

Clippings

❑ Reduction in neural-tube defects after folic acid fortification

In 1998, folic acid fortification of a large variety of cereal products became mandatory in Canada, a country where the prevalence of neural-tube defects was historically higher in the eastern provinces than in the western provinces. This study assessed changes in the prevalence of neural-tube defects in Canada before and after food fortification with folic acid was implemented. The study population included live births, stillbirths, and terminations of pregnancies because of fetal anomalies among women residing in seven Canadian provinces from 1993 to 2002. On the basis of published results of testing of red-cell folate levels, the study period was divided into pre-fortification, partial-fortification, and full-fortification periods. The relationship between baseline rates of neural-tube defects in each province and the magnitude of the decrease after fortification was implemented. A total of 2446 subjects with neural-tube defects were recorded among 1.9 million births. The prevalence of neural-tube defects decreased from 1.58 per 1000 births before fortification to 0.86 per 1000 births during the full-fortification period, a 46% reduction (95% confidence interval, 40 to 51). The magnitude of the decrease was proportional to the prefortification baseline rate in each province, and geographical differences almost disappeared after fortification began. The observed reduction in rate was greater for spina bifida (a decrease of 53%) than for anencephaly and encephalocele (decreases of 38% and 31%, respectively). (N Engl J Med.2007; 357:135-142.)

Comments: Food fortification with folic acid was associated with a significant reduction in the rate of neural-tube defects in Canada. The decrease was greatest in areas in which the baseline rate was high.

❑ Recurrent urinary tract infections in children

The evidence regarding risk factors for recurrent urinary tract infection (UTI) and the risks and

benefits of antimicrobial prophylaxis in children is scant. The aim of this study was to identify risk factors for recurrent UTI in a pediatric primary care cohort, to determine the association between antimicrobial prophylaxis and recurrent UTI, and to identify the risk factors for resistance among recurrent UTIs. From a network of 27 primary care pediatric practices in urban, suburban, and semirural areas spanning 3 states, a cohort of children aged 6 years or younger who were diagnosed with first UTI between July 1, 2001, and May 31, 2006, was assembled. Time-to-event analysis was used to determine risk factors for recurrent UTI and the association between antimicrobial prophylaxis and recurrent UTI, and a nested case-control study was performed among children with recurrent UTI to identify risk factors for resistant infections. Among 74 974 children in the network, 611 (0.007 per person-year) had a first UTI and 83 (0.12 per person-year after first UTI) had recurrent UTI. Factors associated with increased risk of recurrent UTI included white race, age 3 to 4 years and grade 4 to 5 vesicoureteral reflux. Sex and grade 1 to 3 vesicoureteral reflux were not associated with risk of recurrence. Antimicrobial prophylaxis was not associated with decreased risk of recurrent UTI. (JAMA 2007; 298:179-186).

Comments: Among the children in this study, antimicrobial prophylaxis was not associated with decreased risk of recurrent UTI, but was associated with increased risk of resistant infections.

❑ Migraine in adolescents.

The influence of socioeconomic status on the prevalence of migraine is unknown in adolescents. This study investigated the prevalence of migraine in a large sample of adolescents by socio-demographic features. A validated headache questionnaire was mailed to 120,000 households representative of the US population. All individuals in the household were interviewed (probands and their parents). Sex-specific prevalence estimates of migraine in adolescents derived by age, race, and urban vs rural residence, household income, region

of the country, and parental status of migraine, using log-linear models were calculated. A total of 32,015 adolescents were identified. Surveys were returned by 18,714 of them (58.4% response rate). The 1-year prevalence of migraine was 6.3% (5.0% in boys and 7.7% in girls). The prevalence was higher in girls than in boys older than 12 and in whites than African Americans. In families with an annual income lower than \$22,500, the adjusted prevalence of migraine in adolescents without a parental history of migraine was 4.4%; in families earning \$90,000 or more, it was 2.9%. In adolescents with a parental history of migraine, the prevalence in the lower vs the higher income group was 8.6% vs 8.4%. (Neurology 2007; 69: 16-25)

Comments: In adolescents with family history of migraine, household income does not have a significant effect, probably because of the higher biologic predisposition. In those without a strong predisposition, household income is associated with higher prevalence. This suggests social causation rather than social selection, highlighting the need for exploration of environmental risk factors related to low income and migraine and the search for specific comorbidities and stressors in this group.

□ Predicting traumatic lumbar puncture

The objective of this study is to determine if visual and tactile inspection of the spine is useful in the prediction of a difficult or traumatic lumbar puncture (LP). This was a prospective, observational, cohort study conducted in the emergency department (ED) on patients who were undergoing an LP. Physicians prospectively completed a structured data form that included information about the patient, number of prior LPs performed, their assessment of the LP difficulty, and the number of needlesticks required. A "difficult" LP and a "traumatic" tap were defined a priori. Of the 148 patients enrolled, LP was difficult in 47 (32%) patients and traumatic in 23 (16%) patients. The percentage of patients that did not have a visible spine was significantly higher in the difficult and traumatic groups ($P < 0.05$). Among patients where the physician was unable to visualize the spine, there were significantly more difficult LPs. (Am J Emerg Med 2007; 25: 608-611)

Comments: It may be possible to predict which patients will have difficult or traumatic LPs before performing the procedure. Simple bedside assessments of spine visibility and palpability may assist in planning the approach to an LP in patients.

□ Is diagnostic tonsillectomy indicated in all children with asymmetrically enlarged tonsils?

