ABSTRACTS IN URGENT CARE

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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.

Is Oral Antibiotic Therapy Enough for Children with Acute Pyelonephritis?

Key point: A randomized trial failed to prove the acceptability of oral antibiotic monotherapy relative to sequential intravenous and oral therapy, but evidence supporting oral treatment alone as an option is accumulating.

Citation: Bocquet N, Sergent AA, Jais JP, et al. Randomized trial of oral versus sequential IV/oral antibiotic for acute pyelonephritis in children. *Pediatrics*. 2012; 129(2):e269-275.

Children with acute pyelonephritis typically receive intravenous (IV) antibiotic therapy as initial standard treatment. At 10 pediatric centers in France, researchers randomized 171 children (age range, 1–36 months) with their first case of acute pyelonephritis to receive oral cefixime for 10 days or IV ceftriaxone for 4 days followed by oral cefixime for 6 days (sequential antibiotics). All participants had an abnormal dimercaptosuccinic acid (DMSA) scintigraphy result within 8 days of diagnosis and an elevated serum procalcitonin concentration.

Among 96 patients in a per-protocol analysis, the incidence of renal scarring, measured with DMSA scintigraphy 6 to 8 months after treatment, was 31% in the oral cefixime-alone group and 27% in the sequential-therapy group — a nonsignificant difference. The sample size was too small to prove the noninferiority of oral treatment alone (an estimated 349 children would have been needed in each group).

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Bronchitis in Children: Does It Really Exist?

Key point: The authors of this retrospective study suggest that some children with "chronic wet cough" have bacterial infection of the lower airway — also known as bacterial bronchitis

Citation: Zgherea D, Pagala S, Mendiratta M, et al. Bronchoscopic findings in children with chronic wet cough. *Pediatrics* . 2012;129(2): e364-369.

Is protracted bacterial bronchitis a real phenomenon in children? To find out, researchers retrospectively studied 197 children (55% age 0–3 years; 9% >7 years) who had been re-

ferred to an academic pediatric pulmonary clinic from 2004 to 2008. All had experienced "wet cough" for more than 4 weeks and had not responded to what the authors describe as "conventional therapy with antibiotics and corticosteroids." Some patients were referred for reasons other than chronic cough, including possible foreign-body aspiration or wheezing that was unresponsive to bronchodilators; patients identified as having underlying conditions were excluded.

All patients underwent flexible bronchoscopy. The character of the bronchial secretions was recorded, and bronchoalveolar lavage fluid was sent for Gram stain, quantitative bacterial culture, and white-blood-cell differential and count. Of the 197 children, 110 (56%) had visibly purulent bronchitis. Ninety-one patients (46%) had positive cultures detected, which included bacteria colonizing the oropharynx. Of the 108 children 3 years, 33 (30%) were found to have laryngomalacia, tracheomalacia, or both.

Published in *J Watch Ped Adol Med.* February 29, 2012 — Louis M. Bell, MD. ■

Guideline Issued for Managing Acute Bacterial Rhinosinusitis

Key point: Remember that MANY cases of recurrent sinusitis (especially when they manifest as headache with few other symptoms) are in fact undiagnosed migraines.

Citation: Chow AW, Benninger MS, Brook I, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012 doi: 10.1093/cid/cir1043

The guideline, published in *Clinical Infectious Diseases*, first points out that a bacterial cause accounts for 2%–10% of acute rhinosinusitis cases. Among the recommendations:

- Bacterial rather than viral rhinosinusitis should be diagnosed when any of the following occurs:
  - persistent symptoms lasting at least 10 days, without improvement;
  - severe symptoms or high fever and purulent nasal discharge or facial pain for 3–4 days at illness onset;
  - worsening symptoms after an initial respiratory infection, lasting 5–6 days, has started to improve.
- Empirical therapy should be started as soon as acute bacterial rhinosinusitis is diagnosed clinically; amoxicillin-clavulanate, instead of amoxicillin alone, is recommended for both children and adults.
- Macrolides and trimethoprim-sulfamethoxazole are not recommended as empirical therapy, because of high rates of antimicrobial resistance.

