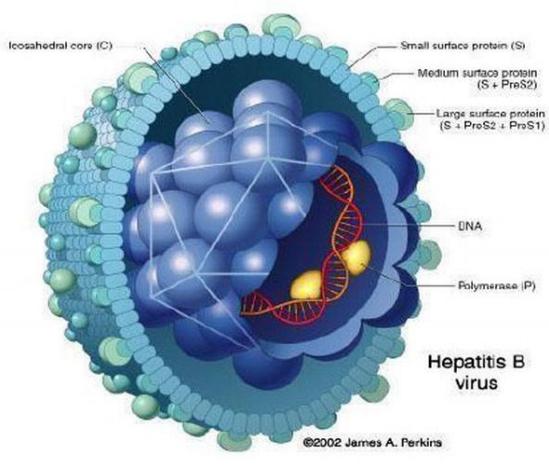
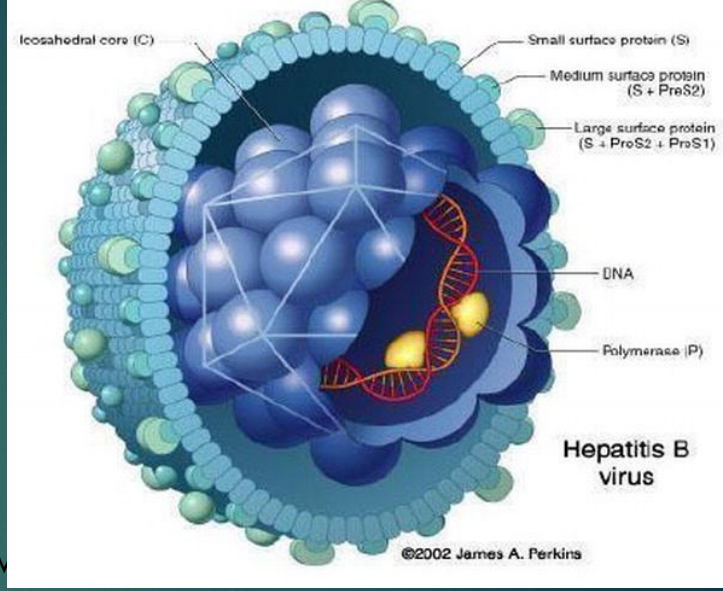


Hepatitis B and the infant vaccine

CHD

SUZANNE HUMPHRIES, MAY 2026

What is HepB virus?



- Double stranded DNA virus that primarily infects liver.
- Acute hepatitis
  - Adults mostly reversible lobular injury; immune system usually v
  - Most adults (~95%) clear the virus completely within 6 months, with full recovery and minimal or no lasting liver damage.
  - Only 10% of infants exposed at birth recover completely on their own
- Chronic hepatitis
  - Smoldering portal/interface inflammation leading to cumulative fibrosis, architectural distortion, cirrhosis, and cancer risk.
  - THIS IS THE BIG CONCERN AND WHY NEWBORN VACCINATION WAS INTRODUCED

Virus Research 259 (2019) 90–96

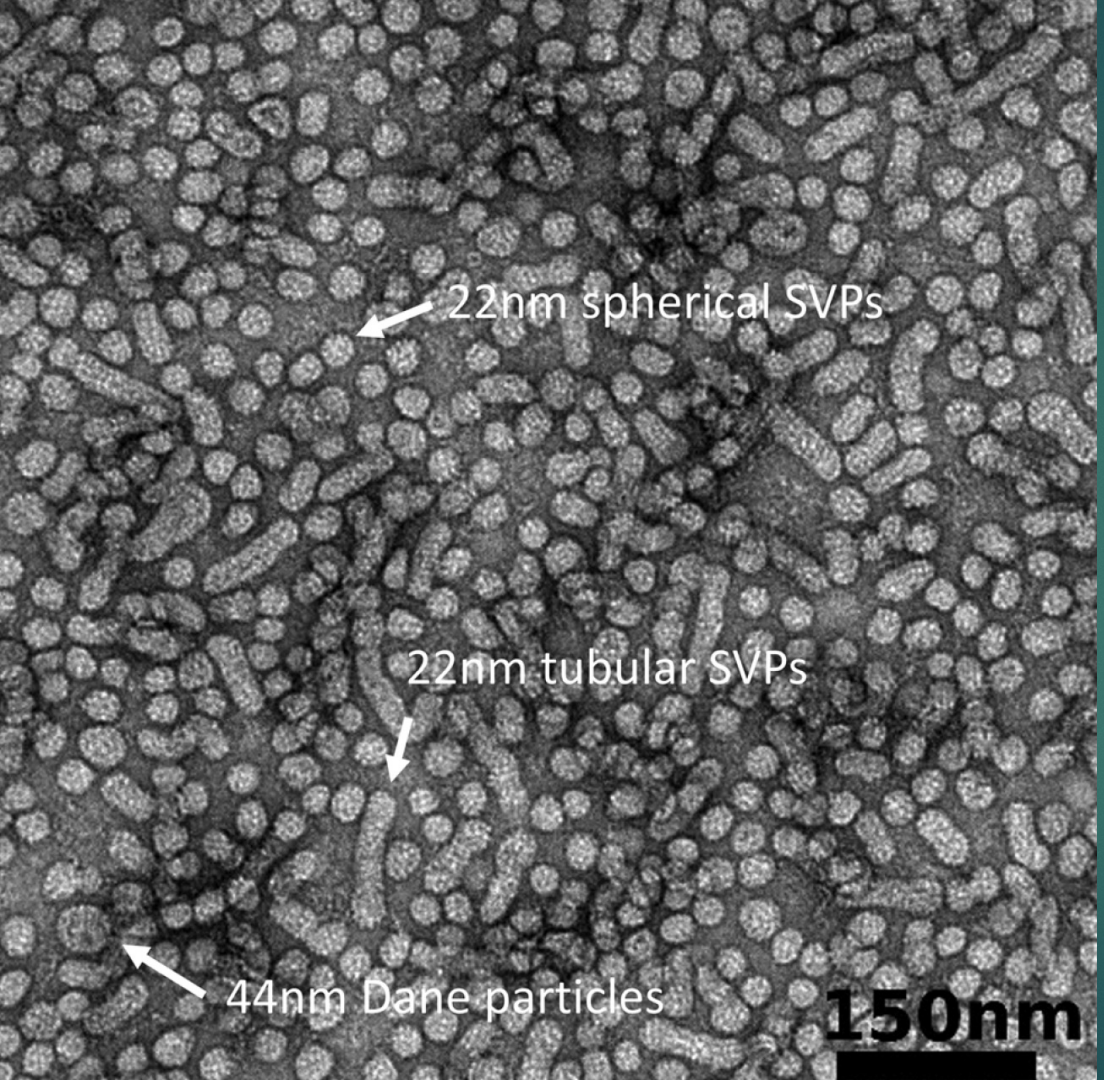
Contents lists available at ScienceDirect

Virus Research

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

Cryo-EM structure of native spherical subviral particles isolated from HBV carriers

Jianhao Cao[a,b,1], Junchang Zhang[c,g,1], Yanmeng Lu[d], Shuhong Luo[a,**], Jingqiang Zhang[e,**], Ping Zhu[b,f,*]



Cao J, Zhang J, Lu Y, Luo S, Zhang J, Zhu P. Cryo-EM structure of native spherical subviral particles isolated from HBV carriers. Virus Res. 2019 Jan 2;259:90-96. doi: 10.1016/j.virusres.2018.10.015. Epub 2018 Nov 12. PMID: 30391399.