The aims of the study were: (i) to determine the necessity for diagnostic tonsillectomy in children with asymmetrically enlarged tonsils; (ii) to determine the accuracy of clinical assessment of tonsillar asymmetry; and (iii) to determine how to manage children with clinical tonsillar asymmetry in a developing-world practice. All children undergoing tonsillectomy or adenotonsillectomy had a clinical assessment of tonsil symmetry done, and all tonsil and adenoid specimens were examined histologically. The maximum diameter and volume of the resected tonsils were measured. A comparison was done of true tonsil asymmetry in patients with asymmetrical tonsils and a subgroup of matched controls with symmetrical tonsils. The 13 patients (7.6%) diagnosed as having clinically asymmetrically enlarged tonsils had no significant pathological diagnosis. In the patients with symmetrical tonsils there were 2 abnormal pathological findings (tuberculosis of the adenoids and T-cell lymphoma of the tonsils and adenoids). (S Afr Med J 2007; 97: 367-370)

Comments: Clinical tonsillar asymmetry is usually apparent rather than real. The incidence of significant pathology in children with asymptomatic, asymmetrical tonsils is low. Diagnostic tonsillectomy is indicated in children with asymmetrically enlarged tonsils associated with constitutional symptoms, cervical lymphadenopathy, rapid tonsil enlargement or significant tonsillar asymmetry.

□ Tacrolimus in the treatment of idiopathic nephrotic syndrome

The immunosuppressant tacrolimus (FK-506) is a calcineurin inhibitor with a widespread use for the prevention of graft rejection in transplantation medicine. Tacrolimus inhibits the activation of an

essential transcription factor for the transcription of cytokine genes in T cells leading to a decreased production of cytokines such as IL-2 and IFN-gamma. As T-cell activation plays a crucial role in the pathogenesis of inflammatory glomerular diseases, there is an increasing number of reports on the use of tacrolimus in nephrotic syndrome. In idiopathic nephrotic syndrome, corticosteroid treatment constitutes the first-line therapy to achieve remission. In the case of steroid resistance or steroid dependence, alternative immunosuppressive strategies are needed. Cyclophosphamide and cyclosporin are well-established drugs in this condition. (Expert Opin Investig Drugs 2007; 16: 1099-1110)

Comments: This article reviews the pharmacodynamics, pharmacokinetics, safety and clinical efficacy of tacrolimus in steroid-resistant and steroid-dependent nephrotic syndrome.

❑ Omeprazole for GER

Gastroesophageal reflux occurs in the majority of infants, with severity ranging from asymptomatic to severe esophagitis and failure to thrive. Omeprazole is recognized as a safe and effective treatment of gastroesophageal reflux in older children, at an initial dosage of 0.7 mg per kg per day. The aim of the present study was to prospectively determine the dosage of omeprazole required to treat symptomatic gastroesophageal reflux in children younger than 2 years. Children under 2 years with clinical suspicion of gastroesophageal reflux underwent 24-hour dual-channel intraesophageal/gastric pH monitoring. A reflux index above 10% in children under 1 year and above 6% in children older than 1 year was deemed significant. Treatment with omeprazole at an initial dosage of 0.7 mg per kg per day (in 2 divided doses) was followed by dual-channel pH study after 14 days. The dosage was increased in increments of 0.7 mg per kg per day, and pH studies were repeated until the gastroesophageal reflux was controlled. The median dosage required was 1.05 mg per kg per day. (J Pediatr Gastroenterol Nutr 2007; 45: 50-55).

Comments: Omeprazole is an effective treatment for gastroesophageal reflux in children younger

than 2 years. The majority responds to a dosage of 0.7 mg per kg per day, but increased dosages up to 2.8 mg per kg per day may be required.

❑ Injectable paromomycin for visceral leishmaniasis in India

Visceral leishmaniasis (kala-azar) affects large, rural, resource-poor populations in South Asia, Africa, and Brazil. Safe, effective, and affordable new therapies are needed. A randomized, controlled, phase 3 open-label study comparing paromomycin, an aminoglycoside, with amphotericin B was conducted. In four treatment centers for visceral leishmaniasis, 667 patients between 5 and 55 years of age who were negative for the human immunodeficiency virus and had parasitologically confirmed visceral leishmaniasis were randomly assigned in a 3:1 ratio to receive paromomycin (502 patients) at a dose of 11 mg per kilogram of body weight intramuscularly daily for 21 days or amphotericin B (165 patients) at a dose of 1 mg per kilogram intravenously every other day for 30 days. Final cure was assessed 6 months after the end of treatment; safety assessments included daily clinical evaluations and weekly laboratory and audiometric evaluations. Paromomycin was shown to be noninferior to amphotericin B. Mortality rates in the two groups were less than 1%. Adverse events, which were more common among patients receiving paromomycin than among those receiving amphotericin B included transient elevation of aspartate aminotransferase levels (>3 times the upper limit of the normal range); transient reversible ototoxicity, and injection-site pain and in patients receiving amphotericin B, as compared with those receiving paromomycin, nephrotoxicity, fevers, rigors, and vomiting. (N Engl J Med 2007; 356: 2571-2581).

Comments: Paromomycin was shown to be noninferior to amphotericin B for the treatment of visceral leishmaniasis in India.

K. Rajeshwari,

Professor Pediatrics,

Maulana Azad Medical College,

New Delhi 110 002.

Email: rajeshwari.dr@gmail.com