The guideline includes an algorithm for sinusitis management, with recommendations for treating patients who do not respond to initial empirical therapy. ■

A Noninvasive Test for Severe Vesicoureteral Reflux

Key point: Urinary proteome analysis showed promise in excluding high-grade VUR.

Citation: Drube J, Schiffer E, Lau E, et al. Urinary proteome analysis to exclude severe vesicoureteral reflux. *Pediatrics*. 2012;129(2): e356-363.

To diagnose vesicoureteral reflux (VUR) currently requires a voiding cystourethrogram (VCUG), which exposes a child to radiation and discomfort. At four hospitals in Europe, researchers examined how well capillary-electrophoresis mass spectroscopy of urinary proteins identifies biomarkers of high-grade VUR. VCUG was used as the gold standard. The study was led by the founder and co-owner of the company that developed the urinary proteome analysis system.

Of 73 children with suspected VUR who met inclusion criteria, 18 with severe (grade IV–V) VUR and 19 without VUR (controls) were randomly selected for identification of urinary proteome patterns. Comparative urinary proteome analysis revealed nine polypeptides associated with severe VUR; all nine candidate biomarkers were excreted in lesser amounts among cases than controls.

The researchers then conducted a blinded analysis of this urinary proteome pattern in the remaining 36 children: 17 with severe, VCUG-identified VUR and 19 without VUR. The noninvasive test detected high-grade VUR with a sensitivity of 88% and a specificity of 79%. The odds ratio of reduced excretion of the nine polypeptides for severe VUR was 28 (95% confidence interval, 4.5–176). The result was independent of age, sex, hypertension, and renal impairment. The estimated negative predictive value of the proteome pattern analysis method was 98%.

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The Risks and Benefits of Aspirin in Primary Prevention of CVD

Key point: Risk for nontrivial bleeding roughly equals benefit in preventing nonfatal myocardial infarction.

Citations: Seshasai SR, Wijesuriya S, Sivakumaran R, et al. Effect of aspirin on vascular and nonvascular outcomes: Meta-analysis of randomized controlled trials. *Arch Intern Med*. 2012; 172(3):209-216. Mora S. Aspirin therapy in primary prevention: To use or not to use? *Arch Intern Med*. 2012;172(3):217-218.

Aspirin's benefits in preventing cardiovascular (CV) events in patients with cardiovascular disease (CVD) are clear. The benefit in patients not known to have CVD is more modest and has not been weighed fully against the risk for bleeding. In this meta-analysis, researchers analyzed data from nine randomized, controlled trials of aspirin use in primary prevention;

most of the 102,000 participants (mean age, 57; 47% men) were at elevated risk for CVD.

During mean follow-up of 6 years, nearly 2200 CV events were identified, including 1540 nonfatal myocardial infarctions (MIs) and 592 fatal events. More than 10,000 nontrivial bleeding events (defined in various studies as gastrointestinal bleeding, hemorrhagic stroke, nasal bleeding, and hematuria) were also identified. Aspirin treatment lowered risk for nonfatal CV events by about 20% (number needed to treat, 162), did not lower risk for fatal CV events, and raised risk for nontrivial bleeding events by 31% (number needed to harm, 73).

Published in *J Watch Gen Med.* March 1, 2012 — Thomas L. Schwenk, MD. ■

Extremity Fracture Pain After Emergency Department Reduction and Casting: Predictors of Pain After Discharge

Key point: Pain control is still insufficient.

Citation: Thompson RW, Krauss B, Kim YJ, et al. Extremity fracture pain after emergency department reduction and casting: Predictors of pain after discharge. *Ann Emerg Med*. 2012 Mar 2 [Epub ahead of print]

The aims of this study are to determine the prevalence of pediatric extremity fracture pain after emergency department (ED) discharge, compare pain severity between fractures requiring simple casting versus sedated reduction and casting, and explore predictors of postdischarge pain.

This is a prospective observational study of children aged 4 to younger than 18 years and presenting to the ED with extremity fracture from May 2010 to February 2011. The Parents' Postoperative Pain Measure, which scores pain according to 15 behavior-related questions, was completed 48 to 72 hours after discharge. A score greater than or equal to 6 of 15 indicates clinically meaningful pain. Univariate tests and multivariable regression analyses were used to compare Parents' Postoperative Pain Measure scores between cohorts.