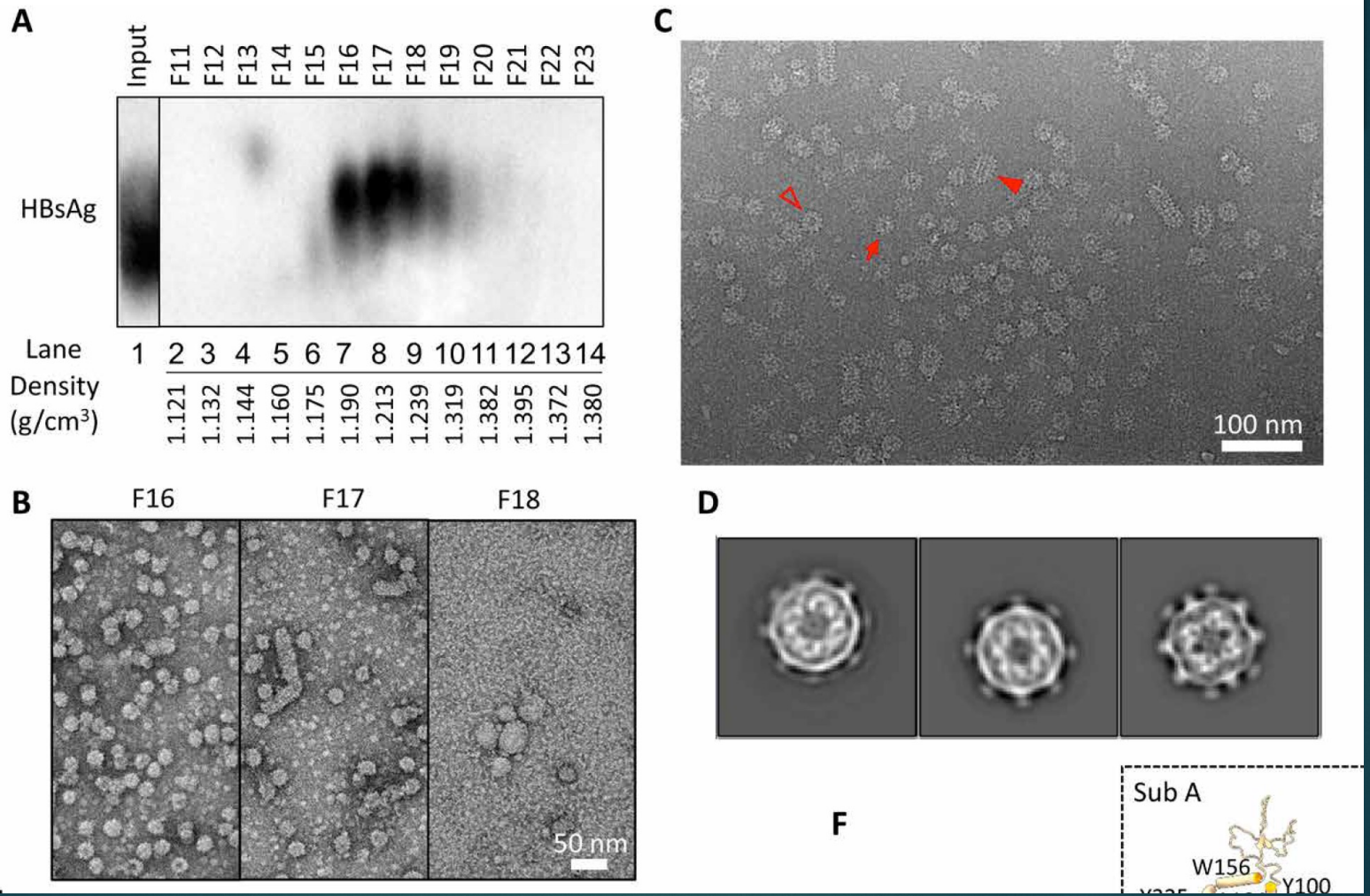
STRUCTURAL BIOLOGY

Cryo-EM structures of human hepatitis B and woodchuck hepatitis virus small spherical subviral particles

Haitao Liu[1], Xupeng Hong[1], Ji Xi[1], Stephan Menne[2], Jianming Hu[1], Joseph Che-Yen Wang[1]*

The loss of detectable hepatitis B surface antigen (HBsAg) is considered a functional cure in chronic hepatitis B. Naturally, HBsAg can be incorporated into the virion envelope or assembled into subviral particles (SVPs) with lipid from host cells. Until now, there has been no detailed structure of HBsAg, and the published SVP structures are controversial. Here, we report the first subnanometer-resolution structures of spherical SVP from hepatitis B virus (HBV) and the related woodchuck hepatitis virus (WHV) determined by cryo–electron microscopy in combination with AlphaFold2 prediction. Both structures showed unique rhombicuboctahedral symmetry with 24 protruding spikes comprising dimer of small HBsAg with four helical domains. The lipid moiety in the SVP is organized in a noncanonical lipid patch instead of a lipid bilayer, which can accommodate the exposed hydrophobic surface and modulate particle stability. Together, these findings advance our knowledge of viral membrane organization and the structures of HBV and WHV spherical SVPs.

https://www.science.org/doi/epdf/10.1126/sciadv.abo4184


A
Input
F11
F12
F13
F14
F15
F16
F17
F18
F19
F20
F21
F22
F23
HBsAg
Lane
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Density
(g/cm³)
1.121 1.132 1.144 1.160 1.175 1.190 1.213 1.239 1.319 1.382 1.395 1.372 1.380
C
100 nm
B
F16
F17
F18
50 nm
D
F
Sub A
W156
Y100

Symptoms acute HepB in infants, children, and adults.

- Most people with HBV experience few or no symptoms.
- 65% are unaware that they carry the virus.
- 30% of people with acute hepatitis B have no symptoms
- Fewer than 10% of the 90% infected exposed newborns have any symptoms
- Most people with chronic HBV also have few or no symptoms,
- Symptoms can include fatigue, fever, malaise, nausea, vomiting, yellowing of skin and eyes (Jaundice), loss of appetite, abdominal pain or bloating, indigestion, headache, itching and muscles or joints aches.

Before a vaccine

- Low risk births in mothers who were tested negative, no infections
- 16k to 18k children were HepB positive before age 10, half of which were infected at birth.
  - Numbers are based on epidemiologic modeling. Non-Asian estimates were about half that.
- 9500 infants per year in USA were infected at birth
  - Translates to 240 per 100K

Worst case scenario: no intervention and no test.

- High risk mothers are about 0.5% of the population.
  - Worst case scenario 400-500 per 100K born to HepB positive mothers per year.
- If no treatment to baby, and **mother has low viral load** (HBeAg neg) 10-25% pass it to baby
- If no treatment to baby and **mother has a high viral load**, 70-90% will pass it to baby
- For any infant infected, 90% of them can go to have CAH
  - Of those, 25% will die at age 40-70

Further breakdown of numbers

- 18-25K infants born each year to mothers who are HepB positive
- All those babies are at risk but 7000-10,000 would become infected (40% average transmission to baby)
- Of those, **6500-9000** would develop chronic hepatitis
- 25% of them, 1625-2250 would go on to die between ages 40 and 70
- So in all, 9% of all infants born to HepB positive mothers could go on do die of hepatitis complications later in life.
- Concerns about contagion from carriers

With testing of mothers

- 18-25K babies born each year to mothers with HepB
- Estimated 800-1200 babies born with HepB despite screening and HepB immune globulin and vaccination
- 720-1080 babies will go on to have CAH
- Testing of mothers and aggressive prophylaxis of infant brings down the CAH from 9000 babies per year to **1080 babies.**

Mother truly HepBsAg negative: zero risk to infant

- But could become infected after the test
- Infection after birth by the hospital or another family member.
- False negative blood test due to hospital error.
  - Very very rare.
    - Escape mutants
    - Window period
    - Low viral load

Why are babies more prone to be carriers and develop CAH?

- Infant immune system is inherently biased to be non-responsive and tolerant as it is developing. It is not a deficiency. Low Th1 cytotoxic responses are by design.
- Virus does not directly harm the liver very much. It is the immune system attacking infected cells that harms the liver. Babies don't react so the virus persists, leading to slow destruction over decades. Eventually the immune tolerance phase will convert to an immune active phase (puberty or adulthood).
- The aluminum in the vaccine is supposed to over ride the natural quiescence of the infant immune system, and force it to go against the normal program.

Reasons given for vaccinating babies

- When the risk is not known
- When other members of the household are HepB positive. Infection later could occur.
- Daycare and school settings

Low risk mother who tested negative

- ZERO risk
- We can't even get an estimate of how often it happens because it is essentially never.

Estimated carriage rates pre vax

- Age 6-19
  - Pre-vaccine era chronic Hep B carriage (HBsAg prevalence) in US children was very low in the general population — around **0.2–0.24%** for ages 6–19 in NHANES 1988–1994.
- Birth to 6 years: Chronic carriage was very low in the broad US population — likely **well under 0.2–0.3%** for birth to 6 years in low-risk groups. Most cases were concentrated in high-risk households (e.g., foreign-born from endemic areas, infected mothers/siblings).
- Even lower for low-risk populations, like 0.1%

CDC Home | Search | Health Topics A-Z

MMWR

Recommendations and Reports

November 22, 1991 / 40(RR-13);1-19

Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation and the title of the report in the subject line of e-mail.

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)

The VACCINE

Birth

Engerix (GSK)
Contains 10 mcg of antigen

11 DESCRIPTION

ENGERIX-B [Hepatitis B Vaccine (Recombinant)] is a sterile suspension of noninfectious HBsAg for intramuscular administration. It contains purified surface antigen of the virus obtained by culturing genetically engineered *Saccharomyces cerevisiae* cells, which carry the surface antigen gene of the hepatitis B virus. The HBsAg expressed in the cells is purified by several physicochemical steps and formulated as a suspension of the antigen adsorbed on aluminum hydroxide. The procedures used to manufacture ENGERIX-B result in a product that contains no more than 5% yeast protein.

Each 0.5-mL pediatric/adolescent dose contains 10 mcg of HBsAg adsorbed on 0.25 mg aluminum as aluminum hydroxide.

The VACCINE

Birth

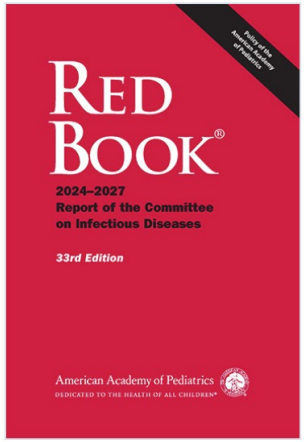
Recombivax(Merck)
Contains 5 mcg of antigen
Contains 7.5 mcg of formaldehyde

All formulations contain approximately 0.5 mg of aluminum (provided as amorphous aluminum hydroxyphosphate sulfate, previously referred to as aluminum hydroxide) per mL of vaccine. In each formulation, hepatitis B surface antigen is adsorbed onto approximately 0.5 mg of aluminum (provided as amorphous aluminum hydroxyphosphate sulfate) per mL of vaccine. The vaccine contains <15 mcg/mL residual formaldehyde. The vaccine is of the *adw* subtype.

