

# MRSA in Nurseries Blamed on Bad Hand Hygiene

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Outbreaks of community-associated methicillin-resistant *Staphylococcus aureus* among healthy, term newborns in Chicago and Los Angeles County hospitals probably originated in the newborn nursery and illustrate the critical importance of consistent hand hygiene, the Centers for Disease Control and Prevention reported.

The CDC helped local health departments in both locations conduct independent investigations into the outbreaks, both of which occurred in 2004. In both outbreaks, the MRSA was a community-acquired rather than a health care-acquired strain.

The Chicago hospital had a cluster of MRSA infections that led authorities to discover 11 cases, of which 9 (82%) were in infants delivered by cesarean section (MMWR 2006;55:329-32).

Nine of the infants were male.

Symptoms were pustules, vesicles, and/or blisters on areas including the neck, groin, perineum, ears, and legs; most patients had lesions on more than one site.

Median age at symptom onset was 7 days, and symptom onset occurred a median of 5 days post discharge from the newborn nursery. The infants were treated with topical antimicrobials in 10 cases, and 3 of those were treated with con-

comitant oral antimicrobials. One was hospitalized. All 11 infants recovered without incident, the CDC reported.

A subsequent investigation found that one physician and one nurse had nasal MRSA colonization.

Both were restricted from work and required to undergo a course of intranasal mupirocin and to then test negative for MRSA.

In the Los Angeles County hospital, 11 cases of infection were discovered in two clusters. All were male newborns, and 7 of the 11 (64%) were delivered via C-section. All the infants had pustular/vesicular lesions in the groin area occurring a median of 3 days after nursery discharge. The median postdelivery stay was 4 days, as in the Chicago cases.

In contrast to the Chicago outbreak, 8 of these 11 infants were hospitalized. They were treated with parenteral antimicrobials and recovered without incident. The remaining infants were either treated with topical antimicrobials or not treated. Laboratory tests showed that the MRSA strain was the same one as in the Chicago outbreak.

Unlike the Chicago hospital, however, the Los Angeles County hospital chose not to test its health care workers for MRSA, reasoning that no employee had more infant contact than the others.

Staff members were instructed regarding proper hand hygiene, and all patient contacts were subsequently required to wear gloves and gowns. A policy of bathing newborns with antibacterial soap before discharge also was begun, and the frequency and intensity of the environmental cleaning of the nursery was reportedly increased.

The editors noted that these cases were similar to cases in a New York City hospital in 2002, in which a community-acquired strain of MRSA was the source of infection in six newborns.

They also observed that male gender has been found to be a risk factor for staphylococcal infection in newborns and that most of the infants in this report were delivered via C-section, which requires a longer hospital stay—although they cautioned that the role of this factor is unclear.

They speculated that the moist environment and friction in the diaper area, where lesions were common, might be a breeding ground for *S. aureus*.

The CDC recommended that hospitals emphasize transmission-prevention methods and promote frequent dressing changes for infants with skin infections. The agency also advised that when MRSA appears, hospitals should review and reinforce infection-control measures in all newborn nurseries and consider requiring all persons coming into contact with the infants to be checked for skin lesions.

The need for universal use of gowns and gloves, antiseptic bathing of newborns, and surveillance cultures of health care workers and the environment is less clear, the CDC said.

Additional information regarding MRSA infections is available at [http://www.cdc.gov/ncidod/dhqp/ar\\_mrsa.html](http://www.cdc.gov/ncidod/dhqp/ar_mrsa.html). ■

## 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.

**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.

**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 (DTaP) vaccine or a vaccine containing an acellular pertussis component, consider carefully whether to give subsequent doses of BOOSTRIX: temperature of  $\geq 40.5^{\circ}\text{C}$  ( $105^{\circ}\text{F}$ ) within 48 hours not due to another identifiable cause; collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours; persistent, inconsolable crying lasting  $\geq 3$  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](http://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: General:** 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 effect 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 3,608 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 DTaP or a combination of DTaP 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.