Two hundred fifty-seven patients were enrolled; 202 (79%) had Parents' Postoperative Pain Measure scores for analysis. Pain scores greater than or equal to 6 were reported by 37 of 102 (36%) of the simple casted and 44 of 100 (44%) of the reduced casted children. There was no difference in scores between the simple (median 4.0) and reduced casted (median 5.0) cohorts (difference 16.7%; 95% confidence interval [CI] -3.0% to 40%). In the multivariate analysis, ED narcotic administration was associated with 24% higher Parents' Postoperative Pain Measure scores (95% CI 0.95% to 53.6%). Children receiving ED narcotics had more than 2 times increased odds of pain scores greater than or equal to 6 after discharge (95% CI 1.24 to 5.39).

Children in both simple casted and reduced casted groups had clinically meaningful pain after ED discharge. Identifying these children is important to improving pain management and discharge care.

Low Risk for Febrile Seizure After DTaP-IPV-Hib Vaccination

Key point: In a population-based study from Denmark, risk for epilepsy was not increased, but a small increased risk for febrile seizures was observed on the day of the first and second vaccine doses.

Citation: Sun Y, Christensen J, Hviid A, et al. Risk of febrile seizures and epilepsy after vaccination with diphtheria, tetanus, acellular pertussis, inactivated poliovirus, and *Haemophilus influenzae* type b. *JAMA*. 2012;307(8):823-831.

As some families become concerned about the risks and adverse effects of immunization, population-based studies can provide useful information about vaccine safety. Using data from the Danish Civil Registry, researchers analyzed the risks for febrile seizures and epilepsy among 378,834 children who were immunized, from 2003 through 2008, with the diphtheria–tetanus toxoids–acellular pertussis–inactivated poliovirus–*Haemophilus influenzae* type b (DTaP-IPV-Hib) vaccine.

Within the first 18 months after vaccination, 7811 children (2%) developed febrile seizures; only 250 seizures occurred during the first 7 days (17 cases after dose 1, 32 after dose 2, and 201 after dose 3). The overall risk for febrile seizures within the first 7 days after vaccination was similar between this cohort and a reference cohort of children who were not within a 7-day postvaccination window. However, on the single days when doses 1 and 2 were given, the risk for febrile seizures was significantly higher in the main cohort than in the reference cohort (hazard ratios: 6.02 for dose 1 and 3.94 for dose 2). Having a febrile seizure during the week after vaccination did not confer any excess risk for subsequent epilepsy or for recurrent febrile seizures. Furthermore, vaccination was not associated with an increased risk for epilepsy.

Published in *J Watch Ped Adol Med.* March 14, 2012 — Peggy Sue Weintrub, MD. ■

Apixaban vs. Aspirin for Secondary Stroke Prevention in Atrial Fibrillation

Key point: This new oral anticoagulant drug significantly reduced the rate of thromboembolism without increasing intracranial hemorrhages.

Citation: Lawrence J, Pogue J, Synhorst D, et al. Apixaban versus aspirin in patients with atrial fibrillation and previous stroke or transient ischaemic attack: A predefined subgroup analysis from AVERROES, a randomised trial. *Lancet Neurol* 2012;11(3): 225-231.

Anticoagulation with warfarin decreases the risk for stroke from atrial fibrillation (AF) significantly more than antiplatelet therapy. However, one third of patients with AF and prior stroke or transient ischemic attack (TIA) who are eligible for warfarin instead receive antiplatelet therapy, often because of concerns about bleeding. For these patients, new drugs are clearly needed that are as effective as warfarin but as safe as aspirin.

To address this need, investigators have performed an industry-sponsored, prespecified subgroup analysis of patients with prior stroke or TIA enrolled in the AVERROES trial. AVERROES compared outcomes with 5 mg twice daily of apixaban (a factor Xa inhibitor currently available in Europe) and with 81 to 324 mg of aspirin daily in 5599 patients with AF and at least one stroke risk factor who were considered ineligible for warfarin therapy. Exclusion criteria included high risk for bleeding or having experienced serious bleeding within the previous 6 months. Mean follow-up was 1.1 years. The current subgroup analysis included the 764 participants with a prior stroke or TIA.

