



EVIDENCE FOR HEALTH PROMOTION

MEDICAL COLLEGE OF GEORGIA
DEPARTMENT OF FAMILY MEDICINE

Volume 1, Issue 1
October, 1999

Welcome to Evidence for Health Promotion Newsletter. The Evidence-Based Health Promotion Newsletter is an initiative of the Department of Family Medicine at the Medical College of Georgia to advance Health Promotion. This bimonthly publication is being produced by the Faculty Development Group to provide evidence-based reviews of current literature regarding practices in health promotion and disease prevention as well as other useful health promotion tips. This newsletter is our effort to provide clinically relevant information to practicing family physicians in Georgia. Please respond to us with any suggestions or questions at (706) 721-4510.

HEPATITIS B

Barash, Craig, et al. Serologic Hepatitis B Immunity in Vaccinated Health Care Workers. *Arch. Intern. Med* Vol 159, July 12, 1999.

(By David M. Jester, MD)

Clinical Question: Does the current system of vaccination of health care worker against Hepatitis B provide adequate protection?

Background: The current Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination against hepatitis B for all high-risk group, including health care workers. In the United States between 1984 and 1993, 8,000 new cases of hepatitis B that were related to occupational exposure. The currently accepted non-response rate is 5%, while the duration of immunity is widely debated in the literature. The Advisory Committee on Immunization Practices (ACIP) recommends testing at 1 to 2 months post vaccination for persons at occupational risk, but does not suggest further periodic testing.

Population Studied: There were 154 participants who were health care workers at Presbyterian Hospital in Philadelphia, PA. The study took place between July 1995 and March 1996. This population was a diverse mix of the typical health care workers seen in the hospital setting in the United States.

Study Design and Validity: The study enrolled participants by placing flyers in their medical center and setting up various meeting sites around their campus. Each individual enrolled had serum checked for hepatitis B surface antigen, hepatitis B core antibody and qualitative and quantitative hepatitis B surface antibody. A questionnaire was used to evaluate date of vaccination, number of doses, whether titers had been checked, titer results as well as age, sex, and job description. Appropriate statistical analyses was performed. Overall, the study design and parameters were acceptable for the clinical question being studied.

Outcomes Measured: The primary outcome of this study was the presence or absence of anti-hepatitis B titers which indicated active immunity in the participants. They also evaluated the number of vaccinations, time since vaccination; current age, age at the time of vaccinations, whether titers had been drawn and if these were positive. This was based upon self report and the authors were not able to provide objective verification of these tests.

Results: In regards to detectable anti-hepatitis B titers, 109/154 (71%) had detectable titers and 45/154 (29%) had no detectable titers. There were no statistical differences in the time since vaccination, number of doses of vaccine, sex, age, or job description among the participants. In regards to previous testing to confirm immunity, 62/154 (40%) had previously had their titers checked, with 48 (77%) of these persons reporting immunity. Twenty-nine percent of the health care workers who had been vaccinated showed no serologic evidence of immunity. Furthermore, 6 subjects were given booster doses, and all of these subjects responded by developing anti-hepatitis B levels.

Recommendations for Clinical Practice: This study supports the continued vaccination of all health care workers against hepatitis B following the current vaccination schedule. They have provided data to support post vaccination testing at 1 to 2 months to document response. The data also suggest that routine anti-hepatitis B monitoring is needed to maintain immunity, as is booster immunization for subjects whose titers fall below the protective levels.

ROTAVIRUS VACCINE

(By Bruce LeClair, MD)

Intussusception Among Recipients of Rotavirus Vaccine, United States, 1998-1999, *Morbidity and Mortality Weekly Report*, July 16, 1999.

This issue of the MMWR describes the epidemiologic features of the 15 cases of intussusception among infants who had received the tetravalent rhesus-based rotavirus vaccine (RRV-TV) reported to the Vaccine Associated Adverse event Reporting System (VAERS) during the period of September 1, 1998-July 7, 1999 and ongoing

studies of intussusception and rotavirus vaccine.