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form/ Strength	Clinically Relevant Nonmedicinal Ingredients
Intramuscular injection	Sterile suspension for injection/ After reconstitution, 1 dose (0.5 ml) contains 25 limit of flocculation (Lf) [30 International Units (IU)] diphtheria toxoid; 10 Lf (40 IU) tetanus toxoid; 25 µg pertussis toxoid (PT); 25 µg filamentous haemagglutinin (FHA); 8 µg pertactin (PRN); 10 µg hepatitis B surface antigen (HBsAg); 40 D-antigen units (DU) of type 1 poliovirus, 8 DU type 2 poliovirus, and 32 DU type 3 poliovirus; 10 µg of adsorbed purified capsular polysaccharide of *Haemophilus influenzae* type b (Hib) (PRP) covalently bound to approximately 25 µg of tetanus toxoid per 0.5 mL dose.	lactose, sodium chloride, aluminum adjuvant (as aluminum salts), water for injection, residual formaldehyde, polysorbate 20 and 80 (Tween 20 and 80), M199, potassium chloride, disodium phosphate, monopotassium phosphate, glycine, neomycin sulphate, polymyxin B sulphate and aluminum phosphate.

Who can be vaccinated?



‹ Prev Next ›

Red Book: 2024–2027 Report of the Committee on Infectious Diseases (33rd Edition) 🛒

BOOK CHAPTER

Immunization in Preterm and Low Birth Weight Infants 🛒

DOI: https://doi.org/10.1542/9781610027373-S1_006_001

Published: 2024

Share Tools

Search within book:

Infants born preterm (at less than 37 weeks of gestation) or low birth weight (less than 2500 g) who are clinically stable should, with few exceptions, receive all routinely recommended childhood vaccines at the same chronologic age as term and normal birth weight infants. Although studies have shown decreased immune responses to several vaccines administered to neonates with very low birth weight (less than 1500 g) and neonates of very early gestational age (less than 29 weeks of gestation), most preterm infants, including infants who receive corticosteroids for bronchopulmonary dysplasia, produce sufficient vaccine-induced immunity to prevent disease. Vaccine dosages administered...

The infamous theory

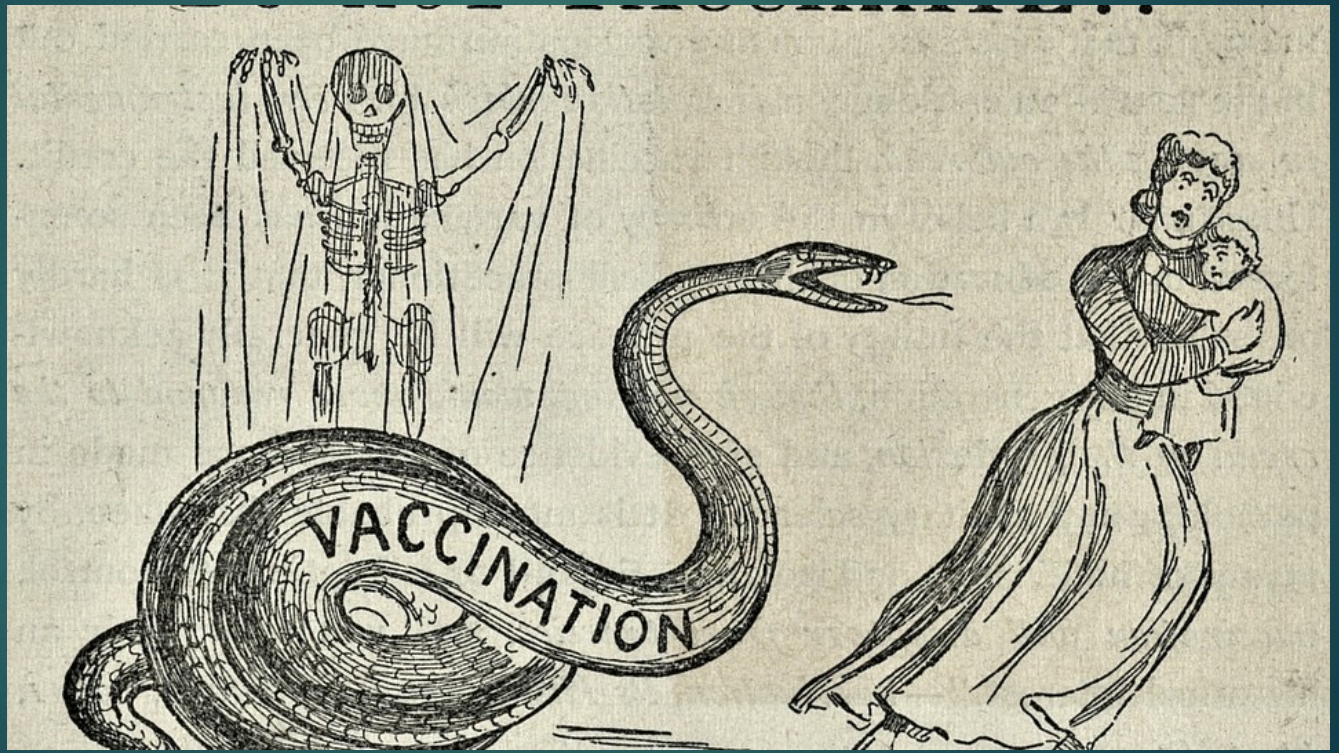
Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System?

Paul A. Offit, MD*; Jessica Quarles‡; Michael A. Gerber, MD§; Charles J. Hackett, PhD‖; Edgar K. Marcuse, MD¶; Tobias R. Kollman, MD#; Bruce G. Gellin, MD**; and Sarah Landry‡

gle B-cell clone per mL), 4) each vaccine contains approximately 100 antigens and 10 epitopes per antigen (ie, 10^3 epitopes), and 5) approximately 10^7 B cells are present per mL of circulating blood,[39] then each infant would have the theoretical capacity to respond to about 10 000 vaccines at any one time (obtained by dividing 10^7 B cells per mL by 10^3 epitopes per vaccine).

Pediatrics 2002 PMID: 11773551

Objections to vaccination



Pourcyrous
1998 PMID:
9481022

Pediatrics

Interleukin-6, C-Reactive Protein, and Abnormal Cardiorespiratory Responses to Immunization in Premature Infants

Massroor Pourcyrous, MD*‡§; Sheldon B. Korones, MD*‡; Dennis Crouse, MD, PhD*‡; and Henrietta S. Bada, MD*‡

ABSTRACT. *Objective.* We report our experience with routine immunization of 89 premature infants in the neonatal intensive care unit because 1) a substantial number of them developed abnormal clinical signs, and 2) all but one of those who received diphtheria, tetanus, and whole-cell pertussis (DTwP) vaccine responded with elevations of interleukin-6 (IL-6) and C-reactive protein (CRP) concentrations that are otherwise characteristic of bacterial disease.

Methodology. We hypothesized that the elevated IL-6 and CRP levels were solely a response to immunization and that treatment with antibiotics was not necessary. We performed this study in two consecutive parts. In part 1, we prospectively evaluated 79 consecutive premature infants who were immunized with DTwP, *Haemophilus* b conjugate vaccine, hepatitis B vaccine, and inactivated polio vaccine, (Hib, HBV, and IPV). IL-6 and CRP were determined before immunization and every 12 hours on three occasions after immunization. In part 2, we studied an additional 10 infants who received acellular pertussis vaccine (DTaP) and who, 2 days later, received Hib, HBV, and IPV immunization simultaneously. We followed the same schedule of IL-6 and CRP determinations as in part 1.

Results. In part 1, 24 infants (30%) developed abnormal cardiorespiratory signs within 24 hours after immunization. CRP and IL-6 values rose to abnormal levels after immunization in all but one infant; that infant was later shown to have a T-cell abnormality. In part 2, 3 infants had abnormal cardiorespiratory signs after simultaneous immunization with Hib, HBV, and IPV, but not after DTaP. IL-6 and CRP levels remained normal in all 10 infants.

Conclusions. Part 1 demonstrates clearly the temporal relationship between IL-6 and CRP increments after DTwP, Hib, HBV, and IPV vaccines. In part 2 (DTaP was substituted for DTwP), there were no elevations of IL-6 or CRP, thus indicating that whole-cell pertussis component of DTwP was responsible for IL-6 and CRP elevations. Abnormal cardiorespiratory signs occurred frequently after immunizations in part 1, but they were unrelated to the magnitude of IL-6 and CRP elevations. The frequency of cardiorespiratory difficulty and its occasional severity suggest a need to monitor premature infants for ~48 hours after routine immunization.
Pediatrics 1998;101(3). URL: http://www.pediatrics.org/cgi/content/full/101/3/e3; *immunization, C-reactive protein, Interleukin-6, premature, bronchopulmonary dysplasia.*

ABBREVIATIONS. IL-6, interleukin-6; CRP, C-reactive protein; WBC, white blood cell; DTwP, diphtheria–tetanus–whole-cell pertussis; HBV, hepatitis B vaccine; DTaP, diphtheria–tetanus–acellular pertussis; IPV, inactivated poliovirus vaccine; Hib, *Haemophilus influenzae* conjugate type b; BPD, bronchopulmonary dysplasia; HIV, human immunodeficiency virus.