In a study conducted in Germany, BOOSTRIX was administered to 319 children 10 to 12 years of age previously vaccinated with 5 doses of acellular pertussis-containing vaccines, 193 of these subjects had previously received 5 doses of INFANRIX. Adverse events were recorded on diary cards during the 15 days following vaccination. Unsolicited adverse events that occurred within 31 days of vaccination (day 0-30) were recorded on the diary card or verbally reported to the investigator. Subjects were monitored for 6 months post-vaccination for physician office visits, emergency room visits, onset of new chronic illness, and serious adverse events. The 6-month follow-up evaluation, conducted via telephone interview, was completed by 90% of subjects.

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 and German-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 20 days following administration of BOOSTRIX. 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  $\leq 4\%$ ). 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) %
<b>Local</b>		
Pain, <sup>†</sup> any	75.3	71.7
Pain, <sup>†</sup> grade 2 or 3	51.2	42.5
Pain, <sup>†</sup> grade 3	4.6	4.0
Redness, any	22.5	19.8
Redness, $>20$ mm	4.1	3.9
Redness, $\geq 50$ mm	1.7	1.6
Swelling, any	21.1	20.1
Swelling, $>20$ mm	5.3	4.9
Swelling, $\geq 50$ mm	2.5	3.2
Arm circumference increase, <sup>‡</sup> $>5$ mm	28.3	29.5
Arm circumference increase, <sup>‡</sup> $>20$ mm	2.0	2.2
Arm circumference increase, <sup>‡</sup> $>40$ mm	0.5	0.3
<b>General</b>		
Fever, <sup>§</sup> $\geq 99.5^{\circ}\text{F}$	13.5	13.1
Fever, <sup>§</sup> $>100.4^{\circ}\text{F}$	5.0	4.7
Fever, <sup>§</sup> $>102.2^{\circ}\text{F}$	1.4	1.0
Headache, any	43.1	41.5
Headache, <sup>¶</sup> 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, <sup>  </sup> any	26.0	25.8
Gastrointestinal symptoms, <sup>  </sup> grade 2 or 3	9.8	9.7
Gastrointestinal symptoms, <sup>  </sup> 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  $\leq 4\%$ ).

§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.

**Solicited Adverse Events in the German Safety Study:** No cases of whole arm swelling were spontaneously reported. Two individuals (2/193) reported large injection site swelling (range 110 to 200 mm diameter), in one case associated with grade 3 pain. Neither individual sought medical attention. These episodes were reported to resolve without sequelae within 5 days. These were the rates of solicited local adverse events and fever within 15 days of vaccination for those subjects who had previously been vaccinated with 5 doses of INFANRIX.

#### Rates of Solicited Adverse Events Reported Within the 15-day\* Post-Vaccination Period Following Administration of BOOSTRIX in Individuals 10 to 12 Years of Age Who Had Previously Received 5 Doses of INFANRIX

Adverse Event	BOOSTRIX (N = 193) % (95% CI)
Pain, any	62.2 (54.9-69.0)
Pain, grade 2 or 3	33.2 (26.6-40.3)
Pain, grade 3	5.7 (2.9-10.0)
Redness, any	47.7 (40.4-55.0)
Redness, $>20$ mm	15.0 (10.3-20.9)
Redness, $\geq 50$ mm	10.9 (6.9-16.2)
Swelling, any	38.9 (31.9-46.1)
Swelling, $>20$ mm	17.6 (12.5-23.7)
Swelling, $\geq 50$ mm	14.0 (9.4-19.7)
Fever, $\geq 99.5^{\circ}\text{F}$	8.8 (5.2-13.7)
Fever, $>100.4^{\circ}\text{F}$	4.1 (1.8-8.0)
Fever, $>102.2^{\circ}\text{F}$	1.0 (0.1-3.7)

N = number of subjects with local/general symptoms sheets completed.  
Grade 2 = Painful when the limb was moved.  
Grade 3 = Spontaneously painful and/or prevented normal activity.  
\*Day of vaccination and the next 14 days.

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.hhs.gov](http://www.vaers.hhs.gov).

**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 DTaP 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 missiles, 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](http://www.BOOSTRIX.com).  
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**References:** 1. Centers for Disease Control and Prevention. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP). Early Release 2006;55(February 23, 2006):1-43. 2. Centers for Disease Control and Prevention. Recommended childhood and adolescent immunization schedule—United States, 2006. *MMWR*. 2006;54(51&52):Q1-Q4.

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