CLINICAL CAPSULES

Hurricane Health Care Threat

Missing pediatric vaccinations is one of the health challenges the country faces from Hurricane Katrina, Anthony Fauci, M.D., said at a press briefing sponsored by the Association of Health Care Journalists.

"One of the problems with natural catastrophes and disasters is that when you interrupt the regularly scheduled childhood vaccinations, then you develop areas of vulnerability of children getting infected with common viruses that you generally don't think of as being a problem, like measles," said Dr. Fauci, director of the National Institute of Allergy and Infectious Diseases, Bethesda, Md. "We've got to keep the children's vaccination schedules up for normal diseases, not necessarily diseases that are peculiar to Katrina."

Keeping up the vaccination schedule in pediatric Hurricane Katrina survivors has been made even more difficult by the fact that many patients' health care records have been destroyed. "So one of the things we have to be sure of is when in doubt, vaccinate," Dr. Fauci said, adding that the hurricane "certainly is an argument for electronic versions of medical records."

STI Vaccination Acceptance

Ninety-three percent of 320 parents and 89% of their 320 adolescents endorsed a vaccine against HIV, said Gregory D. Zimet, Ph.D, and his associates at Indiana University, Indianapolis. Eighty-five percent of parents and 87% of adolescents said that they would get a gonorrhea vaccine if it were available, and 89% and 90% of parents and adolescents, respectively, supported a vaccine for genital herpes. The parents and adolescents were recruited into the study from primary care clinics and private pediatric practices, and responded to anonymous surveys. Parental predictors of vaccine acceptance included a parental history of sexually transmitted infections and a perceived vulnerability of the child to STIs. Adolescent predictors of vaccine acceptance included having parents who accepted the vaccine and having at least one friend who had engaged in sex. Since the ideal age for immunization against STIs would be preadolescence or early adolescence, prior to the onset of sexual activity, parental acceptance and support of vaccination would be central to any program, the investigators noted (J. Adolesc. Health 2005;37:179-86).

MRSA Joins Football Team

An outbreak of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) occurred among 13 players on a high school football team in Pennsylvania, said Jeffrey A. Rihn, M.D., of the University of Pittsburgh and his colleagues (Pediatr. Infect. Dis. J. 2005;24:841-3). The outbreak began during the fourth week of football season, when abscesses appeared in four players, and three of them yielded positive cultures for CA-MRSA. Although the team was educated about hygiene behavior, such as washing hands, treating skin lesions promptly, and not sharing towels, the outbreak eventually included 20 infections. All 102 players and staff members underwent nasal cultures. Overall, 3 of 102 cultures (2.9%) were positive for MRSA and 32 (31.4%) were positive for methicillin-susceptible *S. aureus*; this low prevalence of colonization means surveillance cultures aren't useful for determining risk of CA-MRSA. Mupirocin was not effective at controlling infections due to noncompliance and nonsimultaneous use. Eight infections were treated with drainage and empiric cephalexin or amoxicillin/clavulanate, and the recurrence rate was slightly lower in cases where the choice of antibiotics was guided by culture. In this outbreak, risk factors included playing lineman position, and junior class status, but did not include personal hygiene practices or sharing towels or equipment.

Uncircumcised at Greater UTI Risk

Being uncircumcised and having a fever greater than 39° C were significant risk factors for urinary tract infections (UTIs) in a study of 1,025 infants aged 1-60 days, said Joseph J. Zorc, M.D., of the University of Pennsylvania, Philadelphia, and other members of the Multicenter RSV-SBI study group. Overall, 52% of the 291 boys were uncircumcised, and 21% of these had UTIs, compared with UTI rates of 2% among circumcised boys and 5% among girls. In addition, 23 of 68 male infants who were uncircumcised and had fevers greater than 39° C were diagnosed with urinary tract infections.

Hispanic/Latino boys and Asian boys were significantly more likely to be uncircumcised (78% and 72%, respectively), compared with infants of other ethnicities (28%). Circumcision status was often not documented in the records of patients in whom infections were missed. Physicians may not consider circumcision status as a factor in managing UTIs, and an enhanced urinalysis or empiric treatment while awaiting culture results in the absence of enhanced urinalysis may be merited for uncircumcised infants, the investigators said (Pediatrics 2005;116:644-8).

—Heidi Splete with staff reports

BOOSTRIX®
(Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed) (Tdap)

The following is a brief summary only; see full prescribing information for complete product information.

INDICATIONS AND USAGE: BOOSTRIX is indicated for active booster immunization against tetanus, diphtheria, and pertussis as a single dose in individuals 10 through 18 years of age. The use of BOOSTRIX as a primary series or to complete the primary series has not been studied. As with any vaccine, BOOSTRIX may not protect 100% of individuals receiving the vaccine. BOOSTRIX is not recommended for treatment of actual infections.