In 1982, the American Academy of Pediatrics recommended routine immunization of premature or low birth weight infants at 2 months' postnatal age.[1] Later, a survey showed that only 56% of pediatricians and 34% of family physicians were in compliance with the American Academy of Pediatrics recommendation.[2] Some cautiously used a vaccine dose smaller than recommended or arbitrarily designated various weights at which immunizations were initiated.[2–4] However, clinical trials have shown that decreased doses of vaccine result in ineffective immunologic responses to pertussis vaccine,[4,5] and that the risk of neurologic signs was no higher in premature than in full-term infants.[4,5] Routine immunization of preterm infants beginning at the second postnatal month is now a pervasive practice in the physician's office and in the neonatal intensive care unit as well. During the course of administering these routine immunizations, we observed that a substantial number of premature infants developed abnormal cardiorespiratory signs soon after immunization, often necessitating evaluations for septicemia and therapy with antibiotics. Blood culture results were regularly negative in these infants, but our routine studies showed that C-reactive protein (CRP) values were always elevated. Therefore, we prospectively studied interleukin-6 (IL-6) and CRP responses to immunization, seeking to demonstrate that immunization itself stimulates increases in blood IL-6 and CRP levels, and that usually there is no need for antibiotic therapy.

MATERIALS AND METHODS

mal (<1.0 mg/dL) at a mean of 82 ± 27 hours (39 to 181 hours) after immunization (Fig 1).

In part 1, 3 infants were extremely irritable and 24 infants (30%) had abnormal cardiorespiratory signs that increased in frequency or appeared for the first time. These signs included apnea, bradycardia, and oxygen desaturation that required vigorous stimulation, initiation, or increase in oxygen supplementation. One of these infants required continuous positive airway pressure, and 2 others needed intermittent positive pressure ventilation. Cardiorespiratory signs first appeared within 12 to 24 hours of immunization and usually disappeared 48 hours later; however, in a few infants the abnormal clinical signs persisted for 4 days. Two infants received antibiotics; their blood cultures tested negative. Table 1 compares four groups of infants in part 1 based on the presence or absence of cardiorespiratory signs during 3 days before and 3 days after immunization. The four groups were significantly different as to

not significantly different among groups.

In part 2, 10 infants were immunized. Their mean birth weight was 850 ± 300 (470 to 1370 g). Mean gestational age was 27 ± 2 weeks (24 to 32 weeks). Seven infants were black, and 4 were male. The mean postnatal age at the time of immunization was 62 ± 6 days (54 to 74 days); mean weight was 1850 ± 550 g (1230 to 2640 g). Two infants had occasional cardiorespiratory signs before immunization, and these episodes were unchanged afterward. In 3 infants, however, cardiorespiratory signs began or increased in frequency after the simultaneous immunizations with Hib, HBV, and IPV. Each of these infants required vigorous stimulation, initiation, or increase in oxygen supplementation or bag/mask. IL-6 and CRP levels were not elevated after any of the immuniza-

there were no new abnormal clinical signs after immunization. Two infants were treated with antibiotics, and results of their blood cultures were negative. In part 2, with total absence of abnormally high CRP

tion (whole-cell pertussis) may be an easily demonstrated sign of an underlying T-cell deficiency.

In conclusion, this study demonstrates that abnormal cardiorespiratory signs occur in a substantial number of premature infants after routine immunization, and that the frequency of abnormal clinical responses and their occasional severity indicate a need for cardiorespiratory monitoring for ~48 hours after administration of vaccine. For infants already discharged, caretakers should be made aware of the possibility of adverse reactions, either as a new

Pourcyrous 2007 PMID: 17643770

2007 study same author

Primary Immunization of Premature Infants with Gestational Age <35 Weeks: Cardiorespiratory Complications and C-Reactive Protein Responses Associated with Administration of Single and Multiple Separate Vaccines Simultaneously

MASSROOR POURCYROUS, MD, SHELDON B. KORONES, MD, KRISTOPHER L. ARHEART, PHD, AND HENRIETTA S. BADA, MD

Objective To determine the incidence of cardiorespiratory events and abnormal C-reactive protein (CRP) level associated with administration of a single vaccine or multiple separate vaccines simultaneously.

Study design Prospective observational study on 239 preterm infants at ≥2 months of age in the neonatal intensive care unit (NICU). Each infant received either a single vaccine or multiple vaccines on one day. CRP levels and cardiorespiratory manifestations were monitored for 3 days following immunization.

Results Abnormal elevation of CRP level occurred in 85% of infants administered multiple vaccines and up to 70% of those given a single vaccine. Overall, 16% of infants had vaccine-associated cardiorespiratory events within 48 hours postimmunization. In logistic regression analysis, abnormal CRP values were associated with multiple vaccines (OR, 15.77; 95% CI 5.10-48.77) and severe intraventricular hemorrhage (IVH) (OR, 2.28; 95% CI 1.02-5.13). Cardiorespiratory events were associated marginally with receipt of multiple injections (OR, 3.62; 95% CI 0.99-13.25) and significantly with gastroesophageal reflux (GER) (OR, 4.76; 95% CI 1.22-18.52).

Conclusion CRP level is expected to be elevated in the 48 hours following immunization. In a minority of infants immunized, cardiorespiratory events were associated with presumed need for intervention. Underlying medical conditions and possibly multiple injections are associated with cardiorespiratory events. Precautionary monitoring following immunizations is warranted. *(J Pediatr 2007;151:167-72)*

Newborns from July 2001 to July 2004. Written parental consent was obtained. Subjects for the study were premature infants ≥2 months' postnatal age, who were still in the NICU and were scheduled to receive immunization. Immunization was postponed in infants who were acutely ill, had bacterial infection, or for other reasons as judged by the attending physician. The study was prospective observational and quasi-experimental, and it used a convenience sample. A group of 15 consecutive infants received a randomly chosen single vaccine from five vaccines (DTaP, Hib, inactivated poliovirus vaccine [IPV], hepatitis B vaccine [HBV], or pneumococcal 7-valent conjugate vaccine [PCV7]) or multiple separate vaccines simultaneously. For the single vaccine group, the randomization scheme used multiple blocks of random sequences of five vaccines. To have an adequate number of infants assigned to each single vaccine, every third group of 15 infants was assigned to receive multiple vaccines. In the single vaccine group, infants were given the assigned single vaccine, were monitored for cardiorespiratory events, and were given the remaining vaccines in the primary immunization 3 days later after the end of the monitoring period. Only the administration of the first vaccine in the single vaccine group was considered as part of the study. When assigned to receive multiple vaccines, infants were given two or more vaccines simultaneously in a single day. Thus, an infant was a subject in either the multiple or the single vaccine group.

All infants received acetaminophen 10 mg/kg by mouth before immunization and then every 6 hours within the first 48 hours of immunization. Outcomes examined in this study were cardiorespiratory events and abnormal CRP values observed within 3 days following immunization.

All infants were maintained on cardiorespiratory and

these episodes decreased or remained the same post-immunization. The remaining 16% (39/239) were considered to have immunization-associated cardiorespiratory events; 24 infants were asymptomatic before immunization but had episodes of apnea, bradycardia, or O_2 desaturation after immunization, and 15 infants who already had episodes of apnea, bradycardia, or O_2 desaturation before immunization had increase in the number of episodes after immunization. Twenty-six of 39 infants had initiation of O_2 therapy or increase in FIO_2. The remaining 13 of 39 infants had bag-mask ventilation, an initiation of CPAP or mechanical ventilation, or increase in ventilator settings. The onset of new cardiorespiratory symptoms or worsening cardiorespiratory status was noted 4 to 66 hours (mean ± SD of 25 ±15 hours; median of 21 hours) after immunization. Ninety-five percent (37/39) cardiorespiratory events occurred within 48 hours post-immunization. Table II shows the frequency of cardiorespiratory events with each single vaccine and with multiple separate vaccines simultaneously. Cardiorespiratory events were noted in 32% of those who received multiple vaccines. DTaP was associated with the highest incidence of cardiorespiratory events ($\chi^2 = 15.7$, $df = 4$, $P = .004$) among groups given a single vaccine. HBV administration was not associated with cardiorespiratory events. Improvement or resolution of cardiorespiratory abnormalities was noted within 72 hours of onset of cardiorespiratory manifestation.

of onset of cardiorespiratory manifestation.

Twelve infants had a work-up for septicemia after immunization as directed by the attending physician. These infants had cardiorespiratory events for which intervention was positive pressure ventilation, and they also had elevated CRP values. However, blood cultures were negative and antibiotics were discontinued after 48 to 72 hours of treatment and without any further complication.

model was used, controlling for the demographic and clinical variables listed in Table I. Variables significant at the .05 levels were retained in the model. Abnormal CRP values were associated with administration of multiple vaccines, (OR, 15.77; 95% CI 5.10-48.77) and the presence of IVH grades 3 or 4 (OR, 2.28; 95% CI 1.02-5.13). Cardiorespiratory events were related marginally to multiple vaccines (OR, 3.62; 95% CI 0.99-13.25) and significantly to GER (OR, 4.76; 95% CI 1.22-18.52). Compared with infants who received a single vaccine, infants who received multiple vaccines were almost four times more likely to have immunization-associated cardiorespiratory events and 16 times more likely to have abnormal CRP value (>1.6 mg/dL).