Of the 15 infants with intussusception reported to VAERS, 13 (87%) developed intussusception following the first dose of the three-dose RRV-TV series, and 12 (80%) within 1 week of receiving any dose of RRV-TV. Intussusception was confirmed radiographically in all 15 patients. Eight infants required surgical reduction and one required resection of 7 inches of distal ileum and proximal colon. The histopathology of the resected portion indicated lymphoid hyperplasia (a common finding in intussusception and thought to be the cause) and ischemic necrosis. All infants recovered.

The rate of hospitalization for intussusception among infants aged <12 months in New York 1991-1997 was 51 per 100,000 infant-years. Given this information, 14-16 intussusception cases among infants would be expected by chance alone during the week following receipt of any dose of RRV-TV.

This would seem to indicate that the rate of intussusception was not above that which would have been expected, however, two postlicensure studies, one at Northern California Kaiser Permanente (NCKP) and a second in Minnesota, also indicated the possibility of increased risk. At NCKP nine cases of intussusception were identified during the period of vaccination giving the rate of intussusception at 45 per 100,000 infant-years among never vaccinated compared to 125 per 100,000 infant-years in vaccinated infants (age-adjusted relative risk 1.9 CI=0.5-7.7, $p=0.39$). In the Minnesota study eighteen cases were identified, five of which were among infants who had received RRV-TV giving an observed rate of RRV-TV associated intussusception of 292 per 100,000 infant-years.

While the individual data from each of these sources is not statistically significant due to small numbers of cases (lack of power), the fact that both studies suggest increased risk was enough for the CDC to recommend suspension of administration of RRV-TV at least until November when the rotavirus season reaches its peak. The authors emphasize the need to be observant for sign and symptoms of intussusception in infants who have received the RRV-TV and report it to VAERS.

Recommendations for Clinical Practice:

1. Hold off on the rotavirus vaccinations at least until November when it's likely that the CDC will have further information and recommendations.
2. If you've been giving the rotavirus vaccine, be aware of signs and symptoms of intussusception (persistent vomiting, bloody stools, black stools, abdominal distention, and/or severe colic pain) as early diagnosis may increase the probability that the intussusception can be treated without surgery.
3. Report any potential vaccine associated adverse event to VAERS.

VAERS IS AVAILABLE 24 HOURS A DAY AT (800) 822-7967 OR ON THE WORLD-WIDE WEB <http://www.nip.gov/nip/vaers.htm>

INTRANASAL INFLUENZA VACCINE IN ADULTS

(By Julie Hendrich, MD)

Effectiveness of Live, Attenuated Intranasal Influenza Virus Vaccine in Healthy Working Adults: A Randomized Controlled Trial, *JAMA* 1999;282:137-144.

Clinical Question: Is intranasally administered trivalent, live, attenuated virus (LAIV) vaccine safe and effective in reducing illness among healthy working adults?

Background: Influenza Type A and B viruses cause illness in 10-20% of the population each year accounting for millions of work loss days and physician office visits. Currently, vaccination with inactivated influenza virus is associated with health and economic benefits for healthy working adults. Intranasal LAIV vac-

enza virus is associated with health and economic benefits for healthy working adults. Intranasal LAIV vac-

INTRANASAL INFLUENZA VACCINE IN ADULTS (CONT'D)

(By Julie Hendrich, MD)

cines offer a new option for influenza prevention. This study assesses the safety and effectiveness of intranasally administered trivalent LAIV vaccine among healthy adults for reducing clinical illness, absenteeism and health care use.

Population Studied: 4,561 healthy working adults ages 18-64, working at least 30 hours outside the home, with health insurance, were enrolled from 13 sites across the U.S. in mid-September to mid-November 1997. Patients were excluded if they had a history of hypersensitivity to egg products, had previously received 1997-1998 inactivated influenza vaccine, self-reported pregnancy or risk of pregnancy within previous 3 months or had acute febrile illness within 72 hours. Exclusion also included subjects with indication for routine vaccination with inactivated vaccine. The average age was 38, 84% were caucasian, 54% were female.

Study Design and Validity: The study was a well-designed randomized, double-blind, placebo-controlled trial and the population is similar to that seen by many family physicians. Vaccine was given by study staff member or self-administered under supervision. Subjects were randomized 2:1 to receive intranasal LAIV vaccine or placebo. Post vaccination symptoms and adverse events were recorded at 7 and 28 days following vaccination. Symptom and illness cards were completed daily November 1997-March 1998 to assess occurrence of illness, health care use, and work loss. Outbreak periods of influenza were well-defined at each site. Follow-up of subjects was excellent. Definitions of illness were created to be sensitive and specific for influenza; however, no testing was done to define influenza in study participants.

