2023a). Two single-antigen, recombinant hepatitis B vaccines, Engerix-B® and Recombivax HB®, are licensed for use in the United States for administration at birth. Recombinant vaccines trigger an antibody response without the use of weakened or inactivated viruses or any animal or human products (FDA 2019, FDA 2023, Mayo Clinic 2025). For more than 30 years, ACIP has systematically conducted comprehensive reviews of data related to the safety, effectiveness, and public health impact of hepatitis B vaccination at birth. Each review has served to address gaps and determine whether adjustments to recommendations should be made to further protect individuals and the public from hepatitis B infection, disease, and death. The result of these stepwise reviews has led to a significant decline in reported perinatal HBV infections in the United States (Figure 1); in 2023, only seven cases of perinatal HBV infection were reported to the National Notifiable Diseases Surveillance System (CDC 2025c). As infant and child vaccination confers protection from HBV infection for more than 35 years (Bruce 2022), it has had a critical impact on reducing the overall burden of hepatitis B in the United States, providing important protection of adolescents and adults from sexual and parenteral transmission and protecting infants born to mothers vaccinated in childhood (Figure 1).

Burden of hepatitis B virus in the US population

Approximately 660,000 people in the United States are living with hepatitis B infections, a decline from an estimated peak of 1 million to 1.25 million in the 1980s (Bixler 2023b, CDC 1991). In 2023, the incidence of reported acute hepatitis B was 0.7 cases per 100,000 population, more than a 90% decrease from 1985 (Daniels 2009, CDC 2025c). An estimated 50% of people in the United States living with HBV infection are unaware of their infection status (Bixler 2023b).

The incidence of reported acute HBV infections among children and adolescents has decreased substantially over the past four decades (CDC 2004, CDC 2025c). In 2022, there were no reported cases of acute HBV infections among 1- to 4-year-olds and only two reported cases in 5- to 14-year-olds (CDC 2025d). Over time, acute HBV has also consistently declined in the 20- to 29-year-old category, historically a group at highest risk (CDC 2024a, CDC 2025c). Adults who were born after initiation of the universal birth dose recommendation have substantially lower incidence of acute hepatitis B than those born prior to its implementation (CDC 2025e).

Overall prevalence of any past or present HBV infection is higher among non-US-born persons (11.9%) than in those who are US-born (2.5%) (Kruszon-Moran 2020); an estimated 40% of new HBV diagnoses are among people born in the United States (Le 2020). Prevalence is also higher among Hispanic (3.8%), non-Hispanic Black (10.8%), and Asian (21.1%) people than among those who are non-Hispanic White (2.1%) (Kruszon-Moran 2020).

Approximately 0.5% of US women test HBsAg-positive in pregnancy; in 2021, an estimated 17,827 infants were born to mothers who tested HBsAg-positive in pregnancy (Salihu 2012, Ellington 2015, Walker 2016, Harris 2018, Koneru 2019, CDC 2025e). Nearly half of all women who test HBsAg-positive in pregnancy are US-born (CDC 2025e).

Although national disease surveillance systems have reported fewer than 20 perinatal HBV cases annually since 2018, these figures likely underestimate the true burden owing to gaps in screening, follow-up, reporting, and access to care. One modeling analysis estimated that the true number of perinatal infections may be nearly 1,000 cases per year (Ko 2016). Notably, HBV infections in children less than 24 months are classified as perinatal when there is evidence that the child was born to a mother with documented HBV infection (CDC 2021a). If maternal infection is ruled out, cases in this age-group are reported under the acute HBV case definition instead. Because most infections in children less than 24 months originate from maternal transmission, reported perinatal case totals tend to be higher than acute HBV infections in this age group.

> Despite a marked decline in hepatitis B burden in recent decades, an estimated 50% of those living with HBV infection are unaware of their status. Ongoing infections among pregnant women and adults highlight the need for continued screening and vaccination at birth.

Historical trends in newborn hepatitis B vaccine recommendations and incidence of HBV infection

The history of US newborn hepatitis B vaccination reflects a progressive shift from targeted, risk-based interventions toward a universal approach designed to address gaps in protection (Table 1, Table 2), and a growing recognition of the role of newborn vaccination on individual and population-level protection toward the US goal for the elimination of hepatitis B. As shown in the evidence-based processes outlined in this section, the incidence of HBV infection among infants and children declined by approximately 99%, with estimated annual infections in infants and young children falling from roughly 16,000 in the early 1990s (Armstrong 2001) to fewer than 20 cases of reported perinatal infections per year in recent years (Figure 1) (CDC 2024a, CDC 2025c).

Early strategies were grounded in the assumption that HBV risk factors were readily identifiable and sufficient to guide prevention efforts (Table 1). In 1982, ACIP introduced its initial recommendations targeting hepatitis B vaccination to "high-risk" populations, which included immigrant and refugee populations and their relatives from high-HBV-endemic areas, men who have sex with men, and users of injection drugs (CDC 1982). By 1984, this approach was expanded to include HBsAg screening of pregnant women considered at elevated risk (e.g., those with frequent exposure to blood in occupational settings, recipients of multiple blood transfusions, those having household contacts with HBV), with HBIG and vaccination recommended for infants born to those who test positive (CDC 1984).

Closing the gap in preventing perinatal HBV transmission

Accumulating evidence throughout the 1980s demonstrated that selective screening alone was inadequate to protect infants. With no observable improvement in HBV incidence among infants and young children during this period, studies revealed that 35% to 65% of mothers who tested HBsAg-positive had no identifiable risk factors and would not have been identified using the 1984 screening criteria (CDC 1988). Additional investigations raised concerns that healthcare providers may be reluctant to or not prioritize collection of detailed patient histories needed to inform risk-based screening. Further, many providers had limited familiarity with HBV transmission risks and the recommended procedures for screening and prophylaxis. These findings highlighted some of the inherent limitations of programs dependent on accurate risk assessment and served as the basis for broader, more comprehensive policies.

In response to the evident shortcomings of risk-based screening, ACIP updated its recommendations in 1988, which were adopted by the Centers for Disease Control and Prevention (CDC), for universal HBsAg screening of all pregnant women (CDC 1988). This marked an important shift to advancing measures intended to identify all women with chronic HBV infection so that exposed infants could receive timely and appropriate prophylaxis at birth.

However, implementation of recommendations for universal screening of pregnant women proved to be insufficient for the protection of all infants, as technical and operational challenges posed barriers to achieving universal prenatal screening. Despite the recommendation, up to 18% of pregnant women do not receive HBsAg testing during pregnancy (Kolasa 2017, Harris

2018, Pham 2023). Persistent gaps further demonstrated that even universal HBsAg screening could not reliably prevent all perinatal infections (see section on *Persistent Challenges to Prevention*) and underscored the need for an additional layer of protection. Notably, despite the limitations of universal HBsAg screening, it remains a vital component of HBV prevention efforts. In 2004, the US Preventive Services Task Force (USPSTF) conducted a systematic review and concluded that the benefits of universal HBsAg screening in pregnant women greatly outweighed associated costs, a finding that was reaffirmed again in 2009 and 2019 (USPSTF 2009, USPSTF 2019).

Building on these insights and with the goal of optimizing protection of infants and children from HBV infection and its sequelae, ACIP in 1991 revised its recommendations, which were adopted by CDC, that all newborns be vaccinated for hepatitis B at birth prior to hospital discharge, intended to provide protection for all infants regardless of maternal HBsAg status (CDC 1991). Early implementation of infant vaccination programs for hepatitis B in certain high-risk populations resulted in demonstrable improvement, including a 99% reduction in acute HBV incidence among Alaskan Natives (McMahon 1987) and substantial reductions in American Samoa (Abara 2017), highlighting the potential of a universal approach. As a result of this recommendation, hepatitis B birth-dose coverage increased steadily from less than 1% of infants in the late 1980s (Woodruff 1996) to approximately 80% by 2021 (Hill 2024), a trend that has largely been responsible for the reduction in HBV burden among infants and the general US population over the past three decades.

Continued reviews and refinement of evidence-informed guidelines
Although the 1991 recommendation marked a pivotal change, guidelines involving the administration of hepatitis B vaccine doses to newborns continued to be reviewed and refined as new evidence became available. In 2002, ACIP recommended and CDC adopted the redesign of the Childhood Immunization Schedule to more clearly highlight the value of administering the first dose of hepatitis B vaccine at birth (CDC 2002b). Birth-dose coverage remained relatively low; in 2004, 46% of US newborns received the birth dose and perinatal HBV infections were reported in 48 infants (CDC 2005).

In 2005, ACIP recommended and CDC adopted further updates to strengthen implementation of the birth dose (CDC 2005). The guidance offered more detailed procedural instructions, clarifying best practices related to the timing of vaccine administration, birthweight thresholds, and additional standard procedures. These refinements were aimed at reducing variation in practice, as experts noted that permissive language, allowing deferral of vaccination in certain circumstances, had contributed to some inconsistencies in delivery across birth settings (CDC 2017).

Given these findings, ACIP revised recommendations that were accepted and published by CDC in 2018, which remain in place, that provide guidance for clinicians and establish a clear national standard: All medically stable infants weighing 2,000 grams or more should receive the first dose of a hepatitis B vaccine series within 24 hours of birth (CDC 2017, Schillie 2018). This refinement eliminated ambiguity introduced by previous permissive language. It also aligned US

guidance with the World Health Organization's (WHO's) standard for administering a first dose of hepatitis B vaccine preferably within 24 hours of birth (WHO 2017).

> US hepatitis B vaccination policy has evolved from selective, risk-based strategies to a universal birth-dose approach. A series of evidence-based adjustments to recommendations for universal maternal HBsAg screening and hepatitis B vaccination within 24 hours of birth resulted in a 99% decline in pediatric HBV infections since the early 1990s.

Safety of the hepatitis B vaccine birth dose

This review of data on the safety of single-antigen, recombinant hepatitis B vaccines licensed for use in the United States for administration at birth, focused primarily on clinical trials and studies of large national safety monitoring programs, particularly those that systematically detect, assess, and verify vaccine safety signals. We reviewed information related to both short-term and long-term adverse events (AEs), including those that are mild, moderate, and severe (e.g., local redness and swelling, injection-site pain, rash, fever, dizziness, headache, gastrointestinal symptoms, anaphylaxis, irritability/crying, sepsis, death). The review of long-term AEs included a range of reported outcomes, including developmental disorders/delays, bronchopulmonary dysplasia, and autoimmune disorders. Additional analyses of safety data included a review of the administration of the initial vaccine dose at birth compared with vaccines administered at one month of age or more. Studies that investigated products not licensed for US use, or did not evaluate hepatitis B vaccines administered at birth, were not included in the review.

Overall safety profile of the hepatitis B vaccine birth dose

Administration of the hepatitis B vaccine at birth has consistently been demonstrated to be safe, as evidenced by findings from randomized controlled trials (RCTs), case series using routine safety monitoring systems, and large cohort studies (Table 3). Among term newborns, only mild-to-moderate, short-term reactions were reported, predominately acute reactogenicity (e.g., tenderness, redness and swelling at the injection site, fussiness, transient low-grade fever), with no increased incidence of life-threatening vaccine-related serious adverse events (SAEs) (Bassily 1995, Yerushalmi 1997, Niu 1999, Lewis 2001, Greenberg 2002, Hieu 2002, López 2002, Sapru 2007, Eriksen 2004, Velu 2007, Zhu 2017, Haber 2018, Wood 2018). Additionally, no increased incidence of long-term AEs, SAEs, or deaths were reported through a follow-up period ranging from 21 days to 24 months (Table 3) (Bassily 1995, Niu 1996, Yerushalmi 1997, Niu 1999, Greenberg 2002, Hieu 2002, López 2002, Verstraeten 2003, Eriksen 2004, Sapru 2007, Velu 2007, Zhu 2017, Haber 2018, Wood 2018, Morgan 2025). In particular, the rare deaths following hepatitis B vaccination at birth have been extensively studied and found not to be causally associated with vaccination (Niu 1996, Niu 1999, Greenberg 2002, Eriksen 2004, Haber 2018, Morgan 2025). A single-center study of 5,010 infants noted increased cases of mild-to-moderate fever among vaccinated neonates born in the early 1990s, but with no serious sequelae at 21 days follow-up (Linder 1999). Similar studies from the same era did not identify increased risks—including fever—associated with newborn vaccination compared with controls

(Lewis 2001, Nolan 2001). Additionally, population-level surveillance also revealed no causal patterns for SAEs following administration of hepatitis B vaccine within one month of birth (Table 3) (Niu 1996, Niu 1999, Haber 2018). A recent population-based cohort study among preterm infants demonstrated no increase in bronchopulmonary dysplasia or early mortality among those who received a hepatitis B vaccine birth dose compared to preterm infants who were unvaccinated (Morgan 2025), extending the overall neonatal safety profile in this higher-risk population.