"Our study revealed that some vaccines, including DTaP, even if administered alone were associated with cardiorespiratory adverse events and abnormal CRP values in premature infants in the NICU. However, the incidence of these events was higher following simultaneous administration of multiple vaccines compared with administration of a single vaccine. . .

These associated complications are more likely to occur with current practice of simultaneous administration of multiple vaccines. Also, contrary to previous reports, cardiorespiratory events can be observed even if DTaP is given as a single vaccine. Administration of other vaccines given individually such as PVC7 and Hib also can be associated with cardiorespiratory events."

Another study, huge numbers

Original Investigation

Adverse Events After Routine Immunization of Extremely Low-Birth-Weight Infants

Stephen D. DeMeo, DO; Sudha R. Raman, PhD; Christoph P. Hornik, MD, MPH; Catherine C. Wilson, DNP, NNP-BC, FNP-BC; Reese Clark, MD; P. Brian Smith, MD, MPH, MHS

DeMeo 2015
PMID: 26030302

JAMA Pediatrics

DESIGN, SETTING, AND PARTICIPANTS In this multicenter retrospective cohort study, we studied 13 926 ELBW infants born at 28 weeks' gestation or less who were discharged from January 1, 2007, through December 31, 2012, from 348 NICUs managed by the Pediatrix Medical Group.

EXPOSURES At least one immunization between the ages of 53 and 110 days.

MAIN OUTCOMES AND MEASURES Incidence of sepsis evaluations, need for increased respiratory support, intubation, seizures, and death.

RESULTS Most of the 13 926 infants (91.2%) received 3 or more immunizations. The incidence of sepsis evaluations increased from 5.4 per 1000 patient-days in the preimmunization period to 19.3 per 1000 patient-days in the postimmunization period (adjusted rate ratio [ARR], 3.7; 95% CI, 3.2-4.4). The need for increased respiratory support increased from 6.6 per 1000 patient-days in the preimmunization period to 14.0 per 1000 patient-days in the postimmunization period (ARR, 2.1; 95% CI, 1.9-2.5), and intubation increased from 2.0 per 1000 patient-days to 3.6 per 1000 patient-days (ARR, 1.7; 95% CI, 1.3-2.2). The postimmunization incidence of adverse events was similar across immunization types, including combination vaccines when compared with single-dose vaccines. Infants who were born at 23 to 24 weeks' gestation had a higher risk of sepsis evaluation and intubation after immunization. A prior history of sepsis was associated with higher risk of sepsis evaluation after immunization.

CONCLUSIONS AND RELEVANCE All ELBW infants in the NICU had an increased incidence of sepsis evaluations and increased respiratory support and intubation after routine immunization. Our findings provide no evidence to suggest that physicians should not use combination vaccines in ELBW infants. Further studies are needed to determine whether timing or spacing of immunization administrations confers risk for the developing adverse events and whether a prior history of sepsis confers risk for an altered immune response in ELBW infants.

Table 2. Incidence of Events Before and After Immunization per 1000 Patient-days

Event	Immunization		RR (95% CI)	ARR (95% CI)[a]
	Before	After		
Sepsis evaluation	5.4	19.3	3.5 (3.1-4.1)	3.7 (3.2-4.4)
Increased respiratory support	6.6	14.0	2.1 (1.9-2.4)	2.1 (1.9-2.5)
Intubation	2.0	3.6	1.8 (1.4-2.3)	1.7 (1.3-2.2)
Seizure	0.2	0.1	0.3 (0.1-1.0)	0.3 (0.1-1.1)

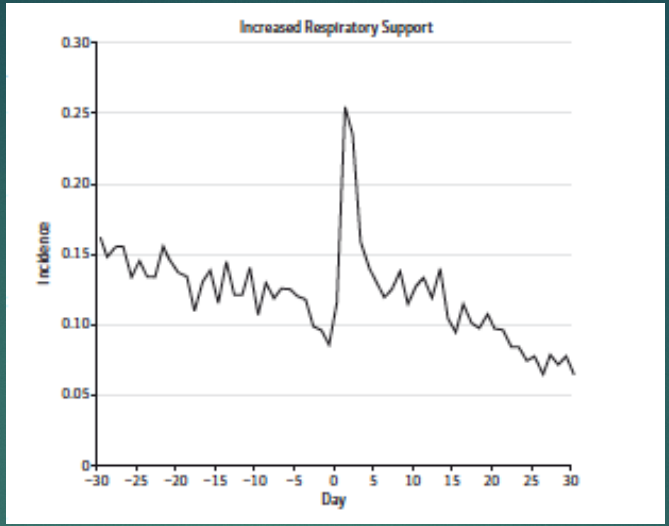
Abbreviations: ARR, adjusted rate ratio; RR, rate ratio.

[a] The ARR was adjusted for gestational age at birth, small for gestational age status, history of sepsis, postnatal age, and postnatal weight.

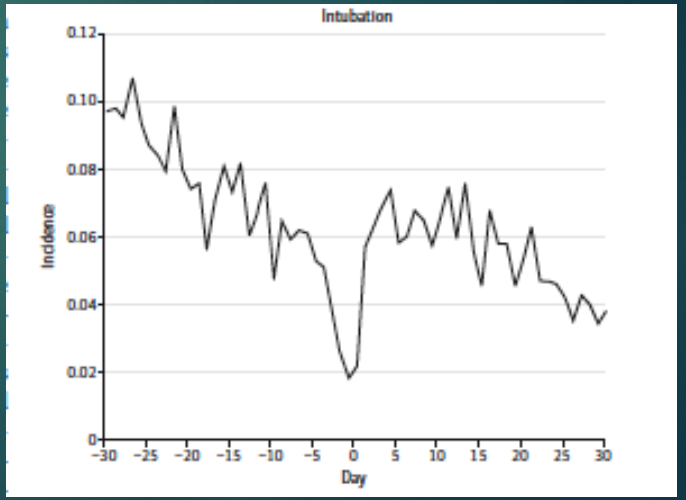
During the preimmunization and postimmunization periods, 5,952 (42.7%) of 13,926 infants received caffeine therapy.

3 total events in each period, respectively.

There were 5 deaths in the postimmunization period. Three of the 5 infants who died in the 3 days after immunization had a diagnosis associated with death available in the data set; 1 infant had a bowel perforation, 1 infant had necrotizing enterocolitis and presumed sepsis, and 1 infant had pneumonia and respiratory failure. The incidence of sepsis evaluations, increased respiratory support, and intubations measured by day, from 30 days before


Increased Respiratory Support
Incidence
0.30
0.25
0.20
0.15
0.10
0.05
0
−30 −25 −20 −15 −10 −5 0 5 10 15 20 25 30
Day


Sepsis Evaluation
Incidence
0.6
0.5
0.4
0.3
0.2
0.1
0
−30 −25 −20 −15 −10 −5 0 5 10 15 20 25 30
Day


Intubation
Incidence
0.12
0.10
0.08
0.06
0.04
0.02
0
−30 −25 −20 −15 −10 −5 0 5 10 15 20 25 30
Day

conclusion

"There was no difference in the incidence of adverse events in combination vaccines vs. single-dose vaccines. These data provide no evidence to suggest that physicians should not use combination vaccines in ELBW infants.

Immunization delay burdens an already fragile patient population with the increased morbidity and mortality of vaccine-preventable diseases through the first year of life."

What about full term infants?

Clinical Trial > Eur J Pediatr. 2013 Jun;172(6):839-42. doi: 10.1007/s00431-013-1946-2. Epub 2013 Jan 29.

Inflammatory responses to hepatitis B virus vaccine in healthy term infants

Istemi Han Celik [1], Gamze Demirel, Fuat Emre Canpolat, Omer Erdeve, Ugur Dilmen

Affiliations + expand

PMID: 23358708 DOI: 10.1007/s00431-013-1946-2

Abstract

Hepatitis B virus (HBV) infection continues to be a serious global health problem. During the course of HBV vaccination, we observed C-reactive protein (CRP) elevation in term infants without sepsis. Therefore, we prospectively studied interleukin-6 (IL-6) and CRP responses to HBV immunization. In 70 healthy term infants without signs and symptoms of sepsis and sepsis risk factors, IL-6, CRP, and white blood cell count levels were determined before and 24 h after immunization. Significant increases in CRP levels were seen 24 h after vaccination ($p < 0.001$). Although CRP levels of 22 infants at second evaluation were above the cutoff level for sepsis (4.82 mg/L), they had no clinical signs and symptoms of sepsis. After 48-72 h, CRP levels of these infants returned to normal levels with no blood culture positivity.

Conclusion: our study showed that HBV vaccine is responsible for CRP elevation in term infants after vaccination at birth. To the best of our knowledge, this is the first study evaluating CRP response to HBV vaccine at birth in term infants. We suggest that this response should be considered in differentiation of early neonatal sepsis to avoid unnecessary antibiotic use.

Original article

Unexplained fever in neonates may be associated with hepatitis B vaccine

Nehama Linder [a], Meirav Raz [b], Lea Sirota [a], Brian Reichman [b], Dan Lubin [b], Jacob Kuint [b], Avner Herman Cohen [c], Asher Barzilai [c]

Dr N Linder.

Abstract

AIM To investigate whether hepatitis B vaccination has increased the number of cases of unexplained neonatal fever.

METHOD The files of all infants born from 1 January 1991 to 31 December 1992, in whom a diagnosis of "injected antibiotic" or "disease of temperature regulation" was recorded, were reviewed. Those who had unexplained fever of 38°C or higher during the first three days of life were divided into two groups: infants who did not receive the hepatitis B vaccine (1991) and infants who did (1992).