CONTRAINDICATIONS: Hypersensitivity to any component of the vaccine is a contraindication (see DESCRIPTION in full prescribing information). Do not use BOOSTRIX after a serious allergic reaction (e.g., anaphylaxis) following any other tetanus toxoid, diphtheria toxoid or pertussis-containing vaccine, or any component of this vaccine (see DESCRIPTION in full prescribing information). Because of the uncertainty as to which component of the vaccine might be responsible, do not give further vaccination with any of these components; or, refer such individuals to an allergist for evaluation. The following events are contraindications to administration of BOOSTRIX: encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous dose of a pertussis-containing vaccine that is not attributable to another identifiable cause; progressive neurologic disorder, uncontrolled epilepsy, or progressive encephalopathy. Do not vaccinate individuals with these conditions until a treatment regimen has been established and the condition has stabilized. BOOSTRIX is not contraindicated for use in individuals with HIV infection.

WARNINGS: The tip cap and the rubber plunger of the needleless prefilled syringes contain dry natural latex rubber that may cause allergic reactions in latex sensitive individuals. The vial stopper is latex-free. If any of the following events occurred in temporal relation to previous receipt of a Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTwP) vaccine or a vaccine containing an acellular pertussis component, consider carefully whether to give subsequent doses of BOOSTRIX: temperature of ≥40.5˚C (105˚F) within 48 hours not due to another identifiable cause; collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours; persistent, inconsolable crying lasting ≥3 hours, occurring within 48 hours; seizures with or without fever occurring within 3 days. Persons who experienced serious Arthus-type hypersensitivity reactions following a prior dose of tetanus toxoid usually have high serum tetanus antitoxin levels and should not be given Tetanus and Diphtheria Toxoids Adsorbed For Adult Use (Td) or Tdap vaccines or even emergency doses of Td more frequently than every 10 years, even if the wound is neither clean nor minor. If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give BOOSTRIX or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks. The decision to administer a pertussis-containing vaccine to individuals with stable central nervous system (CNS) disorders must be made by the physician on an individual basis, with consideration of all relevant factors, and assessment of potential risks and benefits for that individual. Advise the patient, parent, or guardian of the potential increased risk involved (see PRECAUTIONS). A family history of seizures or other CNS disorders is not a contraindication to pertussis vaccine. The Advisory Committee on Immunization Practices (ACIP) has published guidelines for vaccination of persons with recent or acute illness (www.cdc.gov). Do not give BOOSTRIX to individuals with bleeding disorders such as hemophilia or thrombocytopenia, or to persons on anticoagulant therapy unless the potential benefit clearly outweighs the risk of administration. If the decision is made to administer BOOSTRIX to such persons, it should be given with caution with steps taken to avoid the risk of hematoma following the injection.

PRECAUTIONS: Before the injection of any biological, the physician should take all reasonable precautions to prevent allergic or other adverse reactions. Epinephrine injection (1:1,000) and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur. Immunosuppressed persons, including individuals receiving immunosuppressive therapy, may not develop the expected immune response. **Drug Interactions:** Do not mix BOOSTRIX with any other vaccine in the same syringe or vial. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** BOOSTRIX has not been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility. **Pregnancy:** Pregnancy Category C. Animal reproduction studies have not been conducted with BOOSTRIX. It is also not known whether BOOSTRIX can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. BOOSTRIX should be given to a pregnant woman only if clearly needed. Animal fertility studies have not been conducted with BOOSTRIX. In a developmental toxicity study, the effect of BOOSTRIX on embryo-fetal and pre-weaning development was evaluated in pregnant rats. Animals were administered INFANRIX® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) prior to gestation and BOOSTRIX during the period of organogenesis (gestation days 6, 8, 11) and later in pregnancy (gestation day 15), 0.1 mL/rat/occasion (a 45-fold increase compared to the human dose of BOOSTRIX on a body weight basis), by intramuscular injection. No adverse affect on pregnancy and lactation parameters, embryo-fetal or pre-weaning development was observed. There were no fetal malformations or other evidence of teratogenesis noted in this study. **Nursing Mothers:** It is not known whether BOOSTRIX is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when BOOSTRIX is administered to a nursing woman. **Pregnancy Exposure Registry:** Healthcare providers are encouraged to register pregnant women who receive BOOSTRIX in the GlaxoSmithKline vaccination pregnancy registry by calling 1-888-825-5249. **Geriatric Use:** BOOSTRIX is not indicated for use in individuals older than 18 years. **Pediatric Use:** BOOSTRIX is not indicated for use in individuals younger than 10 years (see DOSAGE AND ADMINISTRATION in full prescribing information). For immunization of infants and children younger than 7 years against diphtheria, tetanus, and pertussis, refer to the manufacturers' package inserts for Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) vaccines.