Comparison of birth dose and delayed first dose of the hepatitis B vaccine

We identified four studies that directly compared mild-to-moderate AEs and SAEs between infants who received hepatitis B vaccine at one month of age or older and those who received hepatitis B vaccine within the first few days of birth (Bassily 1995, Nolan 2001, Greenberg 2002) or during the neonatal period (less than 28 days) (Haber 2018). Studies demonstrated no increased risk of any short- or long-term AE or SAE in infants administered the vaccine at birth compared with delayed administration (Table 4).

The safety of hepatitis B vaccines containing thimerosal

Thimerosal-containing hepatitis B vaccines were removed from the market beginning in 1999. A review of safety studies of the hepatitis B vaccine conducted prior to thimerosal removal, summarized in Table 3, found no additional safety signals. Further, extensive studies on the safety of thimerosal have not revealed any risk—including autism spectrum disorder (ASD) or other developmental disorders—associated with any thimerosal-containing vaccines, including the hepatitis B vaccine when administered soon after birth (Stehr-Green 2003, Verstraeten 2003, Parker 2004, Fombonne 2006 Thompson 2007, Schechter 2008, Price 2010, Smith 2010, Iqbal 2013,Yoshimasu 2014, Mrozek-Budzyn 2015).

Several analyses using Vaccine Adverse Event Reporting System (VAERS) and Vaccine Safety Datalink (VSD) datasets have reported correlations between thimerosal-containing hepatitis B vaccines and ASD or other developmental delays, but these studies were noted to have important methodologic limitations, including unverified diagnoses, exposure misclassification, uncontrolled confounding, biased denominators, overlapping populations, and multiple testing (Gallagher 2010, Geier 2013, Geier 2015, Geier 2016, Geier 2018). For example, in a 2016 study, Geier et al. reported associations between early-life thimerosal exposure from certain vaccines, including for hepatitis B, and later ASD diagnosis (Geier 2016). However, methodologic constraints, such as exposure/outcome misclassification (including no control for other sources of mercury exposure), and lack of clinical case validation, limit the ability to assess causality. A 2004 review by the Institute of Medicine found many studies by Geier and colleagues, with similar limitations, to be flawed and “uninterpretable” (IOM 2004).

> The totality of evidence supports the safety of administering a monovalent hepatitis B vaccine at birth. Direct comparisons of the birth dose and delayed first dose identified no differences in safety.

Immunogenicity, efficacy, and effectiveness

Prevention of perinatal HBV transmission

Both hepatitis B vaccines currently licensed in the United States for administration at birth have demonstrated a protective antibody response and efficacy for preventing hepatitis B infection among infants born to mothers infected with HBV (Table 5) (Poovorawan 1989, Stevens 1987, Beasley 1983). Hepatitis B vaccine alone, in the absence of HBIG or other interventions, decreased the risk of HBV infection in infants of HBV-infected mothers by nearly 70% (Beasley 1983, Chen 2017). In combination with HBIG, vaccination reduces the risk of perinatal HBV transmission by 83% to 97% (Schillie 2018, Beasley 1983, Lee 2006).

Among infants born to women who are HBsAg-positive or HBsAg-negative, infant hepatitis B vaccination is seroprotective, defined as hepatitis B surface antibody (anti-HBs) titer 10 mIU/mL or greater, which has previously been shown to protect against HBV infection (Lee 1995, Kang 2015, Schillie 2018, Gorar 2024). Among healthy infants, the first dose of hepatitis B vaccine produces a seroprotective response in approximately 25% of recipients, 63% after the second dose, and 95% after the third dose, with no appreciable variation in vaccine response with varying maternal HBsAg status or HBIG administration (Schillie 2018).

Among healthy infants born to patients who are HBsAg-negative, studies have shown that seroprotection after completion of the hepatitis B vaccine series remains very high, regardless of whether the first dose was given at birth or between one and three months of age. Although later initiation is associated with higher peak anti-HBs titers (Da Villa 1997, Middleman 2014, Schillie 2013, del Canho 1993), acute titers are not necessarily reflective of long-term protection. Studies indicating a slight increase in anti-HBs levels with a delayed initial dose solely evaluated immunogenicity, not duration of protection, against perinatal transmission or acute infection.

Long-term protection

Studies have documented long-term vaccine-induced immunity in people who completed the full hepatitis B series in childhood; no differential durability of protection against infection has been found based on the timing of the first dose of hepatitis B vaccine in infancy (Bruce 2022, McMahon 2009). Among US-born 16- to 19-year-olds who completed a recombinant hepatitis B vaccine three-dose series by 12 months of age, 90% exhibited a seroprotective response to a challenge dose of the vaccine more than 15 years later, indicating a lasting immune response; the post-challenge proportion with seroprotection did not differ between those who initiated vaccination within seven days of birth and those who began at four weeks of age (Middleman 2014). Similar responses were seen 35 years after completion of the hepatitis B vaccine series when initiated after six months of age (Bruce 2022). Results of a meta-analysis indicated that, among children vaccinated in infancy, 90% had seroprotection at 17 years of age (Schönberger 2013). Even when anti-HBs antibody levels are below the standard threshold of seroprotection, protective anamnestic (memory) responses are observed (Middleman 2014, Avdicova 2015). Because of the durability of vaccine-induced immunity, booster doses are not recommended for

immunocompetent children or adolescents (Schillie 2018).

> The hepatitis B birth dose is effective in preventing perinatal transmission and acute infection. Vaccination at birth or delayed vaccination confer a similar and long-lasting protective immune response.

Persistent challenges to the prevention of perinatal and postnatal HBV infection in the United States

Recommendations for universal hepatitis B vaccination at birth were implemented based on a series of ACIP reviews that identified persistent gaps in the protection of infants from perinatal and early postnatal HBV infection. Here we review the information related to challenges in HBV prevention among US infants, with a focus on patients who have HBsAg-negative test results in pregnancy.

Gaps in prenatal detection of HBV infection

Current US guidelines recommend routine HBsAg screening for all pregnant women (ACOG 2023). Although hepatitis B serologic testing has a sensitivity and specificity of greater than 98% (USPSTF 2019), an estimated 0.4% to over 3% of pregnant US women receive no prenatal care (Ayoola 2010, Holcomb 2021, McElfish 2025a, McElfish 2025b) and 12% to 18% do not receive HBsAg testing during pregnancy (Kolasa 2017, Harris 2018, Pham 2023) (Figure 2). Only 20% to 55% of pregnant women testing HBsAg-positive receive follow-up HBV DNA testing as recommended by the American College of Obstetricians and Gynecologists (ACOG) (Walker 2016, Kushner 2018, Pham 2023), and only 42% of pregnancies with an HBV diagnosis received the recommended HBV-directed care (Harris 2018). It is estimated that the National Perinatal Hepatitis B Prevention Program identifies less than half of infants born to infected women (Koneru 2021). Characteristics associated with elevated risk of maternal HBV infection are also associated with missed HBV testing as a part of routine prenatal care (Osterman 2018, McElfish 2025a, Goldfarb 2017, Choi 2025, Lee 2025, McElfish 2025b).

Errors across the continuum of care

Communication of maternal hepatitis B test results among laboratories, prenatal clinics, and obstetric and pediatric hospital care teams is not always timely and accurate (Rosenthal 1995). Failure to provide timely post-exposure prophylaxis to the newborn results in a missed opportunity to prevent perinatal HBV transmission, which can occur due to a lack of written hospital policies and standing orders for the birth-dose (Willis 2010, Shaw 2025, Anderson 2005). While electronic health records have improved provider communications, these records are not foolproof, especially when reporting results to public health systems or across the continuum of care from the laboratory, prenatal care clinic, hospital maternal and infant care teams, and pediatric clinics after discharge.

False-negative test results or maternal HBV infection after prenatal screening
Vaccination at birth protects infants in the event of a false-negative test result or maternal infection after screening. Commercially available clinical enzyme immunoassays range in sensitivity from 97% to 100%, but may have reduced sensitivity for specific HBV genotypes or during early acute infection (Coleman 2006, Ly 2006, Scheiblauer 2010). Further, a negative HBsAg test result in pregnancy does not guarantee that the mother is HBV-uninfected at delivery.

Completion of the hepatitis B vaccine series
Delaying the first dose of hepatitis B vaccine creates a gap in early immune protection against postnatal HBV infection until the infant is vaccinated. There is potential for loss to follow-up between discharge from the hospital and attendance at well-child or pediatric care clinics for vaccination. Initiation of the hepatitis B vaccine series at birth is associated with a higher rate of completion of both the hepatitis B vaccine series and childhood vaccination series overall (Zhao 2013, Oster 2019b, Wilson 2019, Vader 2020). This association, however, is likely driven in part by the fact that receipt of the birth dose is also correlated with increased vaccine acceptance overall and the propensity to vaccinate against all childhood vaccine-preventable diseases.

Prevention of postnatal HBV infection
While vaccinating newborns within 24 hours of birth serves as the cornerstone of prevention against perinatal HBV infection, it also provides protection from postnatal infection. HBV can remain stable on surfaces at room temperature for more than seven days (Bond 1981), and unvaccinated infants are at risk of HBV transmission from household, daycare, or other family and community contacts. Seroprevalence studies have identified a higher risk of HBV exposure among children with one or more household members who test positive for HBsAg, especially siblings (Hurie 1992, Mahoney 1995). It's important to note that addressing household risk alone is not sufficient, as another study found that 21% of children with evidence of past hepatitis B infection had no household members who were HBsAg-positive (Hurie 1992).

> Universal hepatitis B vaccination at birth has served to close real-world gaps in prenatal screening and follow-up that may leave infants vulnerable to infection. Administering the birth dose ensures timely protection against both perinatal and postnatal HBV exposure and is associated with an increased likelihood of completion of the full vaccine series.

Global context of hepatitis B vaccine birth-dose recommendations

Global strategies to eliminate HBV infection and perinatal transmission rely on a multi-pronged approach that includes screening in pregnancy, post-exposure prophylaxis for the infant, and vaccination soon after birth. Countries that have scaled up maternal screening and infant vaccination programs have observed a decline in HBV rates across age categories (Sheena 2022). As such, the WHO has set a country-level target of 90% coverage with the birth dose. In 2024, the US birth dose recommendation was aligned with 115 of 194 WHO member states that also had a universal recommendation for a birth dose of hepatitis B vaccine (WHO 2025).

The hepatitis B childhood vaccination schedule varies considerably across European Union (EU) and European Economic Area (EEA) countries. Only five EU/EEA countries (Bulgaria, Lithuania, Poland, Portugal, and Romania) recommend a universal birth dose of hepatitis B vaccine and all five meet the 90% target set by WHO (ECDC 2025). Although most EU/EEA countries do not have a recommendation for a universal birth dose, all countries provide universal prenatal HBV screening and the majority (77%) of countries with available data report screening over 90% of pregnant women (ECDC 2025). In countries where a birth dose is not universally recommended, post-exposure prophylaxis with hepatitis B vaccine and HBIG at birth are targeted for use among infants born to women with documented HBV infection in pregnancy.

While appropriate to consider US vaccine guidance in the context of global recommendations, US vaccination policies were developed and revised to address real-world challenges related to hepatitis B epidemiology, populations at risk, continuity of care, access to care, costs, and other considerations —that are unique to the US and its healthcare system.

> Universal hepatitis B vaccination at birth serves as a safety net to maximize prevention of perinatal and early postnatal HBV transmission, addressing the real-world challenges that are unique to the US and its healthcare system.