RESULTS In 1992 the incidence of unexplained fever in hepatitis B vaccinated neonates was significantly higher than in the 1991 group of pre-vaccination neonates (35 out of 5819 (0.6%) *vs* 14 out of 5010 neonates (0.28%) respectively, p=0.013).

CONCLUSIONS The increase in the number of cases of unexplained neonatal fever seems to be associated with the introduction of routine hepatitis B vaccination on the first day of life. The possibility that an excess number of neonates will undergo unnecessary procedures and treatment to diagnose unexplained fever justifies planning a controlled study to determine whether these preliminary findings point to a significant problem.

https://doi.org/10.1136/fn.81.3.F206

Statistics from Altmetric.com

Neonatal hepatitis B vaccination impaired the behavior and neurogenesis of mice transiently in early adulthood

Yang 2016 PMID: 27501128

Junhua Yang [1], Fangfang Qi [1], Yang Yang [1], Qunfang Yuan [1], Juntao Zou [1], Kaihua Guo [1], Zhibin Yao [2]

Affiliations + expand

PMID: 27501128 DOI: 10.1016/j.psyneuen.2016.08.002

Abstract

The immune system plays a vital role in brain development. The hepatitis B vaccine (HBV) is administered to more than 70% of neonates worldwide. Whether this neonatal vaccination affects brain development is unknown. Newborn C57BL/6 mice were injected intraperitoneally with HBV or phosphate-buffered saline. HBV induced impaired behavioral performances and hippocampal long-term potentiation at 8 weeks (w) of age without influence at 4 or 12w. At 6w, there was decreased neurogenesis, M1 microglial activation and a neurotoxic profile of neuroimmune molecule expression [increased tumor necrosis factor-α and reduced interferon (IFN)-γ, brain-derived neurotrophic factor and insulin-like growth factor-1] in the hippocampus of the HBV-vaccinated mice. In the serum, HBV induced significantly higher levels of interleukin (IL)-4, indicating a T helper (Th)-2 bias. Moreover, the serum IFN-γ/IL-4 ratio was positively correlated with the levels of neurotrophins and neurogenesis in the hippocampus at the individual level. These findings suggest that neonatal HBV vaccination of mice results in neurobehavioral impairments in early adulthood by inducing a proinflammatory and low neurotrophic milieu in the hippocampus, which follows the HBV-induced systemic Th2 bias.

True placebo-controlled RCTs of Hep B alone at birth in low-risk general-population infants are rare/non-existent due to ethical/practical reasons once efficacy was (supposedly) established.

There are no saline placebo-controlled studies looking at HepB risks given to day old newborns. Why?

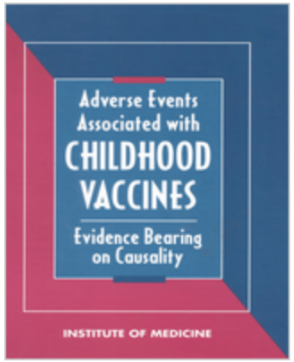
- The recombinant Hep B vaccines (e.g., Recombivax HB, Engerix-B) were licensed based on immunogenicity (antibody response), short-term safety monitoring (often days to weeks post-dose in key trials), and comparisons that sometimes used aluminum-containing placebos or other controls rather than pure saline.
- We are told that it is unethical to do a saline placebo study now, because the safety was long ago established. Was it?

Institute of Medicine false reporting on safety of HepB vaccines.

National Library of Medicine
National Center for Biotechnology Information

Bookshelf Books

Browse Titles Advanced



Adverse Events Associated with Childhood Vaccines

< Prev

Evidence Bearing on Causality

Institute of Medicine (US) Vaccine Safety Committee; Editors: Kathleen R. Stratton, Cynthia J. Howe, and Richard B. Johnston, Jr.

Washington (DC): National Academies Press (US); 1994.

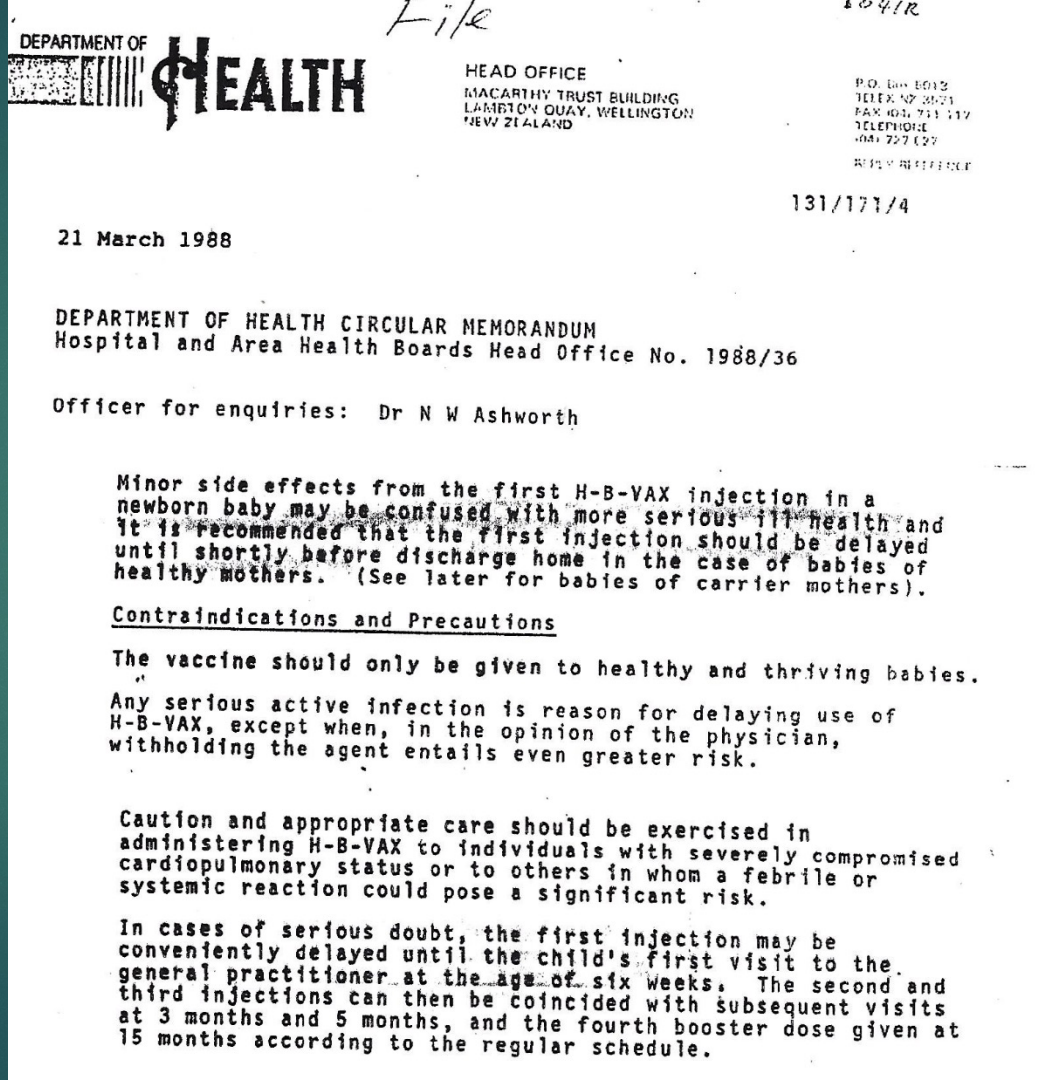
ISBN-10: 0-309-04895-8

Copyright and Permissions

Hardcopy Version at National Academies Press

21 March 1988

MoH memorandum



File

DEPARTMENT OF HEALTH

HEAD OFFICE
MACARTHY TRUST BUILDING
LAMBTON QUAY, WELLINGTON
NEW ZEALAND

131/171/4

21 March 1988

DEPARTMENT OF HEALTH CIRCULAR MEMORANDUM
Hospital and Area Health Boards Head Office No. 1988/36

Officer for enquiries: Dr N W Ashworth

Minor side effects from the first H-B-VAX injection in a newborn baby may be confused with more serious ill health and it is recommended that the first injection should be delayed until shortly before discharge home in the case of babies of healthy mothers. (See later for babies of carrier mothers).

Contraindications and Precautions

The vaccine should only be given to healthy and thriving babies.

Any serious active infection is reason for delaying use of H-B-VAX, except when, in the opinion of the physician, withholding the agent entails even greater risk.

Caution and appropriate care should be exercised in administering H-B-VAX to individuals with severely compromised cardiopulmonary status or to others in whom a febrile or systemic reaction could pose a significant risk.

In cases of serious doubt, the first injection may be conveniently delayed until the child's first visit to the general practitioner at the age of six weeks. The second and third injections can then be coincided with subsequent visits at 3 months and 5 months, and the fourth booster dose given at 15 months according to the regular schedule.

28 May 1988

PARTMENT OF HEALTH

SOUTH AUCKLAND DISTRICT OFFICE
LEYTON HOUSE
MANUKAU CITY CENTRE
MANUKAU CITY
NEW ZEALAND

PRIVATE BAG
MANUKAU CITY
TELEPHONE
(09) 278-5024
FAX (09) 277-6806

Reply ref:

23 May 1988.

HEPATITIS "B" VACCINE - SEVERE ALLERGIC RESPONSE

We have been advised by Dr Nigel Ashworth, National Coordinator that according to Professor Ralph Edwards, The Medical Assessor for medicines adverse reaction, the potential for severe allergic reaction response to Hepatitis "B" vaccine exists.