Outcomes Measured: Primary endpoints measured were the development of illness, missed days from work, visits to health care providers during peak and total outbreak periods. Secondary endpoints measured were vaccine related adverse effects. Blinded study investigators reviewed adverse events following vaccination to determine relationship between event and vaccination.

Results: Vaccine recipients (VR) were less likely to experience febrile illness in all categories. VR also experienced a 27.3% vs. 22.9% reduction in total sick days, and 28.4% vs. 13.17% reduction in work loss days. VR also had fewer visits to health care provider and took fewer antibiotics. They were more likely to experience runny nose or sore throat within seven days after vaccination. There were no significant differences in serious adverse events between groups. A limitation of the study was the lack of confirmation of influenzae by laboratory testing. The investigators attempted to use the severe illness category and population sample size to improve specificity for capturing cases of influenza. Decreased illness in all groups may suggest some cross-reactivity to other viruses.

Recommendations: Trivalent intranasal influenza virus vaccine (LAIV) was well tolerated and effective at reducing severe febrile illness, work absenteeism, health care visits, and antibiotic use in healthy workers. Consideration of routine vaccine use in the workplace may be warranted.

HEPATITIS A

(By Rayvelle Barney, MD)

Hepatitis A Vaccination in Chronic Carriers of Hepatitis B Virus, *The Journal of Pediatrics*, 1999, Vol. 134:(6);784-785.

Clinical Question: What is the efficacy and clinical utility of vaccination against hepatitis A virus (HAV) in children with chronic hepatitis B virus (HBV) infection?

Background: HAV infection typically follows a benign course. However, in a subpopulation of patients, HAV can result in severe

liver disease and subsequent death. Studies have convincingly demonstrated that patients with chronic liver disease, including chronic hepatitis B virus infection, are one such subpopulation that has an increased risk for severe complications following HAV infection. Consequently, in this population, vaccination against HAV may be warranted to prevent such complications and reduce fatalities from HAV infection.

Study Design: The study enrolled 33 children, mean age 10.7. All the participants were chronic hepatitis B surface antigen carriers and all were initially seronegative for anti-HAV. All the participants were in good physical health and the majority (20 patients) had normal liver function tests.

HEPATITIS A (CONT'D)

(By Rayvelle Barney, MD)

Anti-HAV vaccine (HAVRIX, Smith Kline Beecham) was administered intramuscularly in three, 0.5 ml doses of 360 enzyme-linked immunosorbent assay units and administered at 0, 1 and 6 months. Blood samples were analyzed for HAV antibodies at 1, 2, 6, 7 and 12 months. All participants were monitored for localized and generalized reactions.

Results: The vaccine for HAV proved to be immunogenic and well tolerated. Seroconversion rates were 90.9%, 96.9% and 100% after the 1st, 2nd and 3rd respectively. The anti-HAV geometric titer (GMT) rose logarithmically with each dose going from 98.4 to 283.4 to 3776.8 with the 1st, 2nd and 3rd doses respectively. At one-year follow-up, all participants had maintained protective levels of anti-HAV and none of the children had developed HAV infection. The side-effects reported were mild (local redness/swelling, generalized headache, malaise and slight fever). No severe side-effects were reported.

Conclusions and Recommendations: This results of this study should be interpreted cautiously due to: (a) sample size not large enough to rule out possible side effects; (b) relatively short follow-up period; (c) lack of an experimental control group, and; (d) results speak only to carriers for hepatitis B and not to those with chronic liver disease. This study suggests that the anti-HAV vaccine is well tolerated and effective. The vaccine has very good immunogenicity and has been demonstrated to prevent the occurrence of HAV infection in immunized patients over their term of the study. It is recommended that clinicians consider: 1) prophylactically administering anti-HAV to patients with hepatitis B; 2) more specifically, anti-HAV vaccine administration may be most important in children with hepatitis B due to their longer life expectancy and increased ability to elicit a more effective immune response.



Medical College of Georgia
Department of Family Medicine
Research Program
HB-3000F
Augusta, GA 30912