

1 Determinants of Influenza Vaccination in Children with Asthma in Four Health Maintenance Organizations

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Objective: Asthma is one of the most common causes of hospitalization among children. Viral infections, especially influenza, can exacerbate the course of asthma. Although influenza vaccination is recommended for children with asthma, fewer than 10% receive an annual vaccination.

Methods: We assessed the determinants for receipt of the 1994/1995 influenza vaccine in asthmatic children enrolled in four health maintenance organizations participating in the Vaccine Safety Datalink Project. Computerized data were available on all medical and pharmacy encounters of approximately 500,000 children 0-6 years of age. Asthma cases were identified using International Classification of Diseases and asthma medication files. We used logistic regression to identify risk factors for vaccination, adjusting for age, sex, asthma medication, hospitalizations and emergency department (ED) visits during the six months preceding the beginning of the influenza season.

Results: We identified 37,805 children with asthma; only 3,365 (9%) were vaccinated against influenza. Vaccinated children were more likely to have had at least one hospitalization or ED visit for asthma (OR=2.1; 95%CI=1.8-2.5), and were more likely to have three or more prescriptions for a beta agonist drug prior to study entry (OR=10.0; 95%CI=8.9-11.3). However, only 35% and 39% of asthmatic children in each of these categories, respectively, were vaccinated.

Conclusions: Children with more severe asthma are more likely to be vaccinated against influenza, but only a minority of such children is currently vaccinated. Further studies of risk factors for nonvaccination are warranted.

3 Booster Dose Hepatitis B Immunogenicity of a Pentavalent [DTPw/Hib/Hepatitis B] Vaccine at 18 Months of Age Following Monovalent Hepatitis B Vaccine at Birth, and Pentavalent Vaccine at 2, 4 and 6 Months

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Administration of monovalent hepatitis B (HB) vaccine at birth followed by single injections of pentavalent vaccine at 2, 4, 6 and 18 months would fit with existing schedules and promote uptake, simplify administration, and reduce delivery costs. We recently reported that following a 2.5µg or 5µg dose of HB vaccine at birth, three doses of pentavalent vaccine stimulated hepatitis B antibody levels of ≥10mIU/mL in 93.9% of infants (regardless of the dose of HB vaccine given at birth). We now report preliminary HB immunogenicity results following an 18-month pentavalent vaccine booster in a subset (n=182 pre- and 97 1mo. post-booster) of the original cohort of 347 children. The pentavalent vaccine incorporates a whole-cell pertussis-based DTP vaccine (30Lf diphtheria toxoid, 6Lf tetanus toxoid, ≤20x10⁸ inactivated *Bordetella pertussis*: CSL Ltd.), 7.5µg liquid PRP-OMP conjugate Hib vaccine (Merck & Co.), and 5µg HBsAg recombinant hepatitis B vaccine (Merck & Co.). The birth dose was either 2.5µg (low dose) or 5µg HBsAg (standard dose) monovalent recombinant hepatitis B vaccine (Merck & Co.). The pre-booster dose anti-HBs GMT was 17mIU/mL, rising a geometric mean 32-fold to 530mIU/mL after vaccination. Proportions with titres ≥10mIU/mL were 68.1% (95% CI 61%, 75%) before, and 92.8% (95% CI 86%, 97%) after boosting. There were no significant differences in pre- or post-booster titres between those infants who received 2.5µg and 5µg of hepatitis B vaccine at birth.

Conclusion: The data show that there was a vigorous boost to anti-HBs antibody titres following the 18 month vaccination resulting in satisfactory performance of the vaccine with respect to hepatitis B antibody generation. (Funded by CSL Ltd. and Merck & Co., Inc.)

2 Immunogenicity of Attenuated Dengue Virus Vaccines (Pasteur Mérieux Connaught, PMC) in Human Volunteers

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Groups of five flavivirus non-immune volunteers were given one of four monovalent, live, attenuated dengue vaccines (types 1, 2, 3, and 4; PMC). Ten volunteers received combined tetravalent vaccine, and 10 were given placebo (vaccine vehicle alone). Vaccines were administered as a single subcutaneous dose (range 3.6-4.4 log₁₀ pfu). All recipients of dengue-3, dengue-4, and tetravalent vaccine developed transient viremia between days 7-12 after immunization; viremia was rarely detected in dengue-1 or -2 vaccines. Seroconversion (by PRNT or MAC-ELISA) was achieved by all volunteers immunized with types 2, 3, and 4 dengue vaccines, but only 60% of dengue-1 vaccinees. Monovalent vaccines induced type-specific PRNT antibody responses, which persisted out to day 180 in 89% of responders. In 10 tetravalent vaccine recipients, all seroconverted for type 3 dengue virus. Whereas seven volunteers also developed neutralizing antibodies against other virus types, the highest antibody titers in tetravalent vaccinees were against dengue-3 virus. One volunteer in this group developed antibody against three dengue viruses (types 2, 3, and 4) and another demonstrated tetravalent antibody by day 180. Type 3 viremia after tetravalent immunization, detected using type-specific RT-PCR, suggests preferential replication of dengue-3 virus. Potential interactions among dengue virus types may affect the infectivity and immunogenicity of the live, attenuated, tetravalent dengue vaccine.

4 Antipertussis Antibodies Over Time and Protection After Household Exposure to *Bordetella pertussis*

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Vaccine efficacy against WHO-defined pertussis after household exposure to *Bordetella pertussis* was estimated at 75.4% for an acellular five-component DTP, at 42.4% for an acellular two-component DTP, and at 28.5% for a licensed U.S. whole-cell DTP, after three doses at 2, 4 and 6 months of age, in a placebo-controlled trial.¹ Logistic regression analysis showed statistically significant correlations between clinical protection and the levels of IgG antibodies against pertactin, fimbriae 2 and 3, and to a lesser extent, against pertussis toxin in sera at time of exposure.

Multi-component pertussis vaccines of proven high efficacy in the recent Swedish NIAID-sponsored efficacy trials^{1,2} induced higher antibody levels against pertactin and fimbriae 2 and 3 than less efficacious vaccines. Anti-pertactin, and anti-fimbriae 2 and 3, and to a lesser extent anti-pertussis toxin may be used as surrogate markers of protection for multi-component acellular and whole-cell vaccines against pertussis.

References:

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