Accordingly, on his recommendation, the following policy should be adhered to by all involved with Hepatitis "B" Immunization Programme.

1. Allergic Response: If it included anaphylactic shock, hypotension, bronchospasm or angio-neurotic oedema then any further immunization is absolutely contra-indicated. The onset of symptoms should have been within 12 hours after an injection of Hepatitis "B" vaccine in order to classify the above conditions as vaccine related.

2. Urticaria: Children who developed vaccine related urticaria alone, it is recommended that any subsequent vaccinations to be given in a hospital setting preferably after skin testing. Full support facilities must be available in case the reaction is worse the next time.

ANALYSIS OF ADVERSE EVENTS REPORTED AFTER HEPATITIS B VACCINATION IN PRE-SCHOOL CHILDREN

Results of surveillance during the national pre-school immunisation campaign

March to September 1988

CARM ✓

✗ Dr Ralph Edwards - medical assessor, Centre for Adverse Reactions Monitoring

RESULTS

9.0 SUMMARY OF RESULTS

A total of 166,757 children were given at least one hepatitis B vaccine injection. Of these, 2,250 children (1.34%) were found to experience adverse events. These events were reported following 2,490 doses. Since 447,273 doses were received in total, the overall reported incidence of adverse events was 0.56%.

Reporting of adverse events showed a sharp drop-off over the three injections. For the first dose, incidence of adverse events reported was 0.84% (total 166,757 doses given), 0.57% for the second dose (150,515 doses) and 0.18% for the third (130,001 doses given).

Many reports described several symptoms ocurring together, and 5,513 adverse symptoms were reported in all. Onset was within twelve hours of vaccination for 48% of these

Number of specific events

- Urticaria 107
- Asthma or bronchospasm 70
- Swelling, edema or angioedema 47
- Anaphylaxis 2
- Death 2

Anaphylaxis

11.4.1 Anaphylaxis

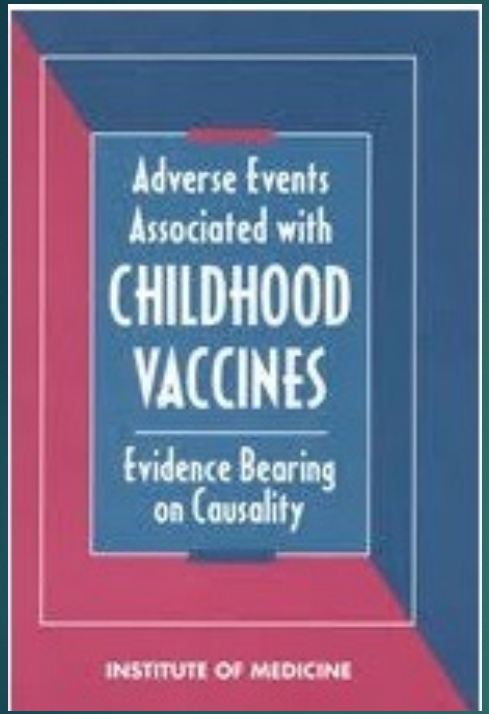
Anaphylaxis occurred in two boys, five minutes after injection in a four-year-old and ten minutes after injection in an infant of four months. In each case, adrenaline was given intramuscularly and the child improved markedly within ten minutes. Both reactions occurred after the third vaccine dose, and neither child had experienced any reaction to former doses.

Death

10.1 Death

Two deaths were reported in association with the vaccination campaign. A boy aged nine months became unwell and grizzly a day after his first vaccine dose, and remained unwell until he was found dead four days after receiving the vaccine.

Another boy, aged three months, had been well until he was found dead three days after receiving his second dose of hepatitis B vaccine. Autopsy revealed no abnormality. An older sibling of this child had previously died a cot death.



IOM official report

Anaphylaxis was not observed in the 166,757 children vaccinated with a plasma-derived vaccine in New Zealand (Morris and Butler, 1992), nor was it observed in 43,618 Alaskan natives who received plasma-derived vaccine (McMahon et al., 1992). The postmarketing surveillance study discussed above (Shaw et al., 1988) investigated only specific adverse neurologic outcomes following receipt of hepatitis B vaccine and provided no data regarding anaphylaxis.

pg 229

Aftermath

Page Three

In May 1988, the Hamilton Department of Health (Wellington) faxed to Hepatitis B co-ordinators in all area health boards a message from the principal medical officer: "We have received approximately 10 reports of *anaphylactoid reactions* occurring in children receiving hepatitis B vaccine. This is . . . a matter of considerable concern . . . Professor Ralph Edwards . . . reports 14 similar reactions . . . since 1985 in Australia and he feels sure that the potential for severe allergic response exists. Accordingly . . . the following policy should be adhered to . . . (1) For children who have developed vaccine-related urticaria alone it is recommended that subsequent vaccinations be given in a hospital setting . . . (2) If the allergic response includes ANAPHYLACTIC SHOCK, HYPOTENSION, BRONCHOSPASM or true ANGIONEUROTIC OEDEMA, then it is considered that any further vaccination is absolutely contraindicated. It is felt that for the above conditions to be classified as vaccine related, the onset of symptoms should be within 12 hours after an injection of hepatitis B vaccine"

Doctors reported problems after the HepB was given at birth.

- More antibiotics
- Immune derangements
- Jaundice in newborns

so nobody has done a study looking at non vaccinated newborns vs vaccinated newborns to compare jaundice rates?

Thought for 10s

No, there are no published studies that directly compare jaundice (hyperbilirubinemia) rates or bilirubin levels between HepB-vaccinated and unvaccinated newborns in a controlled manner.

cdc.gov

Some relevant research on HepB vaccine safety

Hepatitis B vaccines

"Hepatitis B vaccines have several side effects that are caused by the aluminum adjuvant . . . We confirmed by quantitative RT-PCR that hepatitis B vaccine ***changed the expression level of seven genes*** *that were selected biomarkers, which reflected* ***subtoxic/adverse effects of the vaccine, especially subtle liver injury."***

Hamza 2012 PMID: 21691704

Aluminium Hep B vaccine effects

- Mice injected with recomb HepB vaccine
- 144 liver genes changed after one day
  - 52 downregulated, 92 upregulated
  - 7 were closely examined
    - 2 inflammation genes upregulated
    - 2 acute phase inflammation proteins upreg
    - 1 for gluconeogenesis upregulated
    - 2 for bile acid synthesis downregulated

Hamza 2012 PMID: 21691704

They concluded that vaccination altered certain gene expressions, highlighting potential areas for further safety investigation. But those studies are NEVER done are they Grok?

Thought for 5s

No, exact follow-up studies replicating the Hamza 2012 mouse liver gene expression experiment in human term infants have not been done.

2004 Guinea-Bissau Hep B vaccine study

- 6,399 children got MV
- 876 children got MV and 3 doses of HepB vaccine
- Followed to 2 yrs of age
- MV only but no HBV: MR = 0.97
- HBV plus MV compared to MV only
  - @7 ½ months short term MR = 1.62
  - @ 7 ½ - 12 months, MR was 1.81
  - female: male MR 2.20

Garly 2004 PMID: 15626943

“…the vaccine is given in infancy, and there has been no evaluation of its effect on mortality among young children. Because trials would now be considered unethical, any evaluation must be based on observational studies.”

USA: HepB vaccine in 1996

- 225 USA infants given HepB vaccine different doses and routes to see if they would respond better to one dose/route vs another
- Infants who received the standard 10 mcg doses ***had statistically significant growth retardation.*** (another NSE)
  - Growth and weight data (before and after) almost never reported in infant vaccine studies.

Coberly 1996 PMID: 7975851

Vaccine viral escape and the new vaccines soon to be available.

1. Recombivax HB (Merck)

- **Pediatric/Adolescent formulation**: **5 mcg** of HBsAg (hepatitis B surface antigen) in **0.5 mL**
- Given to infants from birth through 19 years of age.

2. Engerix-B (GSK)

- **Pediatric/Adolescent formulation**: **10 mcg** of HBsAg in **0.5 mL**
- Also given to infants from birth through 19 years of age.

Vaccine Viral Escape

Diagnostic and Clinical Relevance of HBV Mutations

Rebecca T. Horvat, PhD, D(ABMM)

Lab Med. 2011;42(8):488-496.

Abstract and Introduction

Abstract

Despite vaccinations, hepatitis B virus (HBV) infections are still very common worldwide. The virus replicates by reverse transcription using a viral polymerase lacking proof-reading ability. This results in the emergence of mutant viruses that can be selected out by host immunity or viral therapeutic agents. Several well-characterized HBV variants have been identified that challenge the effectiveness of the current vaccines. Other mutations result in a change within the HBV surface antigen, resulting in a loss of detection by some diagnostic assays. Additionally, a number of mutations have evolved in response to antiviral therapy. This report is an overview of the HBV mutations leading to vaccine failure, loss of HBV detection by diagnostic assays, increased viral replication, and resistance to antiviral agents.