ADVERSE REACTIONS: A total of 3,289 adolescents were vaccinated with a single dose of BOOSTRIX during clinical trials. An additional 1,092 adolescents 10 to 18 years of age received a non-US formulation of BOOSTRIX (formulated to contain 0.5 mg aluminum per dose) in non-US clinical studies.

The primary safety study, conducted in the United States, was a randomized, observer-blinded, controlled study in which 3,080 adolescents 10 to 18 years of age received a single dose of BOOSTRIX and 1,034 received the control Td vaccine manufactured by Massachusetts Public Health Biologic Laboratories. There were no substantive differences in demographic characteristics between the vaccine groups. Among BOOSTRIX and control vaccine recipients approximately 75% were 10 to 14 years of age and approximately 25% were 15 to 18 years of age. Approximately 98% of participants in this study had received the recommended series of 4 or 5 doses of either DTwP or a combination of DTwP and DTaP in childhood. Data on adverse events were collected by the subjects, parents and/or guardians using standardized diaries for 15 consecutive days following the vaccine dose (i.e., day of vaccination and the next 14 days). Subjects were monitored for unsolicited adverse events that occurred within 31 days of vaccination (day 0-30) using diary cards (day 0-14) supplemented by spontaneous reports and a medical history as reported by subjects, parents, and/or guardians. Subjects were also monitored for 6 months post-vaccination for non-routine medical visits, visits to an emergency room, onset of new chronic illness, and serious adverse events. Information regarding late onset adverse events was obtained via a telephone call 6 months following vaccination. At least 97% of subjects completed the 6-month follow-up evaluation.

The adverse event information from clinical trials provides a basis for identifying adverse events that appear to be related to vaccine use and for approximating rates. However, because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice.

Serious Adverse Events in All Safety Studies: In the US-safety study, no serious adverse events were reported to occur within 31 days of vaccination. During the 6-month extended safety evaluation period, no serious adverse events that were of potential autoimmune origin or new onset and chronic in nature were reported to occur. In non-US studies in which serious adverse events were monitored for up to 37 days, one subject was diagnosed with insulin dependent diabetes. The association of this event with vaccination is unknown. No other serious adverse events of potential autoimmune origin or that were new onset and chronic in nature were reported to occur in these studies.

Solicited Adverse Events in the US-Safety Study: In a US study, the most common local adverse events following administration of BOOSTRIX were pain, redness, and swelling at the injection site. The most common general adverse events were headache and fatigue. Most of these events were reported at a similar frequency in recipients of both BOOSTRIX and Td. Any pain, grade 2 or 3 pain (but not grade 3 alone), and grade 2 or 3 headache (but not grade 3 alone) were reported at a higher rate in recipients of BOOSTRIX. The primary safety endpoint of the US study was the incidence of grade 3 pain (spontaneously painful and/or prevented normal activity) at the injection site within 15 days of vaccination. Grade 3 pain was reported in 4.6% of those who received BOOSTRIX compared with 4.0% of those who received the Td vaccine. The difference in rate of grade 3 pain was within the pre-defined clinical limit for non-inferiority (upper limit of the 95% CI for the difference ≤4%). These were the rates for solicited local and general adverse events within 15 days of vaccination with BOOSTRIX or Td vaccine for the total vaccinated cohort (all enrolled, vaccinated subjects with safety data available analyzed by vaccine received):

Percentage of Individuals 10 to 18 Years of Age Reporting Solicited Local Adverse Events or Solicited General Adverse Events Within the 15-day* Post-Vaccination Period

	BOOSTRIX (N = 3,032)	Td (N = 1,013)
Local		
Pain,† any	75.3	71.7
Pain,† grade 2 or 3	51.2	42.5
Pain,‡ grade 3	4.6	4.0
Redness, any	22.5	19.8
Redness, >20 mm	4.1	3.9
Redness, ≥50 mm	1.7	1.6
Swelling, any	21.1	20.1
Swelling, >20 mm	5.3	4.9
Swelling, ≥50 mm	2.5	3.2
Arm circumference increase,§ >5 mm	28.3	29.5
Arm circumference increase,§ >20 mm	2.0	2.2
Arm circumference increase,§ >40 mm	0.5	0.3
General		
Fever,‖ ≥99.5˚F	13.5	13.1
Fever,‖ >100.4˚F	5.0	4.7
Fever,‖ >102.2˚F	1.4	1.0
Headache, any	43.1	41.5
Headache,† grade 2 or 3	15.7	12.7
Headache, grade 3	3.7	2.7
Fatigue, any	37.0	36.7
Fatigue, grade 2 or 3	14.4	12.9
Fatigue, grade 3	3.7	3.2
Gastrointestinal symptoms,¶ any	26.0	25.8
Gastrointestinal symptoms,¶ grade 2 or 3	9.8	9.7
Gastrointestinal symptoms,¶ grade 3	3.0	3.2