Informed vaccine decision-making

Even with the recommendation for the universal birth dose, parents have the option to choose whether or not their infant receives a hepatitis B vaccine at birth, whether to defer vaccination, or whether to decline vaccination entirely. Providers are required by the National Childhood Vaccine Injury Act to present the appropriate CDC Vaccine Information Sheet (VIS) to parents and guardians as part of the consent process before administering any vaccine, including the hepatitis B birth dose (CDC 2021b). Procedures for obtaining parental consent vary by state and healthcare system (Immunize.org 2025). Though outside of the scope of this report, quality improvement programs have identified strategies that facilitate the consent process, enhance patient-centered care, and improve education and communications between parents and the care team (Sarathy 2021, Nemerofsky 2018, Bradshaw 2020). These programs have included increased utilization of nursing staff to provide information and approvals; standardizing information and timing for obtaining permission for the birth dose; and additional education for physicians, nurses, and parents (Sarathy 2021, Nemerofsky 2018, Bradshaw 2020).

> Improving communications and consent processes related to the hepatitis B vaccine birth dose will further enhance patient education and informed decision making between parents and providers.

Conclusion

The reduction of HBV infection among infants and children in the United States over the past 40 years resulted from a series of evidence-based recommendations. Each sequential modification was based on the systematic review of vaccine safety, efficacy, and effectiveness; HBV incidence; gaps in coverage; and quality improvement programs. Improved coverage of infants at birth, in combination with completion of the full hepatitis B vaccine series, resulted in protection of children and was foundational for interrupting HBV transmission to the next generation and the reduction of hepatitis B-related infection, chronic liver disease, cancer, and death in the entire US population.

In this review, we evaluated vaccine safety and the potential individual and population-level benefits of delaying the first hepatitis B vaccination compared with vaccination at birth. The hepatitis vaccine has consistently been shown to be a safe vaccine, regardless of timing of vaccination. This analysis found no differences in short-term or long-term adverse events related to the birth dose compared with a delayed first dose. No benefits of vaccine efficacy, effectiveness, or long-term protection were identified in delaying the first dose compared with vaccination at birth.

We also evaluated the potential population-level risks of delaying the first dose among infants born to HBsAg-negative mothers compared with those vaccinated at birth. This review found no evidence of any health benefit with delaying the birth dose and identified only risks related to changing current US recommendations for universal hepatitis B vaccination for all medically stable newborns weighing 2,000 grams or more within the first 24 hours of birth.

Figures and Tables

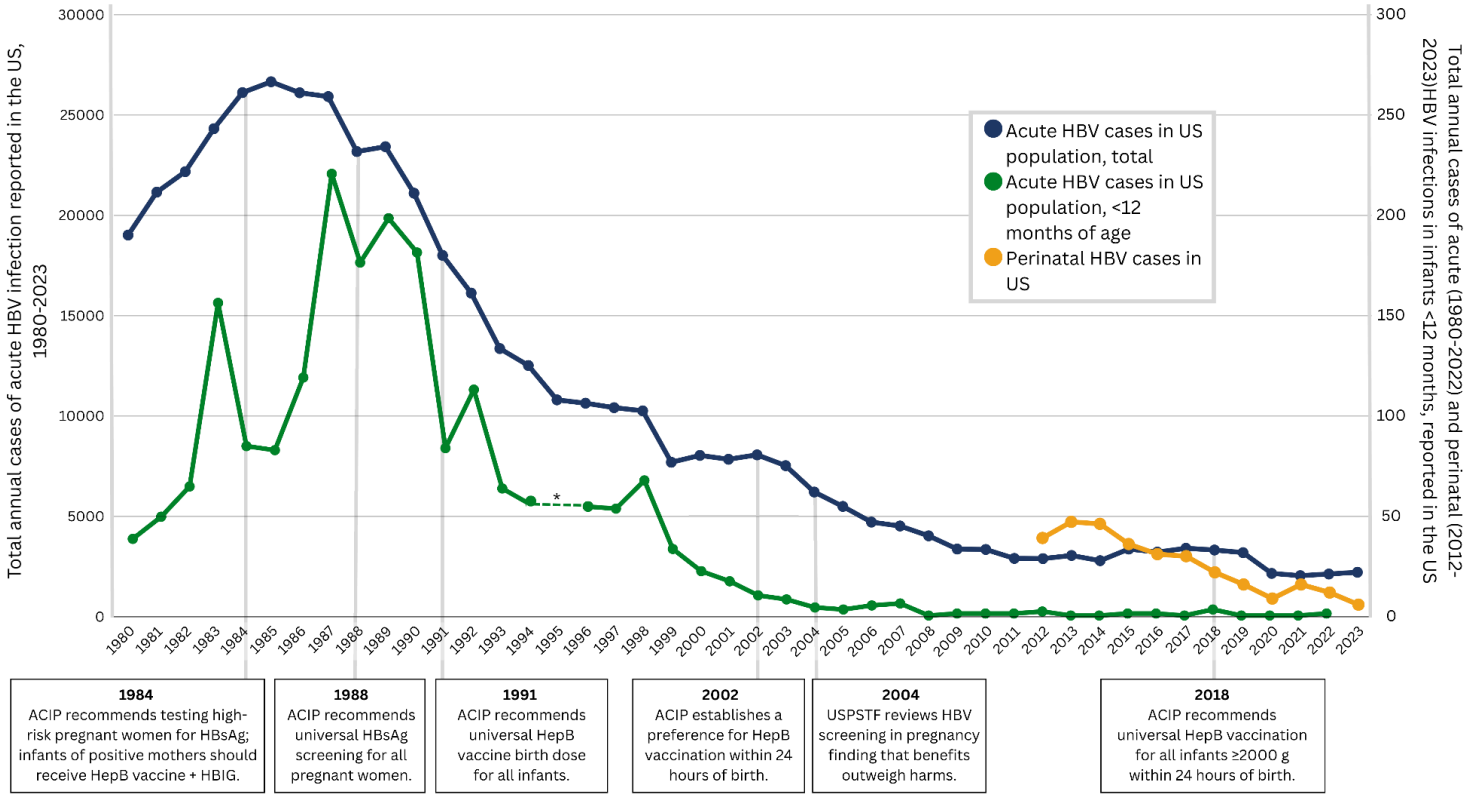

Figure 1: Reported number of acute hepatitis B cases in the United States by year, 1980-2023 and related policy milestones

*No data reported for these years

Abbreviations: ACIP: Advisory Committee on Immunization Practices; HBIG: hepatitis B immunoglobulin; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HepB: hepatitis B; g: grams; USPSTF: United States Preventive Service Task Force

CDC case definitions distinguish acute HBV infection in children <24 months from perinatal HBV infection; cases identified as perinatal infections are based on the epidemiologic link to the mother with documented HBV infection, and reported under the Perinatal Hepatitis B Position Statement (16-ID-06). If the mother is known to not be infected with HBV, the acute hepatitis B case definition is used (CDC 2024b, CDC 2021a). The two definitions are mutually exclusive.

Sources:

- Acute HBV cases in US population, total: CDC 2009: 1980-2007; CDC 2014: 2008-2012; CDC 2018: 2012-2016; CDC 2022: 2016-2020; CDC 2025: 2019-2023
- Acute HBV cases in US population, <12 months of age: CDC 2025g (recurring annual report corresponding to each year of data): 1980-2015; CDC WONDER - NNDSS Annual Summary Data: 2016-2022
- Perinatal HBV cases in US: CDC 2009: 2001, 2004, 2007; CDC 2011: 2005; Ward 2008: 2006; Nelson 2019: 2012-2016; CDC viral hepatitis surveillance reports (CDC 2025h; recurring annual report corresponding to each year of data): 2015-23

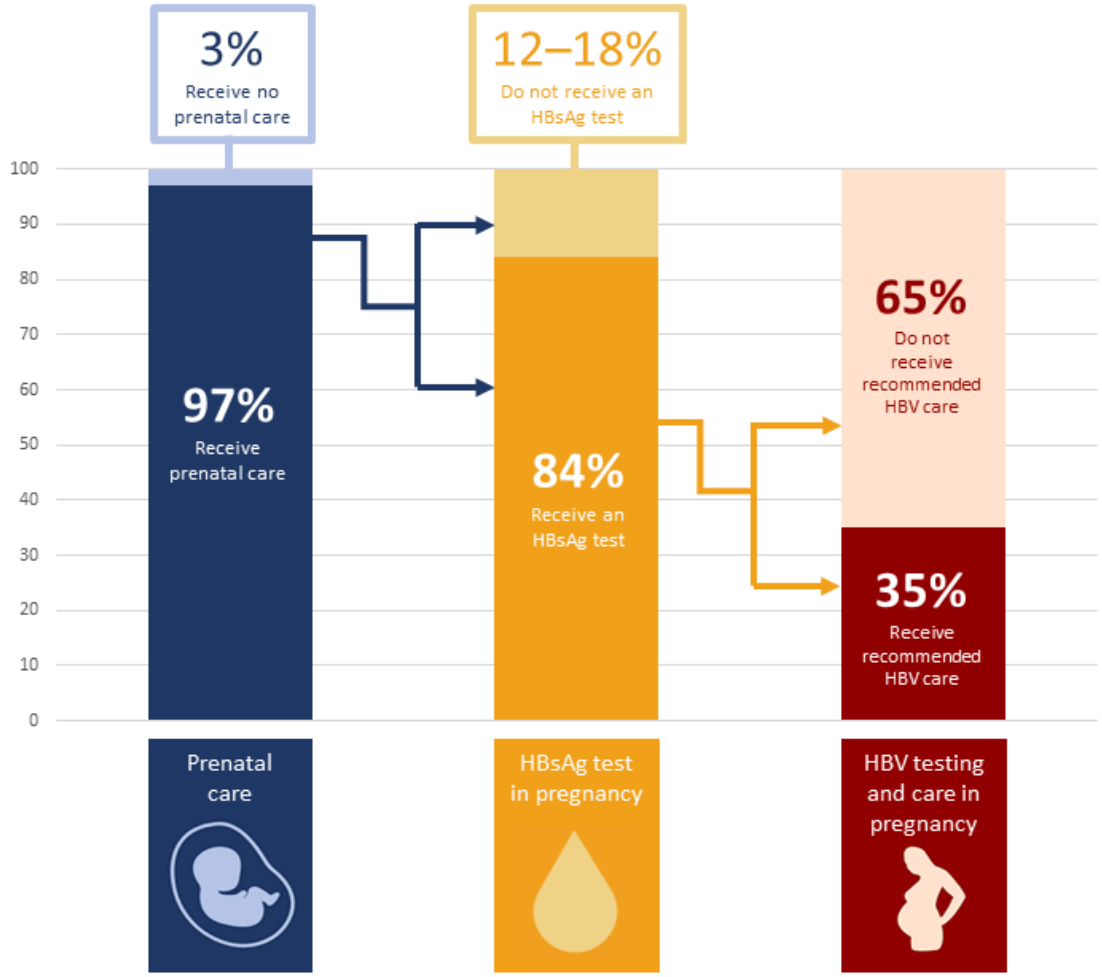

Figure 2: Continuum of care for prenatal HBV screening and care of pregnant women before and after delivery.
Approximately 35% of those who test positive for HBsAg in pregnancy receive recommended follow-up HBV testing and care; 65% do not receive recommended follow-up and care.