Introduction

Hepatitis B virus (HBV) infection continues to be a global public health issue. The World Health Organization (WHO) reports that approximately 2 billion people worldwide have been infected with HBV and approximately 350 million individuals suffer from HBV-induced chronic liver disease.[1] Without intervention, 15% to 40% of chronic HBV-infected individuals will develop cirrhosis, end-stage liver disease, hepatocellular carcinoma (HCC), or will require liver transplantation.[1,2]

Chronic disease is the most common presentation of HBV infection. The chronic nature of HBV results in individuals producing a high level of virus with few symptoms.[3] Hepatitis B virus infects and replicates in the host hepatocyte cells producing high levels of virus. During HBV replication, the virus uses reverse transcription to copy its DNA genome. However, this HBV polymerase lacks proof-reading ability, allowing mutations to occur. This leads to a heterogeneous population of HBV with altered genomes. Under selective pressure from the host immune response and/or antiviral therapy, viruses with mutations emerge as the dominant viral population. This review presents an overview of HBV biology, diagnostic laboratory assays, vaccines, antiviral agents, and the association with specific HBV mutations.

However, in the last 20 years a number of HBV mutants have emerged. The fluid nature of HBV lends itself to rapid change due to the imprecise RNA polymerase allowing random heterogeneity. This permits selection of mutated HBV by host immunity and antiviral therapy. A number of well-characterized HBV mutations have been recognized, leading to vaccine failure, loss of HBV detection by diagnostic assays, increased viral replication leading to hepatic damage, and resistance to antiviral agents.

From a CDC scientist

Asian Journal of Transfusion Science

Home
Current issue
Instructions
Submit article

Asian J Transfus Sci. 2007 Jul-Dec; 1(2): 62–70.
doi: 10.4103/0973-6247.33445

PMCID: PMC3168123

Hepatitis B virus S gene escape mutants

Michael A. Purdy

Division of Viral Hepatitis, MS-A33, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Atlanta, GA 30329, USA

Correspondence to:Michael A. Purdy, Division of Viral Hepatitis, MS-A33, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Atlanta, GA 30329, USA. E-mail: mup3@cdc.gov

Escape Mutants

As stated above, vaccination with HBsAg has been efficacious in the pre-exposure setting; however, occult infections began to be noted in the late 1980's[55,56] and the first case of a vaccine-induced escape mutant, in a child in southern Italy, who received passive-active post-exposure immunization, was described in 1990.[57] Mutations within the S gene are known to be responsible for occult hepatitis B infections, reactivation of hepatitis B,[58,59] diagnostic assay failure[58,60–63] and reinfection in HBV-infected recipients of orthotopic liver transplantations.[17,64] Occult infections create public health concerns because asymptomatic carriers can be blood donors.[65–67] These mutations are stable and can be transmitted horizontally and vertically.[56,68–71]

HBV replicates to high titers in infected individuals. Because it replicates through an RNA intermediate synthesized by reverse transcriptase, mutant viral genomes[59,72] and quasi-species[71–77] are generated. This results in the production of viral mutants during naturally occurring infections.[78,79] Vaccination and the administration of HBIG and anti-viral drugs like lumavidine exert evolutionary pressures to select mutants.[70,80]

Research with childhood vaccinations shows that mutations accumulate with higher frequency in vaccinated than unvaccinated children, with more mutations emerging in children vaccinated with plasma-derived vaccine than recombinant vaccine.[80] Vaccinated children generated a preferential accumulation of mutations in the second loop of the MHR, while unvaccinated children generated random mutations.[81] The prevalence of mutations increases over time[80,82] and the frequency of amino acid variation per site increases with age.[73] There is also an accumulation of S gene mutations in HBV related end-stage liver disease.[83]

- Prevalence of vaccine-escape mutations in studied populations is often in the range of ~6–18% among certain chronic HBV patients (higher in some genotypes like D), with complex (multiple) mutations rarer but increasing in some areas over time (e.g., in genotype D cohorts). tandfonline.com
- They are more noted in high-vaccination settings (e.g., parts of Asia) or breakthrough cases, but breakthrough infections in fully vaccinated people remain rare. Some mutants also cause diagnostic issues (false-negative HBsAg tests). medcraveonline.com

New vaccines on the horizon

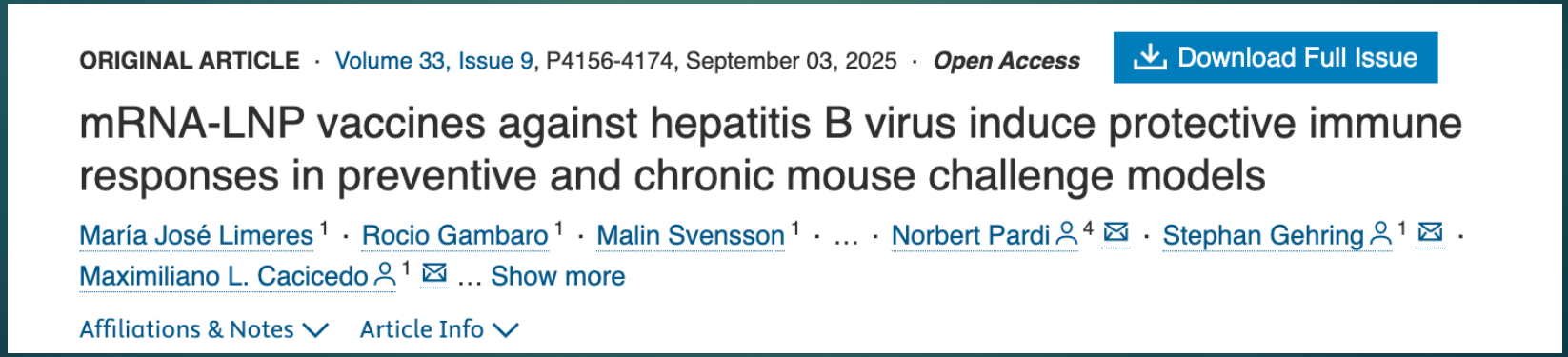
- Next-generation Hepatitis B (HBV) vaccines aim to overcome limitations of standard "second-generation" recombinant vaccines (which contain only small surface antigen, S-HBsAg, produced in yeast). These limitations include non-response in ~5–15% of people, reduced effectiveness against some vaccine-escape mutants (e.g., G145R), and the need for more doses or stronger responses in certain populations.

Article | Open access | Published: 05 September 2022

Neutralization of hepatitis B virus with vaccine-escape mutations by hepatitis B vaccine with large-HBs antigen

mRNA vaccines coming to a clinic near you…

- Preclinical mRNA-LNP vaccines encoding HBsAg have induced stronger antibody and T-cell responses than approved protein vaccines in some studies, with potential for better breadth. However, these remain early-stage and not yet optimized or tested specifically for vaccine-escape mutants (VEMs) in humans.

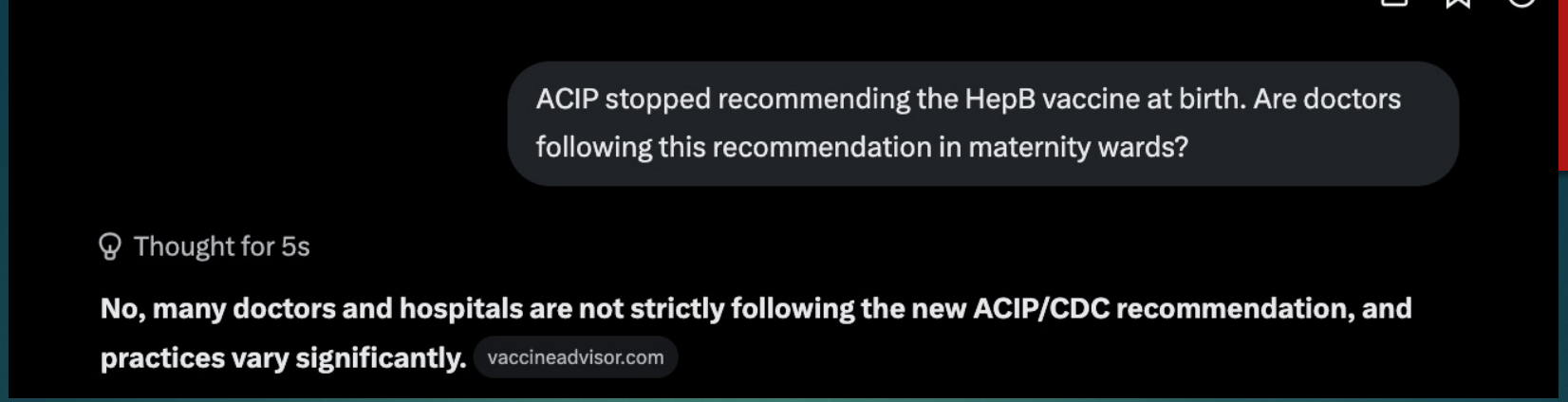


ORIGINAL ARTICLE · Volume 33, Issue 9, P4156-4174, September 03, 2025 · *Open Access* Download Full Issue

mRNA-LNP vaccines against hepatitis B virus induce protective immune responses in preventive and chronic mouse challenge models

María José Limeres [1] · Rocio Gambaro [1] · Malin Svensson [1] · … · Norbert Pardi [4] · Stephan Gehring [1] · Maximiliano L. Cacicedo [1] … Show more

Affiliations & Notes Article Info



Many hospitals and pediatric groups (e.g., AAP) continue strongly recommending the birth dose.