In the subgroup, the cumulative annual risk for ischemic stroke was 7.46% with aspirin versus 2.12% with apixaban (hazard ratio, 0.33). The rate of intracranial hemorrhage was 1.56% with aspirin versus 1.17% with apixaban. Major bleeding occurred more often with apixaban (4.10%) than with aspirin (2.89%).

Published in *J Watch Neuro.* March 6, 2012 — Hooman Kamel, MD. ■

Macrolide Resistance of Group A Streptococcus

Key point: Acute rheumatic fever developed in two children treated for streptococcal pharyngitis with azithromycin.

Citation: Logan LK, McAuley JB, Shulman ST. Macrolide treatment failure in streptococcal pharyngitis resulting in acute rheumatic fever. *Pediatrics*. 2012;129(3): e798.

Macrolide resistance in group A *Streptococcus* (GAS) — and the unfortunate consequences of such resistance — are of increasing concern worldwide. Investigators in the U.S. recently presented two case reports from their own practice and reviewed the literature for relevant studies published between 2000 and 2011.

The case reports described two children in whom streptococcal pharyngitis was diagnosed by rapid antigen-detection test; both were treated with azithromycin. Soon thereafter, they presented with migratory arthritis, increased antistreptolysin O titers, leukocytosis, and elevated erythrocyte sedimentation rates. They were determined to have acute rheumatic fever and recovered without sequelae. In one case, a subsequent throat culture revealed an erythromycin-resistant strain of GAS. Macrolide resistance was presumed (but not proven) for the GAS strain causing pharyngitis in the second case.

Macrolide resistance in GAS is generally caused by an active efflux pump or by ribosomal target site modification. Such resistance — first reported in the 1950s — became much more common in the 1970s, following greatly increased macrolide consumption in some countries. The literature review yielded resistance rates ranging from 1% (in Cyprus, 2003–2004) to 98% (among children in China, 2007). In the U.S., single-center studies have shown rates as high as 48% during a single season; multicenter surveillance studies have found rates between 3% and 9% in 2000–2003, rising to between 12% and 15% at the same centers in 2007.

Published in *J Watch Infect Diseases.* March 14, 2012 — Robert S. Baltimore, MD. ■

Incidence of Bacteremia in Infants Aged 1 Week to 3 Months

Key point: Incidence of bacteremia in previously healthy full-term infants was 2.2%, and Escherichia coli was the most common pathogen.

Citation: Greenhow TL, Hung Y-Y, Herz AM. Changing epidemiology of bacteremia in infants aged 1 week to 3 months. *Pediatrics.* 2012 Mar;129:e590.

To evaluate the epidemiology of infant bacteremia, investigators retrospectively analyzed charts of previously healthy full-term infants aged 1 week to 3 months who had undergone blood cultures at a California hospital system from 2005 through 2009. Of 4255 blood cultures, 2.2% were positive for a pathogen and 5.8% were positive for contaminants (coagulase-negative staphylococci, *Micrococcus* species, and diphtheroids). Pathogens included *Escherichia coli* (56%), group B *Streptococcus* (21%), and methicillin-sensitive *Staphylococcus aureus* (8%). Ten bacteremic patients also had meningitis, and 7 were described as "ill appearing." There were no cases of *Listeria monocytogenes* or meningococcemia and only one case of enterococcal bacteremia.

Ninety-eight percent of patients with *E. coli* bacteremia also had *E. coli* bacteriuria. Of the *E. coli* strains, 44% were resistant to ampicillin, 6% to gentamicin, and 2% to cefazolin; none were resistant to ceftriaxone. Overall, 93% of bacteremic patients had documented temperature >38°C at or before presentation; two hypothermic patients died soon after presentation. Mean white blood cell counts did not differ significantly between bacteremic infants and nonbacteremic controls. Multivariate logistic regression analysis did not identify any predictors of bacteremia.

Published in *J Watch Emergency Med.* March 16, 2012 — Katherine Bakes, MD. ■