Abbreviations: HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus
Sources: Ayoola 2010, Holcomb 2021, McElfish 2025a, Kolasa 2017, Harris 2018, Pham 2023

Table 1: Chronological summary of ACIP reviews and revised recommendations of hepatitis B screening and prophylaxis among pregnant women and infants

Year	Source	Birth Dose Recommendation(s)	Supporting Evidence	Gaps Addressed/Rationale
1984	CDC 1984	Infants born to HBsAg-positive women should receive the first dose of HepB vaccine within 7 days of birth (added as complement to HBIG).	Clinical trials show high efficacy of HepB vaccine + HBIG in preventing chronic infection among infants born to HBsAg-positive mothers; demonstration that vaccine response is not impaired by HBIG.	Enhanced protection for infants born to women with HBsAg-positive test results.
1991	CDC 1991	Universal HepB vaccination for all infants regardless of maternal HBsAg status. Preference that the first dose is administered before hospital discharge.	Data showed highest risk for chronic HBV infection during infancy and early childhood; evident failures of risk-based screening programs. High HBV burden among US children—including an estimated ~16,000 infections annually in children ≤10 years in the early 1990s (Armstrong 2001)—with disparities by race and ethnicity. Successful examples of universal infant vaccination programs for HBV.	Provided a safety net to help mitigate the limitations of risk-based screening programs.
2002	CDC 2002b	Redesigned Childhood Immunization Schedule format to highlight preference for administration of first HBV vaccine dose at birth.	Low birth-dose coverage following the 1999 pause, fell from 47% pre-1999 to 11%; recovering only to 33% in the first year after pause was lifted, despite renewed availability of thimerosal-free vaccines (Luman 2004).	Re-emphasized the birth dose as standard practice to help overcome low uptake and restore clarity following the 1999 pause.
2005	CDC 2005	Medically stable infants ≥2,000 g born to HBsAg-negative mothers should receive the first HepB vaccine dose before hospital discharge. Permissive language for delaying first dose in rare circumstances.	Low birth-dose coverage (46% in 2004), despite >92% of children aged 19-35 months completing the 3-dose series. Ongoing challenges with screening. High chronic HBV infection risk in infants and younger children. Safety and immunogenicity of birth dose reviewed.	Provided further clarification on birth dose guidelines.
2018	Schillie 2018	Universal HepB vaccine birth dose within 24 hours for all medically stable infants ≥2,000 g. Removal of prior permissive language.	High risk of chronic HBV infection in infants and young children. Limitations of screening programs, with up to 16% of pregnant women not tested for HBsAg. Birth-dose coverage below national targets. Alignment with WHO's ≤24-hour guidance. Prior language could be interpreted as setting-specific (i.e., using hospital discharge date as timing does not account for alternative birth facilities).	Standardized timing of HepB vaccine birth dose and removed ambiguity.

Abbreviations: ACIP: Advisory Committee on Immunization Practices; HBIG: hepatitis B immune globulin; HBsAG: hepatitis B surface antigen; HepB: hepatitis B; HBV: hepatitis B virus; g: grams; WHO: World Health Organization

Table 2: Birth-dose guidelines by maternal HBsAg status

Year	Source	HBsAg-negative	HBsAg-positive	Unknown HBsAg status
1984	CDC 1984	n/a	"The first dose should be given within 7 days of birth and may be given concurrently with HBIG [preferably administered ≤12 hours of birth] but at a separate site."	"If a mother's HBsAg-positive status is not discovered until after delivery, prophylaxis should still be administered if a venous (not cord) blood sample from the infant is HBsAg-negative."
1991	CDC 1991	"The first dose can be administered during the newborn period, preferably before the infant is discharged from the hospital, but no later than when the infant is 2 months of age."	"Infants born to mothers who are HBsAg-positive should receive the appropriate doses of hepatitis B vaccine and HBIG within 12 hours of birth. Both should be administered by intra-muscular injection. Hepatitis B vaccine should be administered concurrently with HBIG but at a different site."	"Women admitted for delivery who have not had prenatal HBsAg testing should have blood drawn for testing. While test results are pending, the infant should receive hepatitis B vaccine within 12 hours of birth, in a dose appropriate for infants born to HBsAg-positive mothers."
2005	CDC 2005	"For all medically stable infants weighing >2,000 g at birth and born to HBsAg-negative mothers, the first dose of vaccine should be administered before hospital discharge."	"All infants born to HBsAg-positive women should receive single-antigen hepatitis B vaccine and HBIG <12 hours of birth, administered at different injection sites."	"While test results are pending, all infants born to women without documentation of HBsAg test results should receive the first dose of single-antigen hepatitis B vaccine (without HBIG) within 12 hours of birth"
2018	Schillie 2018	"For all medically stable infants weighing ≥2,000 grams at birth and born to HBsAg-negative mothers, the first dose of vaccine should be administered within 24 hours of birth."	"All infants born to HBsAg-positive women should receive HepB vaccine and HBIG within 12 hours of birth, administered at different injection sites."	"While maternal HBsAg test results are pending, infants with birth weights ≥2,000 grams born to women with an unknown HBsAg status should receive the first dose of HepB vaccine (without HBIG) within 12 hours of birth."

Abbreviations: HBIG: hepatitis B immune globulin; HBsAG: hepatitis B surface antigen; HepB: hepatitis B

Table 3: Summary of published data on adverse events following hepatitis B birth-dose vaccination of vaccines with (denoted by *) and without thimerosal

Study	Study Design	Sample Size	Comparison Groups	Outcomes Assessed	Outcome Window	Last Follow Up	Mild or Moderate Adverse Events (AEs) Following Vaccination	Serious Adverse Events (SAEs) Following Vaccination
Morgan 2025	Cohort	818	Group A: received HepB birth dose Group B (reference): no HepB birth dose	Bronchopulmonary dysplasia and mortality in preterm infants	0-3 months after vaccination	3 months after vaccination	n/a	HepB vaccination was not associated with higher rates of bronchopulmonary dysplasia or all-cause mortality
Wood 2018	RCT	219	Group A: received HepB birth dose concomitant with acellular pertussis vaccine Group B (control): received HepB birth dose alone	Local and systemic effects	0-2 days after vaccination	32 weeks after vaccination	Most frequent AEs were restlessness (31%), drowsiness (28%), vomiting (23%), local erythema (20%), and irritability (20%); mild fever (≥38°C) was documented in 0.7% infants	Among 219 infants, grade 3 severity reactions (defined as AEs preventing normal everyday activities or requiring significant medical intervention) included restlessness (3%), irritability (0.9%), feeding (0.9%), and drowsiness (0.9%)
Haber 2018¥	Case series	Population surveillance (US; 2005-2015)	n/a	Local and systemic effects and mortality	n/a due to study design	n/a due to study design	Analysis of VAERS data identified no new or unexpected safety concerns	No disproportional reporting of SAEs following HepB vaccination were identified
Zhu 2017	RCT	378	Group A: received Engerix-B vaccine at birth (reference) Group B: received Hepavax-Gene TF vaccine at	Local and systemic effects	0-8 days after vaccination	12 months after vaccination	Most frequent AE was fever (≥38°C in <2% and ≥39°C in 0.4%)	No SAEs attributable to vaccination were reported

			birth					
Velu 2007	RCT	38	Group A: received Engerix-B vaccine at birth Group B: received GeneVac B vaccine at birth Group C: received Shanvac B vaccine at birth	Local and systemic effects	0-7 months after vaccination	7 months after vaccination	Most frequent AEs were mild fever (7.8%), moderate fever (5.2%), local swelling (6.8%), and local erythema (5.2%)	No SAEs reported
Sapru 2007	RCT	130	Group A: received Engerix-B vaccine at birth Group B: received GeneVac B vaccine at birth	Local and systemic effects	0-18 weeks after vaccination	18 weeks after vaccination	Low incidence of fever (4.6%) and few mild/moderate local or systemic AEs reported	No SAEs reported
Eriksen 2004*	Cohort	361,696	Group A: received HepB vaccine in the first month of life Group B (reference): did not receive a HepB vaccine in the first month of life	Mortality	0-29 days after vaccination	29 days	n/a	No increase in infant deaths attributed to HepB vaccination
Verstraeten 2003	Cohort	Phase 1: 124,170	Group A: 1-month cumulative Hg	Neurodevelop mental disorders	7 months	7 months	n/a	No consistent association between exposure to thimerosal and neurodevelopment

		Phase 2: 16,717	exposure Group B: 3-month cumulative Hg exposure Group C: 7-month cumulative Hg exposure					outcomes identified
López 2002	Non-RCT clinical trial	117	No comparison groups	Local and systemic effects	0-30 days after vaccination	6 months of age	Low incidence of mild/moderate, self-limited symptoms, most frequently injection site redness (11.4%) and drowsiness (5.1%)	No SAEs reported
Hieu 2002*	RCT	105	Group A: received Hepavax-Gene vaccine at birth Group B (control): received Engerix-B vaccine at birth	AEs	0-15 days after vaccination	24 months of age	Minor, self-limiting events (mild fever) in 2% infants	No SAEs reported
Greenberg 2002	RCT	280	Group A: received DTPa-HepB combination vaccine at 2, 4, and 6 months Group B (control): received HepB vaccine at birth, 1, and 6 months; DTPa at 2, 4, and 6 months	Local and systemic effects and mortality	0-14 days after vaccination	7 months after vaccination	Mild and moderate, self-limiting reactions, most frequently injection site soreness, fussiness, and sleeping more or less	No SAEs or deaths reported

Lewis 2001	Cohort	5655	Group A: received HepB vaccine on day of birth or next day Group B: received HepB vaccine within 21 days of birth Group C (reference): not vaccinated within 21 days of birth	Local and systemic effects, neurological disorders	0-21 days after vaccination	21 days after vaccination	No significantly increased AEs in vaccinated vs unvaccinated	No SAEs reported
Niu 1999*¥	Case series	Population surveillance (US; 1991-1998)	n/a	SAEs and mortality	n/a due to study design	n/a due to study design	n/a	No consistent SAE pattern associated with HepB vaccination; neonatal deaths determined not to be related to vaccination
Linder 1999	Cohort	5010	Group A: born in 1991 (before introduction of routine HepB immunization) Group B: born in 1992 (after introduction of routine HepB immunization)	Fever	Within birth hospitalization	Birth hospitalization	Significantly higher rates (all mild-moderate and self-limited) of fever in infants vaccinated for hepatitis B (0.6% vs 0.28%).	n/a due to study design
Yerushalmi 1997*	RCT	205	Group A: received Bio-Hep-B vaccine at birth Group B (control):	Local and systemic effects	0-5 days after vaccination	12 months after vaccination	Mild and transient AEs; specifically, irritability (11.5% of 52 study participants) and local pain and/or swelling (7.5% each)	No SAEs reported

			received Engerix-B vaccine at birth					
Niu 1996*¥	Case series	Population surveillance (US; 1991-1995)	n/a	AEs and mortality	n/a due to study design	n/a due to study design	Majority of reported AEs were non-serious; mild/moderate AEs not specified	Serious reports consisted of short, fever-related hospitalizations; no deaths or severe neurologic disease were determined to be attributable to vaccination
Bassily 1995*	RCT	178	Group A: received HepB vaccine at birth, 2, and 6 months of age Group B: received HepB vaccine at 2, 4, and 6 months of age Group C (control): no HepB vaccine	Local side effects and fever	0-7 days after vaccination	18 months after vaccination	Mild and self-limited effects, specifically injection site reactions (2.8%) and low-grade fever of ≤38.8°C for 1-2 days (5.6%)	No SAEs reported

* Study vaccine(s) contained thimerosal
¥ Study focused on population-level surveillance; all AE reports in a population over time
Abbreviations: AE: adverse event; DTPa: diphtheria-tetanus toxoids-acellular pertussis; HepB: hepatitis B; Hg: mercury; n/a: not applicable; RCT: randomized controlled trial; SAE: serious adverse event; VAERS: Vaccine Adverse Event Reporting System

Table 4: Selected studies on the adverse event comparison of hepatitis B birth-dose and delayed-dose vaccination schedules

Study	Study Design	Sample Size	Outcomes Assessed	Birth Dose Schedule	Delayed First Dose Schedule	Key Findings
Haber 2018	Case series	Population surveillance (US; 2005-2015)	Local and systemic effects and mortality	0, 2, 6 months	2, 4, 6 months	Short-term AEs were mild to moderate for both schedules No significant safety signals from either schedule
Greenberg 2002	RCT	280	Local and systemic effects and mortality	Single-antigen HepB vaccine at 0, 1, 6 months; DTPa + Hib + OPV vaccines at 2, 4, 6 months	DTPa-HepB + Hib + OPV vaccines at 2, 4, 6 months	Short-term AEs were mild to moderate for both schedules Delayed first HepB dose was associated with higher local AEs and a few higher systemic symptoms at certain visits No vaccine-related SAEs were reported
Nolan 2001	RCT	2156	Local and systemic effects	Single-antigen HepB vaccine at 0 months, followed by pentavalent vaccine at 2, 4, 6 and 18 months	Pentavalent vaccine at 2, 4, 6 and 18 months	No signal of added AEs from the birth dose
Bassily 1995	RCT	178	Local side effects and fever	0, 2, 6 months	2, 4, 9 months	Short-term AEs were mild to moderate for both schedules After birth dose: local reactions (2.8%), fever (5.6%); Delayed first dose: local reactions (7.2%), fever (7.2%) No SAEs through 18 months