Td = Tetanus and Diphtheria Toxoids Adsorbed For Adult Use manufactured by Massachusetts Public Health Biologic Laboratories.
N = number of subjects in the total vaccinated cohort with local/general symptoms sheets completed.
Grade 2 = Local: painful when the limb was moved; General: interfered with normal activity.
Grade 3 = Local: spontaneously painful and/or prevented normal activity; General: prevented normal activity.
*Day of vaccination and the next 14 days.
†Statistically significantly higher (P<0.05) following BOOSTRIX as compared to Td vaccine.
‡Grade 3 injection site pain following BOOSTRIX was not inferior to Td (upper limit of two-sided 95% CI for the difference in the percentage of subjects ≤4%).
§Mid-upper region of the vaccinated arm.
‖Oral temperatures or axillary temperatures.
¶Gastrointestinal symptoms included nausea, vomiting, diarrhea and/or abdominal pain.

Mid-upper arm circumference was measured by the adolescent or their parent/guardian prior to injection and daily for 15 days following vaccination. There was no significant difference between BOOSTRIX recipients and Td recipients in the proportion of subjects reporting an increase in mid-upper arm circumference in the vaccinated arm. The incidence of unsolicited adverse events reported in the 31 days after vaccination was comparable between the 2 groups.

As with any vaccine, there is the possibility that broad use of BOOSTRIX could reveal adverse events not observed in clinical trials.

Postmarketing Reports: Worldwide voluntary reports of adverse events received for BOOSTRIX in persons 10 to 18 years of age since market introduction of this vaccine are listed below. This list includes serious events or events which have causal connection to components of this or other vaccines or drugs. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. *Blood and lymphatic system disorders:* Lymphadenitis, lymphadenopathy. *Cardiac disorders:* Myocarditis. *Injection site reactions:* Induration, inflammation, mass, nodule, warmth, local reaction. *Metabolism and nutrition disorders:* Diabetes mellitus insulin-dependent. *Musculoskeletal and connective tissue disorders:* Arthralgia, back pain, myalgia. *Nervous system disorders:* Convulsion, encephalitis, facial palsy, paraesthesia. *Skin and subcutaneous tissue disorders:* Exanthem, Henoch-Schönlein purpura, rash. In addition, extensive swelling of the injected limb has been reported following administration of BOOSTRIX.

Reporting Adverse Events: Report the occurrence following immunization of any event set forth in the Vaccine Injury Table from the National Childhood Vaccine Injury Act including: Anaphylaxis or anaphylactic shock within 7 days, encephalopathy or encephalitis within 7 days, brachial neuritis within 28 days, or an acute complication or sequelae (including death) of an illness, disability, injury, or condition referred to above, or any events that would contraindicate further doses of vaccine, according to this prescribing information. These events should be reported to VAERS. The VAERS toll-free number is 1-800-822-7967. Reporting forms may also be obtained at the VAERS website at www.vaers.org.

DOSAGE AND ADMINISTRATION: Recommended Dose: BOOSTRIX should be administered as a single 0.5 mL injection by the intramuscular route into the deltoid muscle of the upper arm in individuals 10 through 18 years of age. Do not administer this product subcutaneously or intravenously. There are no data to support repeat administration of BOOSTRIX. Five years should elapse between the subject's last dose of the recommended series of childhood DTwP and/or DTaP vaccine and the administration of BOOSTRIX. Limited data are available on the use of BOOSTRIX following Tetanus and Diphtheria Toxoids Adsorbed For Adult Use (Td) vaccine. **Additional Dosing Information:** ***Wound Management:*** Clinicians should refer to guidelines for tetanus prophylaxis in routine wound management. Adolescents 10 to 18 years of age who have completed a primary series against tetanus and who sustain wounds which are minor and uncomplicated, should receive a booster dose of a tetanus toxoid-containing vaccine only if they have not received tetanus toxoid within the preceding 10 years. In case of tetanus-prone injury (e.g., wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missles, crushing, burns, and frostbite) in an adolescent who is in need of tetanus toxoid, BOOSTRIX can be used as an alternative to Tetanus and Diphtheria Toxoids Adsorbed For Adult Use (Td) vaccine in patients for whom the pertussis component is also indicated (see INDICATIONS AND USAGE).

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Full prescribing information for BOOSTRIX is available at www.BOOSTRIX.com.

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References: 1. Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases.* Atkinson W, Hamborsky J, Wolfe S, eds. 8th ed. Washington DC: Public Health Foundation; 2004:75–88, A26–A27. **2.** Data on file, BOR305, GlaxoSmithKline.

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