On Vasopressin Cardiac Arrest, Playground Injuries, Suturing Children's Faces, Travelers' Diarrhea, and a Boxed Warning for Fluoroquinolones

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Each month, Dr. Nahum Kovalski reviews a handful of abstracts from, or relevant to, urgent care practices and practitioners. For the full reports, go to the source cited under each title.

Vasopressin Not Helpful for Out-of-Hospital Cardiac Arrest

Key point: For now, epinephrine remains the only evidence-based drug option in CPR.

Citation: Gueugniaud P-Y, David J-S, Chanzy E, et al. Vasopressin and epinephrine vs. epinephrine alone in cardiopulmonary resuscitation. *N Engl J Med*. 2008;359:21-30.

The ideal drug regimen for use in CPR is a subject of controversy. Epinephrine is the recommended vasopressor agent, but results of some studies suggest that combining epinephrine with vasopressin may confer additional benefit.

Investigators analyzed data on 2,894 patients in France who experienced out-of-hospital cardiac arrest and were randomized to receive successive injections of 1 mg of epinephrine and either 40 IU of vasopressin or saline placebo. The primary outcome was survival to hospital admission.

The average patient age was about 62, and about three quarters of the events were witnessed. The mean time from collapse to arrival of emergency personnel was seven minutes, and the mean time from collapse to injection of study drug was 21 minutes. Automated external defibrillation was administered to about 80% of patients.

The primary endpoint did not differ significantly between the combination-therapy group and the epinephrine-only group (20.7% vs. 21.3%, respectively). There were also no significant between-group differences in rates of return of spontaneous circulation (28.6% vs. 29.5%), survival to hospital discharge (1.7% vs. 2.3%), or one-year survival (1.3% vs. 2.1%).

This study tested a new drug strategy for out-of-hospital cardiac arrest, which failed to improve upon epinephrine, the agent currently recommended in guidelines.

[Published in *J Watch Cardiol*, July 2, 2008—Harlan M. Krumholz, MD, SM.] ■

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Children Need to Play... Safely

Key point: Monkey bars cause the most playground injuries.

Citation: Loder RT. The demographics of playground equipment injuries in children. *J Pediatr Surg*. 2008;43:691-699.

Given the risk for obesity, children in the U.S. need to stay active. But they also need to be protected from injury.

The author of this study used the National Electronic Injury Surveillance System (NEISS) database of emergency department visits for 2002–2004 to investigate injuries associated with playground equipment in children younger than 18 years.

The overall incidence of playground equipment injuries peaked in the summer, and the incidence of such injuries at school peaked in the spring and fall.

Based on NEISS data since 1991, the frequency of injuries associated with swings and slides has decreased, but the frequency of injuries caused by monkey bars has not.

It is unlikely active play can be made risk-free, but data such as these can be useful in identifying ways to reduce risk. Par-

ents, school administrators and others who supervise children should be cautioned to not use these data to reduce children's opportunities to play.

[Published in *J Watch Pediatr and Adolesc Med*, July 2, 2008—William P. Kanto, Jr., MD.] ■

Absorbable Sutures for Repair of Pediatric Facial Lacerations

Key point: Cosmetic outcomes with absorbable sutures are similar to those with nonabsorbable sutures.

Citation: Luck RP, Flood R, Eyal D, et al. Cosmetic outcomes of absorbable versus nonabsorbable sutures in pediatric facial lacerations. *Pediatr Emerg Care*. 2008;24(3):137-142.

Absorbable sutures offer several advantages over nonabsorbable sutures—including ease of use, less skin reactivity, and lower cost—but their use in children has not been well studied. In a prospective, randomized trial, researchers compared the two types of sutures for repair of acute pediatric facial lacerations of 1 cm to 5 cm. Patients were excluded if the lacerations had irregular borders, resulted from mammalian bites, were contaminated, occurred more than eight hours before presentation, or could be repaired with a topical adhesive.

Children 1–18 years of age were randomized to wound closure with either 5–0 or 6–0 fast-absorbing surgical gut or nonabsorbable nylon.

At three-month follow-up, wounds were photographed, and three pediatric emergency physicians who were blinded to group assignment assessed cosmetic appearance (the primary outcome) using a 100 mm continuous cosmesis visual analog scale (VAS; with a score of 100 representing the best scar). A between-group difference of ≥15 mm was defined as being clinically important. Wounds were assessed at five to seven days for infection (defined as requirement for systemic antibiotics) and dehiscence (defined as requirement for additional sutures).

Overall, 23 of 49 patients in the absorbable-suture group and 24 of 39 in the nonabsorbable-suture group completed the study.

At three months, mean VAS scores between the absorbable-suture and nonabsorbable-suture groups differed by only 1.4 mm (92.3 mm and 93.7 mm). Correlation among the blinded observers was good (r=0.42). Two patients, both in the absorbable-suture group, had wound dehiscence. No wound infections occurred.

The data indicate that the two suture strategies are equivalent, at least for highly vascular facial wounds. Absorbable sutures do not require subsequent visits for removal, and fears that they might increase wound inflammation seem to be unfounded.