Abbreviations: AE: adverse event; DTPa: diphtheria-tetanus toxoids-acellular pertussis; HepB: hepatitis B; Hib: *Haemophilus influenzae* type b; OPV: oral poliovirus vaccine; RCT: randomized controlled trial; SAE: serious adverse event

Table 5: Efficacy, effectiveness, and immunogenicity of newborn dose of hepatitis B vaccine

Study	Study Design	Population	Sample Size	Vaccine Product(s)	Findings
Gorar 2024	RCT	Healthy newborns born to mothers testing HBsAG-negative	218	ENGERIX (10 ug)	95.8% of infants receiving a birth dose had seroprotection, significantly higher than the control group rate at 58.7% which received the routine Pakistan vaccination schedule
Kang 2015	RCT	Healthy newborns	506	Yeast-derived recombinant HepB vaccine (10-ug or 5-ug/0.5 mL doses)	10-ug group achieved higher anti-HBs titers than 5ug group Maternal serostatus did not influence HepB vaccine immunogenicity at either dosage
Qu 2014	RCT	Newborns in Qidong, China who were randomly assigned to the vaccination or control group	72,733	3-dose, 5-µg-plasma-derived HBV vaccination series (Merck) for newborns assigned to vaccine group; children assigned to control group were eligible for a catch-up vaccination series with the 10-µg GSK recombinant vaccine in 200-2001	VE against HBV-related primary liver cancer: 84% (95% CI, 23%-97%) VE against end-stage chronic liver disease: 70% (95% CI, 15%-89%) VE against fulminant hepatitis mortality: 69% (95% CI, 34%-85%)
Hieu 2002	RCT	Full-term, healthy infants born to mothers testing HBsAg and HBeAg positive	105	Hepavax-Gene and Engerix-B	All individuals had a titer greater than 10 mIU/mL, with no statistically significant difference in immune status based on vaccine type received
Bassily 1995	RCT	Healthy neonates born to mothers testing HBsAg-seronegative at the Ministry of Health Center for Maternity and Child Care at Moharam Bek, Alexandria, Egypt	590	2.5 µg of recombinant DNA hepatitis B vaccine (Recombivax HB; Merck Sharp & Dohme, West-point, PA)	Good (51-300 mIU anti-HBs/mL) or Excellent (> 300 mIU/mL) immune responses occurred in 85% of the infants in group receiving doses at birth, 2, and 6 months, and in 96% of the infants in the group receiving doses at 2, 4, and 9 months
del Canho 1993	RCT	Healthy newborns born to mothers testing HBsAg-negative who attended the prenatal clinic of the University Hospital Dijkzigt Rotterdam in the Netherlands	162	20 µg of recombinant DNA yeast-derived vaccine (Engerix-B)	All infants developed anti-HBs levels of at least 10 IU/L, 97% at least 100 IU/L, regardless of vaccination scheme (months 0, 1, and 6, months 0, 1, 2, and 11, or months 3, 4, 5, and 11)

Beasley 1983	RCT	Cases: infants mothers testing positive for HBsAg and HBeAg, born in two large Taipei hospitals Controls: infants born at the same hospital whose parents refused vaccination, or were randomized to receive the placebo from a previous HBIG trial	243	20 g of lots 751/800 and 773/801, titer provided by Merck Sharp and Dohme Laboratories, West Point, PA, and were identical with the commercially available preparation	Efficacy of vaccine alone: 75% Efficacy of HBIG alone: 71% Efficacy of vaccine + HBIG: 94%
Middleman 2014	Non-RCT clinical trial	16-19-year-olds who completed the 3-dose HepB vaccine series as infants	420	Engerix-B	More than 90% of study participants who were vaccinated as infants demonstrated a seroprotective immune response to a challenge dose of the same vaccine
Da Villa 1997	Non-RCT clinical trial	Infants born in 1983 or 1989	710	Plasma-derived vaccine (2 or 3 doses) or DNA recombinant vaccine (2 or 3 doses)	Anti-HBs protection persisted more frequently in participants vaccinated after the third month of life Loss of anti-HBs later in life does not mean a loss of HepB protection
Lee 1995	Non-RCT clinical trial	Newborns of mothers testing HBsAg-negative, or children attending kindergarten	1,364	B-Hepavac II (either 5-ug or 2.5-ug doses)	Half-dose resulted in reduced seroprotection in newborns (anti-HBs ≥10 mIU/mL), but overall seroconversion rates were similar between age and dose groups
Chen 2017	Meta-analysis of RCTs	Infants born to HBV carriers	2,706	Recombinant or plasma-derived HepB vaccine (aggregated for meta-analysis)	RRs (95% CIs) of perinatal transmission from HBV carriers to infants, relative to placebo/none: Vaccine alone: 0.32 (0.21-0.50) Vaccine + HBIG: 0.12 (0.06-0.22)
Schönberger 2013	Meta-analysis of observational studies	Children vaccinated with any HepB vaccine before 6 months of age	28,329	Any HepB vaccine	Long-term protection (90%) at 17 years for children of non-carrier mothers vaccinated with the currently recommended vaccine schedule
Chang 2021	Cohort	Healthy individuals in Taiwan	1,611	Plasma-derived HepB vaccine (pre-November 1992), or recombinant yeast vaccine (post-November 1992)	Prevalence rate of HBsAG in children and adults born after the implementation of the universal HepB vaccination program: 0.4% (94/1,042) vs. prevalence rate of HBsAG

					in subjects born before implementation of the program: 7.7% (44/569)
Poovorawan 1989	Cohort	Healthy newborns born to mothers testing HBsAG and HBeAg-positive; without concomitant HBIG	58	10-ug dose of yeast-recombinant HepB vaccine	Infants becoming carriers: 3.4% at 12 months of follow up Protective efficacy rate against the chronic carrier state during the first 12 months of life was 95%
Stevens 1987	Cohort	Infants born to Asian-American mothers testing HBsAg and HBeAg-positive; all infants received a single 0.5-mL HBIG dose within 24 hours of birth	Total = 122 Plasma-derived vaccine group = 39 Yeast-recombinant vaccine group = 83	10-ug dose of plasma-derived HepB vaccine; 5ug dose of yeast-recombinant HepB vaccine	Infants becoming carriers: Plasma derived vaccine: 10.2% Yeast-recombinant vaccine: 4.8%
Abbreviations: anti-HBs: hepatitis B surface antibody; HBIG: hepatitis B immune globulin; HBeAG: hepatitis B e-antigen; HBsAG: hepatitis B surface antigen; HBV: hepatitis B virus; HepB: hepatitis B; PA: Pennsylvania; RCT: randomized controlled trial; RR: relative risk; VE: vaccine efficacy					

Abbreviations

ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
AE	Adverse event
AI	Artificial intelligence
Anti-HBs	Hepatitis B surface antibody
ASD	Autism spectrum disorder
CDC	Centers for Disease Control and Prevention
CIDRAP	Center for Infectious Disease Research and Policy
EEA	European Economic Area
EU	European Union
HBsAg	Hepatitis B surface antigen
HBIG	Hepatitis B immune globulin
HBV	Hepatitis B virus
RCT	Randomized controlled trial
SAE	Serious adverse event
USPSTF	US Preventive Services Task Force
VAERS	Vaccine Adverse Event Reporting System
VIS	Vaccine Information Sheet
VSD	Vaccine Safety Datalink
WHO	World Health Organization

References

1. AAP (2017). "Elimination of Perinatal Hepatitis B: Providing the First Vaccine Dose within 24 Hours of Birth." Pediatrics **140**(3): e20171870. https://doi.org/10.1542/peds.2017-1870

2. Abara, W. E., Collier, M. G., et al. (2017). "Impact of Universal Infant Hepatitis B Vaccination in the US-Affiliated Pacific Islands, 1985–2015." Vaccine **35**(7): 997–1000. https://doi.org/https://doi.org/10.1016/j.vaccine.2017.01.020

3. ACOG (2023). "Viral Hepatitis in Pregnancy." https://www.acog.org/clinical/clinical-guidance/clinical-practice-guideline/articles/2023/09/viral-hepatitis-in-pregnancy

4. Anderson, T. A. and Wexler, D. L. (2005). "States Report Hundreds of Medical Errors in Perinatal Hepatitis B Prevention." Hepatitis B. https://www.immunize.org/wp-content/uploads/protect-newborns/guide/chapter2/case-reports.pdf

5. Armstrong, G. L., Mast, E. E., et al. (2001). "Childhood Hepatitis B Virus Infections in the United States before Hepatitis B Immunization." Pediatrics **108**(5): 1123–1128. https://doi.org/10.1542/peds.108.5.1123

6. Avdicova, M., Crasta, P. D., et al. (2015). "Lasting Immune Memory against Hepatitis B Following Challenge 10–11 Years after Primary Vaccination with Either Three Doses of Hexavalent Dtpa-HBV-Ipv/Hib or Monovalent Hepatitis B Vaccine at 3, 5 and 11–12 Months of Age." Vaccine **33**(23): 2727–2733. https://doi.org/https://doi.org/10.1016/j.vaccine.2014.06.070

7. Ayoola, A. B., Nettleman, M. D., et al. (2010). "Time of Pregnancy Recognition and Prenatal Care Use: A Population-Based Study in the United States." Birth **37**(1): 37–43. https://doi.org/10.1111/j.1523-536X.2009.00376.x

8. Bassily, S., Kotkat, A., et al. (1995). "Comparative Study of the Immunogenicity and Safety of Two Dosing Schedules of Hepatitis B Vaccine in Neonates." Am J Trop Med Hyg **53**(4): 419–422. https://doi.org/10.4269/ajtmh.1995.53.419

9. Beasley, R. P., Hwang, L. Y., et al. (1983). "Prevention of Perinatally Transmitted Hepatitis B Virus Infections with Hepatitis B Immune Globulin and Hepatitis B Vaccine." Lancet **2**(8359): 1099–1102. https://doi.org/10.1016/s0140-6736(83)90624-4

10. Bixler, D., Roberts, H., et al. (2023a). "Progress and Unfinished Business: Hepatitis B in the United States, 1980-2019." Public Health Rep: 333549231175548. https://doi.org/10.1177/00333549231175548

11. Bixler, D., Barker, L., et al. (2023b). "Prevalence and Awareness of Hepatitis B Virus Infection in the United States: January 2017 - March 2020." Hepatol Commun **7**(4): e0118. https://doi.org/10.1097/HC9.0000000000000118

12. Bond, W. W., Favero, M. S., et al. (1981). "Survival of Hepatitis B Virus after Drying and Storage for One Week." Lancet **1**(8219): 550–551. https://doi.org/10.1016/s0140-6736(81)92877-4

13. Bradshaw, C., DiFrisco, E., et al. (2020). "Improving Birth Dose Hepatitis B Vaccination Rates: A Quality Improvement Intervention." Hosp Pediatr **10**(5): 430–437. https://doi.org/10.1542/hpeds.2019-0294

14. Bruce, M. G., Bruden, D., et al. (2022). "Protection and Antibody Levels 35 Years after Primary Series with Hepatitis B Vaccine and Response to a Booster Dose." Hepatology **76**(4): 1180–1189. https://doi.org/10.1002/hep.32474

15. CDC (1982). "Recommendation of the Immunization Practices Advisory Committee (ACIP) Inactivated Hepatitis B Virus Vaccine." https://www.cdc.gov/mmwr/preview/mmwrhtml/00001116.htm

16. CDC (1984). "Recommendation of the Immunization Practices Advisory Committee (ACIP) Postexposure Prophylaxis of Hepatitis B." https://www.cdc.gov/mmwr/preview/mmwrhtml/00022736.htm

17. CDC (1988). "Recommendations of the Immunization Practices Advisory Committee Prevention of Perinatal Transmission of Hepatitis B Virus: Prenatal Screening of All Pregnant Women for Hepatitis B Surface Antigen." https://www.cdc.gov/mmwr/preview/mmwrhtml/00000036.htm

18. CDC (1991). "Hepatitis B Virus: A Comprehensive Strategy for Eliminating Transmission in the United States through Universal Childhood Vaccination: Recommendations of the Immunization Practices Advisory Committee (ACIP)." https://www.cdc.gov/mmwr/preview/mmwrhtml/00033405.htm

19. CDC (2002a). "Achievements in Public Health: Hepatitis B Vaccination --- United States, 1982--2002." https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5125a3.htm

20. CDC (2002b). "Notice to Readers: Recommended Childhood Immunization Schedule --- United States, 2002." https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5102a4.htm

21. CDC (2004). "Acute Hepatitis B among Children and Adolescents --- United States, 1990--2002." https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5343a4.htm

22. CDC (2005). "A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee

on Immunization Practices (ACIP) Part 1: Immunization of Infants, Children, and Adolescents." https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm

23. CDC (2009). "Surveillance for Acute Viral Hepatitis --- United States, 2007." https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5803a1.htm

24. CDC (2011). "Assessing Completeness of Perinatal Hepatitis B Virus Infection Reporting through Comparison of Immunization Program and Surveillance Data --- United States." https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6013a4.htm

25. CDC (2014). "Index of U.S. 2012 Surveillance Data for Viral Hepatitis | CDC." https://archive.cdc.gov/www_cdc_gov/hepatitis/statistics/2012surveillance/index.htm

26. CDC (2017). "Advisory Committee on Immunization Practices (ACIP) Summary Report : October 19-20, 2016, Atlanta, Georgia." https://stacks.cdc.gov/view/cdc/45555

27. CDC (2018). "2016 Surveillance Data for Viral Hepatitis | CDC." https://archive.cdc.gov/www_cdc_gov/hepatitis/statistics/2016surveillance/index.htm

28. CDC (2021a). "Hepatitis B, Perinatal Infection 2017 Case Definition | CDC." https://ndc.services.cdc.gov/case-definitions/hepatitis-b-perinatal-virus-infection-2017/.

29. CDC (2021b). "Vaccine Information Statement: Facts About VISS | CDC." https://www.cdc.gov/vaccines/hcp/vis/about/facts-vis.html

30. CDC (2022). "2020 Viral Hepatitis Surveillance Report." 2020 Viral Hepatitis Surveillance Report. https://www.cdc.gov/hepatitis-surveillance-2020/about/index.html

31. CDC (2024a). "2022 Viral Hepatitis Surveillance Report." 2022 Viral Hepatitis Surveillance Report. https://www.cdc.gov/hepatitis-surveillance-2022/about/index.html

32. CDC (2024b). "Hepatitis B, Acute and Chronic 2024 Case Definition | CDC." https://ndc.services.cdc.gov/case-definitions/hepatitis-b-acute-and-chronic-2024/.

33. CDC (2025a). "ACIP Presentation Slides: September 18-19, 2025 Meeting." Advisory Committee on Immunization Practices (ACIP). https://www.cdc.gov/acip/meetings/presentation-slides-september-18-19-2025.html

34. CDC (2025b). "ACIP Meeting Information." Advisory Committee on Immunization Practices (ACIP). https://www.cdc.gov/acip/meetings/index.html

35. CDC (2025c). "2023 Viral Hepatitis Surveillance Report." 2023 Viral Hepatitis Surveillance Report. https://www.cdc.gov/hepatitis-surveillance-2023/about/index.html

36. CDC (2025d). "NNDSS Annual Summary Data 2016-2022 Request." https://wonder.cdc.gov/nndss-annual-summary.html

37. CDC (2025e). "ACIP Meeting Materials for Public Posting: Hepatitis B Birth Dose Briefing Document." Advisory Committee on Immunization Practices (ACIP). https://www.cdc.gov/acip/downloads/slides-2025-09-18-19/hep-b-birth-dose-briefing-508.pdf

38. CDC (2025f). "Clinical Overview of Perinatal Hepatitis B." Hepatitis B. https://www.cdc.gov/hepatitis-b/hcp/perinatal-provider-overview/index.html

39. CDC. (2025g). "MMWR Summaries of Notifiable Diseases." from https://stacks.cdc.gov/gsearch?terms=summary+of+notifiable+diseases

40. CDC (2025h). "Viral Hepatitis Surveillance Reports." Viral Hepatitis. https://www.cdc.gov/hepatitis/php/statistics-surveillance/index.html

41. Chang, K.-C., Chang, M.-H., et al. (2021). "Universal Infant Hepatitis B Virus (HBV) Vaccination for 35 Years: Moving toward the Eradication of HBV." The Journal of Infectious Diseases **225**(3): 431–435. https://doi.org/10.1093/infdis/jiab401

42. Chen, Z. X., Zhuang, X., et al. (2017). "Comparative Effectiveness of Prophylactic Strategies for Perinatal Transmission of Hepatitis B Virus: A Network Meta-Analysis of Randomized Controlled Trials." Open Forum Infect Dis **4**(4): ofx225. https://doi.org/10.1093/ofid/ofx225

43. Choi, S., McElfish, P. A., et al. (2025). "Disparities in Prenatal Care Utilization among Racial/Ethnic and Nativity Subgroups in the United States." Prev Med **192**: 108238. https://doi.org/10.1016/j.ypmed.2025.108238

44. CIDRAP (2025). "Vaccine Integrity Project - CIDRAP." https://www.cidrap.umn.edu/vaccine-integrity-project

45. Coleman, P. F. (2006). "Detecting Hepatitis B Surface Antigen Mutants - Volume 12, Number 2—February 2006 - Emerging Infectious Diseases Journal - CDC." https://doi.org/10.3201/eid1202.050038

46. Da Villa, G., Pelliccia, M. G., et al. (1997). "Anti-Hbs Responses in Children Vaccinated with Different Schedules of Either Plasma-Derived or HBV DNA Recombinant Vaccine." Research in Virology **148**(2): 109–114. https://doi.org/10.1016/s0923-2516(97)89893-7

47. Daniels, D., Grytdal, S., et al. (2009). "Morbidity and Mortality Weekly Report (MMWR): Surveillance Summaries, May 2009 / Vol. 58 / No. Ss-3." https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5803a1.htm

48. de Villiers, M. J., Nayagam, S., et al. (2021). "The Impact of the Timely Birth Dose Vaccine on the Global Elimination of Hepatitis B." Nature Communications **12**(1): 6223. https://doi.org/10.1038/s41467-021-26475-6

49. Deerin, J. F., Clifton, R., et al. (2021). "Hepatitis B Birth Dose Vaccination Patterns in the Military Health System, 2014-2018." Vaccine **39**(15): 2094–2102. https://doi.org/10.1016/j.vaccine.2021.03.010

50. del Canho, R., Grosheide, P. M., et al. (1993). "Immunogenicity of 20 Micrograms of Recombinant DNA Hepatitis B Vaccine in Healthy Neonates: A Comparison of Three Different Vaccination Schemes." J Med Virol **41**(1): 30–34. https://doi.org/10.1002/jmv.1890410107

51. Dionne-Odom, J., Cozzi, G. D., et al. (2022). "Treatment and Prevention of Viral Hepatitis in Pregnancy." Am J Obstet Gynecol **226**(3): 335–346. https://doi.org/10.1016/j.ajog.2021.09.002

52. Drutz, J. B., Julie (2025). "Hepatitis B Virus Immunization in Infants, Children, and Adolescents - UpToDate." UpToDate. https://www.uptodate.com/contents/hepatitis-b-virus-immunization-in-infants-children-and-adolescents

53. Dugovich, A. M., Cox, T. H., et al. (2023). "First Hepatitis B Vaccine Uptake in Neonates Prior to and during the Covid-19 Pandemic." Vaccine **41**(17): 2824–2828. https://doi.org/10.1016/j.vaccine.2023.03.039

54. ECDC (2025). "Hepatitis B Vaccination Policies, Practices and Challenges to Achieving Hepatitis Elimination in the European Union and European Economic Area." https://www.ecdc.europa.eu/en/publications-data/hepatitis-b-vaccination-policies-practices-and-challenges-achieving-hepatitis

55. Edmunds, W. J., Medley, G. F., et al. (1993). "The Influence of Age on the Development of the Hepatitis B Carrier State." Proc Biol Sci **253**(1337): 197–201. https://doi.org/10.1098/rspb.1993.0102

56. Ellington, S. R., Flowers, L., et al. (2015). "Recent Trends in Hepatic Diseases during Pregnancy in the United States, 2002-2010." Am J Obstet Gynecol **212**(4): 524 e521–527. https://doi.org/10.1016/j.ajog.2014.10.1093

57. Eriksen, E. M., Perlman, J. A., et al. (2004). "Lack of Association between Hepatitis B Birth Immunization and Neonatal Death: A Population-Based Study from the Vaccine Safety Datalink Project." Pediatr Infect Dis J **23**(7): 656–662. https://doi.org/10.1097/01.inf.0000130953.08946.d0

58. Euler, G. L., Wooten, K. G., et al. (2003). "Hepatitis B Surface Antigen Prevalence among Pregnant Women in Urban Areas: Implications for Testing, Reporting, and Preventing Perinatal Transmission." Pediatrics **111**(5 Pt 2): 1192–1197. https://doi.org/10.1542/peds.111.S1.1192

59. FDA (2019). "Recombivax HB." FDA. https://www.fda.gov/vaccines-blood-biologics/vaccines/recombivax-hb

60. FDA (2023). "Engerix-B." FDA. https://www.fda.gov/vaccines-blood-biologics/vaccines/engerix-b

61. Fombonne, E., Zakarian, R., et al. (2006). "Pervasive Developmental Disorders in Montreal, Quebec, Canada: Prevalence and Links with Immunizations." Pediatrics **118**(1): e139–150. https://doi.org/10.1542/peds.2005-2993

62. Gallagher, C. M. and Goodman, M. S. (2010). "Hepatitis B Vaccination of Male Neonates and Autism Diagnosis, NHIS 1997-2002." J Toxicol Environ Health A **73**(24): 1665–1677. https://doi.org/10.1080/15287394.2010.519317

63. Geier, D. A., Hooker, B. S., et al. (2013). "A Two-Phase Study Evaluating the Relationship between Thimerosal-Containing Vaccine Administration and the Risk for an Autism Spectrum Disorder Diagnosis in the United States." Transl Neurodegener **2**(1): 25. https://doi.org/10.1186/2047-9158-2-25

64. Geier, D. A., Kern, J. K., et al. (2015). "Thimerosal Exposure and Increased Risk for Diagnosed Tic Disorder in the United States: A Case-Control Study." Interdiscip Toxicol **8**(2): 68–76. https://doi.org/10.1515/intox-2015-0011

65. Geier, D. A., Kern, J. K., et al. (2016). "A Longitudinal Cohort Study of the Relationship between Thimerosal-Containing Hepatitis B Vaccination and Specific Delays in Development in the United States: Assessment of Attributable Risk and Lifetime Care Costs." J Epidemiol Glob Health **6**(2): 105–118. https://doi.org/10.1016/j.jegh.2015.06.002

66. Geier, D. A., Kern, J. K., et al. (2018). "Premature Puberty and Thimerosal-Containing Hepatitis B Vaccination: A Case-Control Study in the Vaccine Safety Datalink." Toxics **6**(4): 67. https://doi.org/10.3390/toxics6040067

67. Goldfarb, S. S., Smith, W., et al. (2017). "Disparities in Prenatal Care Utilization among U.S. Versus Foreign-Born Women with Chronic Conditions." J Immigrant Minority Health **19**(6): 1263–1270. https://doi.org/10.1007/s10903-016-0435-x

68. Gorar, Z. A. and Butt, Z. A. (2024). "Impact of Hepatitis B Birth Dose on Immune Response in Pakistani Children: An Open-Label, Non-Inferiority Randomized Controlled Trial, Implications for Achieving SDG Target." Infect Dis (Lond) **56**(1): 1–10. https://doi.org/10.1080/23744235.2023.2258208

69. Greenberg, D. P., Wong, V. K., et al. (2002). "Safety and Immunogenicity of a Combination Diphtheria-Tetanus Toxoids-Acellular Pertussis-Hepatitis B Vaccine Administered at Two, Four and Six Months of Age Compared with Monovalent Hepatitis B Vaccine Administered at Birth, One Month and Six Months of Age." Pediatr Infect Dis J **21**(8): 769–777. https://doi.org/10.1097/00006454-200208000-00014

70. Haber, P., Moro, P. L., et al. (2018). "Safety of Currently Licensed Hepatitis B Surface Antigen Vaccines in the United States, Vaccine Adverse Event Reporting System (VAERS), 2005-2015." Vaccine **36**(4): 559–564. https://doi.org/10.1016/j.vaccine.2017.11.079