[Published in *J Watch Emerg Med*, April 25, 2008—Jill M. Baren, MD, MBE, FACEP, FAAP.] ■

Efficacy and Safety of a Vaccine Patch Against Travelers' Diarrhea Caused by Enterotoxigenic *Escherichia* coli

Key point: Protective efficacy of the LT patch was 75%.

Citation: Frech SA, DuPont HL, Bourgeois AL, et al. Use of a patch containing heat-labile toxin from *Escherichia coli* against travellers' diarrhoea: A phase II, randomised, double-blind, placebo-controlled field trial. Lancet. 2008;371:2019-2025.

Enterotoxigenic *Escherichia coli* (ETEC), a major public health problem, is the leading cause of diarrhea among children in developing countries and of travelers' diarrhea. ETEC causes diarrhea via heat-labile enterotoxin (LT) and/or heat-stable enterotoxin (ST). LT is found in two-thirds of cases.

Antibody to LT has been shown to provide protection against ETEC, but LT antigen is too toxic to be administered by the oral, nasal, or parenteral route. Frech and colleagues hypothesized that an LT vaccine applied to the skin would be immunogenic and prevent ETEC diarrhea. In early studies, LT delivered via skin patch produced good immune responses.

The authors examined the safety, immunogenicity, and efficacy of LT transcutaneous immunization against travelers' diarrhea in persons traveling from the United States to Mexico or Guatemala.

Healthy adult travelers with access to one of 14 U.S. regional vaccination centers were eligible. Vaccination was performed in the United States, and surveillance was conducted in Mexico and Guatemala. Participants were stratified by gender and destination city.

Each traveler had patches of either LT or placebo applied on alternate upper arms a minimum of three weeks (first dose) and one week (second dose) before departure. On each occasion, the skin was marked and prepared with a mild abrasive, and the patch was left in place for six hours.

Participants reported to the clinic within 24 hours of arrival in Mexico or Guatemala and returned weekly for blood draws, stool examination, and review of a diary card that recorded adverse events. Ciprofloxacin was given to persons with moderate to severe diarrhea. Stools were examined for LT, LT/ST, or ST by DNA hybridization assay or toxin-specific polymerase chain reaction and were also tested for other stool pathogens by standard laboratory procedures.

An intention-to-treat analysis included 201 subjects who received the first dose of vaccine. Per-protocol analysis was performed on the 170 subjects who also received the second dose and reported for all clinical study-site visits.

The mean duration of stay was 12.4 days (11.8 days for the LT patch group vs. 12.8 days for the placebo group). The vaccine was well tolerated; most adverse events were mild. Upon arrival in and exit from Mexico or Guatemala, titers of IgG and IgA antibodies to LT were significantly higher in the LT patch group than in the

placebo group; 15% of the LT patch group (nine travelers) and 22% of the placebo group (24 travelers) developed diarrhea (p=.3117).

The rate of moderate-to-severe diarrhea from any cause was higher in the placebo group (21% vs 5%); the protective efficacy of the LT patch was 75% (p=.0070). The number of cases of severe diarrhea was also significantly higher in the placebo group.

Among travelers in whom a pathogen was identified, 11 of 12 persons given placebo and all three persons given LT vaccine had ETEC identified. Persons infected with ETEC who had received the LT patch had significantly fewer stools per episode and diarrhea of shorter duration than placebo recipients.

This study documents that an LT-containing vaccine patch applied to the skin is safe and feasible for the prevention of ETEC diarrhea. The vaccine patch reduced both the rate of occurrence and the severity of ETEC diarrhea, providing a meaningful benefit to recipients. ■

Fluoroquinolone-Related Tendinitis and Tendon Rupture

Key point: A boxed warning must be added to the prescribing information for systemic fluoroquinolones.

Citation: U.S. Food and Drug Administration. Information for healthcare professionals: Fluoroquinolone antimicrobial drugs [ciprofloxacin (marketed as Cipro and generic ciprofloxacin), ciprofloxacin extended-release (marketed as Cipro XR and Proquin XR), gemifloxacin (marketed as Factive), levofloxacin (marketed as Levaquin), moxifloxacin (marketed as Avelox), norfloxacin (marketed as Noroxin), and ofloxacin (marketed as Floxin and generic ofloxacin]).

On July 8, 2008, the FDA announced that the prescribing information for systemic fluoroquinolones must now include a boxed warning regarding the risk for tendinitis and tendon rupture.

The prescribing information for these drugs has long listed tendon-related problems as potential adverse events, but the incidence of these events has not declined, prompting the FDA to require the stronger warning. The manufacturers must also develop and distribute a medication guide for patients.

The risk for tendinitis and tendon rupture is especially increased in patients over 60 years of age, those who are concomitantly taking steroids, and those who have received kidney, heart, or lung transplants.

Patients should be warned of this risk and should be advised to stop taking the fluoroquinolone at the first sign of tendon pain, swelling, or inflammation, to avoid exercise or use of the affected area, and to seek medical advice about switching to a non-fluoroquinolone antimicrobial.

[Published in *J Watch Infect Dis*, July 16, 2008—Lynn L. Estes, PharmD.] ■