71. Haber, P. S., S. (2024). Chapter 10: Hepatitis B. Epidemiology and Prevention of Vaccine-Preventable Diseases, CDC. https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-10-hepatitis-b.html

72. Harris, A. M., Isenhour, C., et al. (2018). "Hepatitis B Virus Testing and Care among Pregnant Women Using Commercial Claims Data, United States, 2011-2014." Infect Dis Obstet Gynecol **2018**(1): 4107329. https://doi.org/10.1155/2018/4107329

73. HHS (2025). "Viral Hepatitis National Strategic Plan | HHS.Gov." https://www.hhs.gov/hepatitis/viral-hepatitis-national-strategic-plan/index.html

74. Hieu, N. T., Kim, K. H., et al. (2002). "Comparative Efficacy, Safety and Immunogenicity of Hepavax-Gene and Engerix-B, Recombinant Hepatitis B Vaccines, in Infants Born to HBsAg and HBeAg Positive Mothers in Vietnam: An Assessment at 2 Years." Vaccine **20**(13-14): 1803–1808. https://doi.org/10.1016/s0264-410x(01)00518-7

75. Hill, H. A., Yankey, D., et al. (2024). "Decline in Vaccination Coverage by Age 24 Months and Vaccination Inequities among Children Born in 2020 and 2021 - National Immunization Survey-Child, United States, 2021-2023." MMWR Morb Mortal Wkly Rep **73**(38): 844–853. https://doi.org/10.15585/mmwr.mm7338a3

76. Holcomb, D. S., Pengetnze, Y., et al. (2021). "Geographic Barriers to Prenatal Care Access and Their Consequences." Am J Obstet Gynecol MFM **3**(5): 100442. https://doi.org/10.1016/j.ajogmf.2021.100442

77. Hurie, M. B., Mast, E. E., et al. (1992). "Horizontal Transmission of Hepatitis B Virus Infection to United States-Born Children of Hmong Refugees." Pediatrics **89**(2): 269–273. https://www.ncbi.nlm.nih.gov/pubmed/1734395

78. Immunize.org (2025). "Vaccine Information Statements (VISS) Overview." Immunize.org. https://www.immunize.org/vaccines/vis/about-vis/.

79. IOM (2004) "Immunization Safety Review: Vaccines and Autism." Immunization Safety Review: Vaccines and Autism. https://doi.org/10.17226/10997

80. Iqbal, S., Barile, J. P., et al. (2013). "Number of Antigens in Early Childhood Vaccines and Neuropsychological Outcomes at Age 7-10 Years." Pharmacoepidemiol Drug Saf **22**(12): 1263–1270. https://doi.org/10.1002/pds.3482

81. Juon, H. S., Sheler, D. T., et al. (2022). "Racial Disparities in Hepatitis B Birth Dose in the Washington Metropolitan Region, 2018-2020." Vaccines (Basel) **10**(7): 1121. https://doi.org/10.3390/vaccines10071121

82. Kang, G., Ma, F., et al. (2015). "Efficacy of Antigen Dosage on the Hepatitis B Vaccine Response in Infants Born to Hepatitis B-Uninfected and Hepatitis B-Infected Mothers." Vaccine **33**(33): 4093–4099. https://doi.org/10.1016/j.vaccine.2015.06.081

83. Kimberlin, D. W., Barnett, E. D., et al. (2021) "Hepatitis B." Red Book: 2021–2024 Report of the Committee on Infectious Diseases. https://doi.org/10.1542/9781610027373

84. Ko, S. C., Fan, L., et al. (2016). "Estimated Annual Perinatal Hepatitis B Virus Infections in the United States, 2000-2009." J Pediatric Infect Dis Soc **5**(2): 114–121. https://doi.org/10.1093/jpids/piu115

85. Kolasa, M. S., Tsai, Y., et al. (2017). "Hepatitis B Surface Antigen Testing among Pregnant Women, United States 2014." Pediatr Infect Dis J **36**(7): e175–e180. https://doi.org/10.1097/INF.0000000000001516

86. Koneru, A., Schillie, S., et al. (2019). "Estimating Annual Births to Hepatitis B Surface Antigen–Positive Women in the United States by Using Data on Maternal Country of Birth." Public Health Reports® **134**(3): 255–263. https://doi.org/10.1177/0033354919836958

87. Koneru, A., Fenlon, N., et al. (2021). "National Perinatal Hepatitis B Prevention Program: 2009-2017." Pediatrics **147**(3): e20201823. https://doi.org/10.1542/peds.2020-1823

88. Kruszon-Moran, D., Paulose-Ram, R., et al. (2020). "Prevalence and Trends in Hepatitis B Virus Infection in the United States, 2015-2018." NCHS Data Brief(361): 1–8. https://www.ncbi.nlm.nih.gov/pubmed/32487291

89. Kushner, T., Shaw, P. A., et al. (2018). "Incidence, Determinants and Outcomes of Pregnancy-Associated Hepatitis B Flares: A Regional Hospital-Based Cohort Study." Liver Int **38**(5): 813–820. https://doi.org/10.1111/liv.13594

90. Le, M. H., Yeo, Y. H., et al. (2020). "Chronic Hepatitis B Prevalence among Foreign‐Born and U.S.‐Born Adults in the United States, 1999‐2016." Hepatology **71**(2). https://journals.lww.com/hep/fulltext/2020/02000/chronic_hepatitis_b_prevalence_among_foreign_born.5.aspx

91. Lee, C., Gong, Y., et al. (2006). "Effect of Hepatitis B Immunisation in Newborn Infants of Mothers Positive for Hepatitis B Surface Antigen: Systematic Review and Meta-Analysis." BMJ **332**(7537): 328–336. https://doi.org/10.1136/bmj.38719.435833.7C

92. Lee, J., Howard, K. J., et al. (2025). "Trends and Racial/Ethnic Disparities in Prenatal Care (PNC) Use from 2016 to 2021 in the United States." J. Racial and Ethnic Health Disparities **12**(5): 3095–3106. https://doi.org/10.1007/s40615-024-02115-9

93. Lee, S. S., Lo, Y. C., et al. (1995). "A Reduced Dose Approach to Hepatitis B Vaccination for Low-Risk Newborns and Preschool Children." Vaccine **13**(4): 373–376. https://doi.org/10.1016/0264-410x(95)98260-h

94. Lewis, E., Shinefield, H. R., et al. (2001). "Safety of Neonatal Hepatitis B Vaccine Administration." Pediatr Infect Dis J **20**(11): 1049–1054. https://doi.org/10.1097/00006454-200111000-00009

95. Li, J., Gao, Z., et al. (2024). "Global, Regional, and National Total Burden Related to Hepatitis B in Children and Adolescents from 1990 to 2021." BMC Public Health **24**(1): 2936. https://doi.org/10.1186/s12889-024-20462-4

96. Linder, N., Raz, M., et al. (1999). "Unexplained Fever in Neonates May Be Associated with Hepatitis B Vaccine." Arch Dis Child Fetal Neonatal Ed **81**(3): F206–207. https://doi.org/10.1136/fn.81.3.f206

97. López, P., Rubiano, L., et al. (2002). "Immunogenicity and Reactogenicity of DTPw-HB/Hib Vaccine Administered to Colombian Infants after a Birth Dose of Hepatitis B Vaccine." Expert Rev Vaccines **1**(3): 277–283. https://doi.org/10.1586/14760584.1.3.277

98. Luman, E. T., Fiore, A. E., et al. (2004). "Impact of Thimerosal-Related Changes in Hepatitis B Vaccine Birth-Dose Recommendations on Childhood Vaccination Coverage." JAMA **291**(19): 2351–2358. https://doi.org/10.1001/jama.291.19.2351

99. Ly Thoai, D., Servant-Delmas, A., et al. (2006). "Sensitivities of Four New Commercial Hepatitis B Virus Surface Antigen (HBsAg) Assays in Detection of HBsAg Mutant Forms." Journal of Clinical Microbiology **44**(7): 2321–2326. https://doi.org/10.1128/jcm.00121-06

100. Mahoney, F. J., Lawrence, M., et al. (1995). "Continuing Risk for Hepatitis B Virus Transmission among Southeast Asian Infants in Louisiana." Pediatrics **96**(6): 1113–1116. https://doi.org/10.1542/peds.96.6.1113

101. Margolis, H. S., Coleman, P. J., et al. (1995). "Prevention of Hepatitis B Virus Transmission by Immunization: An Economic Analysis of Current Recommendations." JAMA **274**(15): 1201–1208. https://doi.org/10.1001/jama.1995.03530150025029

102. Massey, J., Nair, A., et al. (2018). "Hospital, Maternal and Birth Factors Associated with Hepatitis B Vaccination at Birth: West Virginia, 2015." Pediatr Infect Dis J **37**(7): 691–696. https://doi.org/10.1097/INF.0000000000001953

103. Mayo Clinic. (2025). "Hepatitis B Vaccine (Intramuscular Route) - Side Effects & Uses." Mayo Clinic, from https://www.mayoclinic.org/drugs-supplements/hepatitis-b-vaccine-intramuscular-route/description/drg-20068700

104. McElfish, P. A., Caldwell, A., et al. (2025a). "Sociodemographic Factors Associated with Prenatal Care Utilization in Arkansas, United States." Prev Med Rep **51**: 102983. https://doi.org/10.1016/j.pmedr.2025.102983

105. McElfish, P. A., Caldwell, A. R., et al. (2025b). "Disparities in Prenatal Care Utilization in the United States." Matern Child Health J: 1–9. https://doi.org/10.1007/s10995-025-04150-2

106. McMahon, B., Heyward, W., et al. (1987). "A Comprehensive Programme to Reduce the Incidence of Hepatitis B Virus Infection and Its Sequelae in Alaskan Natives." The Lancet **330**(8568): 1134–1136. https://doi.org/10.1016/S0140-6736(87)91557-1

107. McMahon, B. J., Dentinger, C. M., et al. (2009). "Antibody Levels and Protection after Hepatitis B Vaccine: Results of a 22-Year Follow-up Study and Response to a Booster Dose." The Journal of Infectious Diseases **200**(9): 1390–1396. https://doi.org/10.1086/606119

108. Middleman, A. B., Baker, C. J., et al. (2014). "Duration of Protection after Infant Hepatitis B Vaccination Series." Pediatrics **133**(6): e1500–1507. https://doi.org/10.1542/peds.2013-2940

109. Morgan, H. J., Nold, M. F., et al. (2025). "Hepatitis B Vaccination of Preterm Infants and Risk of Bronchopulmonary Dysplasia: A Cohort Study, Australia." Bull World Health Organ **103**(3): 187–193. https://doi.org/10.2471/BLT.24.291683

110. Mrozek-Budzyn, D., Majewska, R., et al. (2015). "Early Exposure to Thimerosal-Containing Vaccines and Children's Cognitive Development. A 9-Year Prospective Birth Cohort Study in Poland." Eur J Pediatr **174**(3): 383–391. https://doi.org/10.1007/s00431-014-2412-5

111. Nelson, N. H., Essi (2019). Webinar Series - Hepatitis B: Education and Support for Health Departments, NACCHO.org.

112. Nelson, N. P., Jamieson, D. J., et al. (2014). "Prevention of Perinatal Hepatitis B Virus Transmission." J Pediatric Infect Dis Soc **3 Suppl 1**(Suppl 1): S7–s12. https://doi.org/10.1093/jpids/piu064

113. Nemerofsky, S. L., Akingboye, B., et al. (2018). "Sustained Improvement in Administration of the Hepatitis B Vaccine Birth Dose: A Quality Improvement Initiative." Am J Med Qual **33**(3): 313–320. https://doi.org/10.1177/1062860617732635

114. Niu, M. T., Davis, D. M., et al. (1996). "Recombinant Hepatitis B Vaccination of Neonates and Infants: Emerging Safety Data from the Vaccine Adverse Event Reporting System." Pediatr Infect Dis J **15**(9): 771–776. https://doi.org/10.1097/00006454-199609000-00007

115. Niu, M. T., Salive, M. E., et al. (1999). "Neonatal Deaths after Hepatitis B Vaccine: The Vaccine Adverse Event Reporting System, 1991-1998." Arch Pediatr Adolesc Med **153**(12): 1279–1282. https://doi.org/10.1001/archpedi.153.12.1279

116. Nolan, T., Hogg, G., et al. (2001). "A Combined Liquid Hib (Prp-Ompc), Hepatitis B, Diphtheria, Tetanus and Whole-Cell Pertussis Vaccine: Controlled Studies of Immunogenicity and Reactogenicity." Vaccine **19**(15-16): 2127–2137. https://doi.org/10.1016/s0264-410x(00)00403-5

117. Oster, N. V., Williams, E. C., et al. (2019a). "Sociodemographic, Clinical and Birth Hospitalization Characteristics and Infant Hepatitis B Vaccination in Washington State." Vaccine **37**(38): 5738–5744. https://doi.org/10.1016/j.vaccine.2019.03.050

118. Oster, N. V., Williams, E. C., et al. (2019b). "Hepatitis B Birth Dose: First Shot at Timely Early Childhood Vaccination." Am J Prev Med **57**(4): e117–e124. https://doi.org/10.1016/j.amepre.2019.05.005

119. Osterman, M. J. K. and Martin, J. A. (2018). "Timing and Adequacy of Prenatal Care in the United States, 2016." Natl Vital Stat Rep **67**(3): 1–14. https://www.ncbi.nlm.nih.gov/pubmed/29874159

120. Parker, S. K., Schwartz, B., et al. (2004). "Thimerosal-Containing Vaccines and Autistic Spectrum Disorder: A Critical Review of Published Original Data." Pediatrics **114**(3): 793–804. https://doi.org/10.1542/peds.2004-0434

121. Pham, T. T. H., Maria, N., et al. (2023). "Gaps in Prenatal Hepatitis B Screening and Management of HBsAg Positive Pregnant Persons in the U.S., 2015-2020." Am J Prev Med **65**(1): 52–59. https://doi.org/10.1016/j.amepre.2023.01.041

122. Poovorawan, Y., Sanpavat, S., et al. (1989). "Protective Efficacy of a Recombinant DNA Hepatitis B Vaccine in Neonates of Hbe Antigen-Positive Mothers." JAMA **261**(22): 3278–3281. https://doi.org/10.1001/jama.1989.03420220092033

123. Price, C. S., Thompson, W. W., et al. (2010). "Prenatal and Infant Exposure to Thimerosal from Vaccines and Immunoglobulins and Risk of Autism." Pediatrics **126**(4): 656–664. https://doi.org/10.1542/peds.2010-0309

124. Qu, C., Chen, T., et al. (2014). "Efficacy of Neonatal HBV Vaccination on Liver Cancer and Other Liver Diseases over 30-Year Follow-up of the Qidong Hepatitis B Intervention Study: A Cluster Randomized Controlled Trial." PLOS Medicine **11**(12): e1001774. https://doi.org/10.1371/journal.pmed.1001774

125. Rosenthal, P., Wood, D. L., et al. (1995). "Hepatitis B Virus Serology in Pregnant Women: Transmittal of Results from Obstetricians to Pediatricians in California." Pediatr Infect Dis J **14**(11): 927–931. https://doi.org/10.1097/00006454-199511000-00001

126. Salihu, H. M., Connell, L., et al. (2012). "Prevalence and Temporal Trends of Hepatitis B, Hepatitis C, and Hiv/Aids Co-Infection during Pregnancy across the Decade, 1998-2007." J Womens Health (Larchmt) **21**(1): 66–72. https://doi.org/10.1089/jwh.2011.2979

127. Sapru, A., Kulkarni, P. S., et al. (2007). "Immunogenicity and Reactogenicity of Two Recombinant Hepatitis B Vaccines in Small Infants: A Randomized, Double-Blind Comparative Study." J Trop Pediatr **53**(5): 303–307. https://doi.org/10.1093/tropej/fmm016

128. Sarathy, L., Cirillo, C., et al. (2021). "Improving Timeliness of Hepatitis B Vaccine Birth Dose Administration." Hosp Pediatr **11**(5): 446–453. https://doi.org/10.1542/hpeds.2020-002766

129. Schechter, R. and Grether, J. K. (2008). "Continuing Increases in Autism Reported to California's Developmental Services System: Mercury in Retrograde." Arch Gen Psychiatry **65**(1): 19–24. https://doi.org/10.1001/archgenpsychiatry.2007.1

130. Scheiblauer, H., El-Nageh, M., et al. (2010). "Performance Evaluation of 70 Hepatitis B Virus (HBV) Surface Antigen (HBsAg) Assays from around the World by a Geographically Diverse Panel with an Array of HBV Genotypes and HBsAg Subtypes." Vox Sanguinis **98**(3p2): 403–414. https://doi.org/https://doi.org/10.1111/j.1423-0410.2009.01272.x

131. Schillie, S., Walker, T., et al. (2015). "Outcomes of Infants Born to Women Infected with Hepatitis B." Pediatrics **135**(5): e1141–1147. https://doi.org/10.1542/peds.2014-3213

132. Schillie, S., Vellozzi, C., et al. (2018). "Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices." MMWR Recomm Rep **67**(1): 1–31. https://doi.org/10.15585/mmwr.rr6701a1

133. Schillie, S. F. and Murphy, T. V. (2013). "Seroprotection after Recombinant Hepatitis B Vaccination among Newborn Infants: A Review." Vaccine **31**(21): 2506–2516. https://doi.org/10.1016/j.vaccine.2012.12.012

134. Schonberger, K., Riedel, C., et al. (2013). "Determinants of Long-Term Protection after Hepatitis B Vaccination in Infancy: A Meta-Analysis." Pediatr Infect Dis J **32**(4): 307–313. https://doi.org/10.1097/INF.0b013e31827bd1b0

135. Shaw, S. C., Shaw, J., et al. (2025). "Healthcare Worker Perspectives on System-Level Barriers to Hepatitis B Birth Dose Vaccination: An Analysis in Five Urban U.S. Hospitals." Human Vaccines & Immunotherapeutics. https://www.tandfonline.com/doi/abs/10.1080/21645515.2025.2567043

136. Sheena, B. S., Hiebert, L., et al. (2022). "Global, Regional, and National Burden of Hepatitis B, 1990-2019: A Systematic Analysis for the Global Burden of Disease Study 2019." The Lancet Gastroenterology & Hepatology **7**(9): 796–829. https://doi.org/10.1016/S2468-1253(22)00124-8

137. Smith, L. B., O'Brien, C., et al. (2024). Well-Child Visits in Medicaid in 2019 and 2020: An Analysis of over 9 Million Black and White Medicaid-Enrolled Children from 18 States, Urban Institute.

138. Smith, M. J. and Woods, C. R. (2010). "On-Time Vaccine Receipt in the First Year Does Not Adversely Affect Neuropsychological Outcomes." Pediatrics **125**(6): 1134–1141. https://doi.org/10.1542/peds.2009-2489

139. Stehr-Green, P., Tull, P., et al. (2003). "Autism and Thimerosal-Containing Vaccines: Lack of Consistent Evidence for an Association." Am J Prev Med **25**(2): 101–106. https://doi.org/10.1016/s0749-3797(03)00113-2

140. Stevens, C. E., Taylor, P. E., et al. (1987). "Yeast-Recombinant Hepatitis B Vaccine. Efficacy with Hepatitis B Immune Globulin in Prevention of Perinatal Hepatitis B Virus Transmission." JAMA **257**(19): 2612–2616. https://doi.org/10.1001/jama.257.19.2612

141. Thompson, W. W., Price, C., et al. (2007). "Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years." N Engl J Med **357**(13): 1281–1292. https://doi.org/10.1056/NEJMoa071434

142. USPSTF (2009). "Screening for Hepatitis B Virus Infection in Pregnancy: U.S. Preventive Services Task Force Recommendation Statement." Ann Intern Med **150**(12): 869–873. https://doi.org/10.7326/0003-4819-150-12-200906160-00011

143. USPSTF (2019). "Screening for Hepatitis B Virus Infection in Pregnant Women: U.S. Preventive Services Task Force Statement." JAMA **322**(4): 349–354. https://doi.org/10.1001/jama.2019.9365

144. Vader, D. T., Lee, B. K., et al. (2020). "Hepatitis B Birth Dose Effects on Childhood Immunization in the U.S." Am J Prev Med **58**(2): 208–215. https://doi.org/10.1016/j.amepre.2019.10.007

145. Velu, V., Nandakumar, S., et al. (2007). "Comparison of Three Different Recombinant Hepatitis B Vaccines: Genevac-B, Engerix B and Shanvac B in High Risk Infants Born to HBsAg Positive Mothers in India." World J Gastroenterol **13**(22): 3084–3089. https://doi.org/10.3748/wjg.v13.i22.3084

146. Verstraeten, T., Davis, R. L., et al. (2003). "Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized Health Maintenance Organization Databases." Pediatrics **112**(5): 1039–1048. https://doi.org/10.1542/peds.112.5.1039

147. Walker, T. Y., Smith, E. A., et al. (2016). "Characteristics of Pregnant Women with Hepatitis B Virus Infection in 5 US Public Health Jurisdictions, 2008-2012." Public Health Rep **131**(5): 685–694. https://doi.org/10.1177/0033354916663183

148. Ward, J. W. (2008). "Time for Renewed Commitment to Viral Hepatitis Prevention." American Journal of Public Health **98**(5): 779–781. https://doi.org/10.2105/ajph.2008.136275

149. WHO (2017). "Hepatitis B Vaccines: WHO Position Paper – July 2017." https://www.who.int/publications/i/item/WER9227

150. WHO (2025). "WHO Immunization Data Portal - Global." Immunization Data. http://immunizationdata.who.int

151. Willis, B. C., Wortley, P., et al. (2010). "Gaps in Hospital Policies and Practices to Prevent Perinatal Transmission of Hepatitis B Virus." Pediatrics **125**(4): 704–711. https://doi.org/10.1542/peds.2009-1831

152. Wilson, P., Taylor, G., et al. (2019). "Missed Hepatitis B Birth Dose Vaccine Is a Risk Factor for Incomplete Vaccination at 18 and 24 Months." J Infect **78**(2): 134–139. https://doi.org/10.1016/j.jinf.2018.09.014

153. Wolf, E. R., Donahue, E., et al. (2021). "Barriers to Attendance of Prenatal and Well-Child Visits." Acad Pediatr **21**(6): 955–960. https://doi.org/10.1016/j.acap.2020.11.025

154. Wood, N., Nolan, T., et al. (2018). "Immunogenicity and Safety of Monovalent Acellular Pertussis Vaccine at Birth: A Randomized Clinical Trial." JAMA Pediatr **172**(11): 1045–1052. https://doi.org/10.1001/jamapediatrics.2018.2349

155. Woodruff, B. A., Stevenson, J., et al. (1996). "Progress toward Integrating Hepatitis B Vaccine into Routine Infant Immunization Schedules in the United States, 1991 through 1994. Connecticut Hepatitis B Project Group." Pediatrics **97**(6 Pt 1): 798–803. https://www.ncbi.nlm.nih.gov/pubmed/8657517

156. Yerushalmi, B., Raz, R., et al. (1997). "Safety and Immunogenicity of a Novel Mammalian Cell-Derived Recombinant Hepatitis B Vaccine Containing Pre-S1 and Pre-S2 Antigens in Neonates." Pediatr Infect Dis J **16**(6): 587–592. https://doi.org/10.1097/00006454-199706000-00009

157. Yoshimasu, K., Kiyohara, C., et al. (2014). "A Meta-Analysis of the Evidence on the Impact of Prenatal and Early Infancy Exposures to Mercury on Autism and Attention Deficit/Hyperactivity Disorder in the Childhood." Neurotoxicology **44**: 121–131. https://doi.org/10.1016/j.neuro.2014.06.007

158. Zhao, Z. and Murphy, T. V. (2013). "Which Newborns Missed the Hepatitis B Birth Dose Vaccination among U.S. Children?" Prev Med **57**(5): 613–617. https://doi.org/10.1016/j.ypmed.2013.08.012

159. Zhu, F., Deckx, H., et al. (2017). "Comparative Efficacy, Safety and Immunogenicity of Hepavax-Gene Tf and Engerix-B Recombinant Hepatitis B Vaccines in Neonates in China." Pediatr Infect Dis J **36**(1): 94–101. https://doi.org/10.1097/INF.0000000000001361