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We now have implemented Audioslides (http://www.jpeds.com/content/authorinfo#audio). These brief, webinar-style presentations accompany published articles on jpeds.com and ScienceDirect to put the article in context, in the authors’ own words. Beginning in April 2016, authors of accepted manuscripts automatically receive an e-mailed invitation to create an AudioSlides presentation. Audioslides are not peer-reviewed, but the Editors will review all Audioslides for accuracy; presentations that inflate or “spin” the article’s findings will be removed at the Editors’ discretion.

Audioslides and database linking are optional services, but we encourage authors to take advantage of them; we believe that these features will help authors increase the visibility and comprehension of their important work. Have you tried Audioslides and database linking? If so, we welcome your feedback (journal.pediatrics@cchmc.org).

We are now living in an era of postmillennium development goals and, although a significant number of them have been completed, a significant proportion of targets remain to be accomplished. Malnutrition is still a concern that affects millions worldwide. In this issue of The Journal, Chowdhury et al present a large scale population-based survey in Bangladesh, extracted from the Bangladesh Demographic Health Survey (2011). This could be considered a large and representative sample of a region where prevention of malnutrition is (and it should be kept as) a priority as a public health intervention. This study shows that there are still important factors (some of them modifiable) related to malnutrition in growing economies, such as parental education, socioeconomic and community status, religion, region of residence, and food security. Although these and other factors are well known to many of us, the importance of this report relies on its effect on our collective memory to not lower our guard on the issues that are proven to improve global health outcomes and better opportunities for development. This could be relevant for specialists in child nutrition and public health.

Is there a growing worldwide epidemic of attention-deficit hyperactivity disorder (ADHD)? Prevalence rates of up to 15% have been reported in Western countries (World Psychiatry 2003;2:104-13). This rise could be due to a true increase, more intensive case ascertainment, or overdiagnosis.

Previous research has conflicted on how much the relative age of a child at school entry contributes to diagnosis. In this issue of The Journal, Chen et al examine cohort data obtained from 378,881 children ages 4 to 17 years followed in the Taiwan National Health Insurance Database from 1997 to 2011, and they determine odds of diagnosis of ADHD or its treatment based upon relative age. Comparing children born in August (the Taiwanese cutoff birthdate for school entry is August 31) with those born in September, the investigators found that the children born in August had precise,
statistically significant, and robustly elevated odds ratios for being diagnosed with ADHD and receiving medication. Thus, relative age, which may be a proxy of neurocognitive ability, plays into the diagnosis of ADHD and perhaps its overdiagnosis.

We should note that this study now documents the variable prevalence of ADHD diagnosis and treatment in an Asian country. All clinicians and parents worldwide should pay careful attention to the relative age of a child compared with classmates when a diagnosis of or treatment for ADHD is being considered. Immaturity is not the same as ADHD.

Kids clot, too—just not like adults
— William S. Ferguson, MD

Much of our practice regarding venous thromboembolism (VTE) in children is extrapolated from adult data—less than optimal given the pediatrician’s refrain that “children are not just small adults.” The relative rarity of VTE in children has certainly contributed to this lack of knowledge. In this issue of The Journal, Sabapathy et al report on their analysis of 11 years of data on pediatric VTE extracted from the Quebec health care databases, which provided a large and robust population-based data set. The current report is comparable in both scope and methodology with an earlier report covering all age groups from the same researchers.

As expected, the incidence of VTE among children (0.29 VTE per 10 000 person-years) was much lower than for adults (approximately 12 per 10 000 person-years overall, climbing exponentially with increasing age). The incidence was especially low throughout early childhood (0.03-0.04 per 10 000 person-years for ages 1-10 years). Whereas the major risk factors for thrombosis—cancer, surgery, presence of a central venous catheter—were similar to those found in adults, only one-half of cases had an identifiable risk factor, a rate lower than previously reported for either children or adults. Other differences included a higher incidence among females compared with males (even prior to puberty) and a lower death rate. Although the 6.4% all-cause mortality in this cohort is not trivial, by comparison 20% adults diagnosed with VTE die within 1 year.

Over the past few decades, pediatricians have become much more aware of the risk of VTE, especially among critically-ill, hospitalized patients. Still, the finding that one-half of patients who were diagnosed with VTE had no identifiable risk factor suggests that we may still be missing cases. VTE is not only associated with substantial risks of subsequent morbidity and mortality, but is also amenable to treatment and prevention. This should prompt all of us who care for pediatric patients to keep the possibility of VTE in mind, especially for those whose underlying condition does not fit into the groups classically felt to be at risk.

Perinatally-acquired herpes simplex virus infection and empiric acyclovir therapy
— Sarah S. Long, MD

Administration of acyclovir empirically in very young infants coming to medical attention with nonspecific (usually febrile) symptoms is gaining a foothold in the US, predominantly because increased mortality has been associated with even a 1-day delay in therapy of herpes simplex virus (HSV) infection. Narrowing use of acyclovir to a particularly at-risk group of infants having this uncommon infection would be ideal. In an attempt to add granularity to characteristics of infants infected with HSV, authors from children’s hospitals in St Louis and Salt Lake City compiled cases of 49 infants admitted over 11 years.

Most (88%) infants with HSV came to first medical attention ≤28 days of age. The majority had classic signs of HSV disease but 16% had only nonspecific symptoms. The latter group were either ≤14 days of age or had cerebrospinal fluid (CSF) pleocytosis or both. The few patients coming to attention after 28 days of age had overt symptoms and signs of HSV central nervous system (CNS) or skin–eye–mouth disease.

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All such studies of HSV end up with small case numbers. However, collectively, a view may emerge. The frequency of HSV infection and the likelihood that very young infants come to medical attention with only nonspecific symptoms probably varies depending on incidence of genital HSV infection in the population served and primary use of hospital emergency departments where full investigation of very young infants is almost universal. Nonspecific presentations are almost always early presentations of CNS infections, and most infants have overt manifestations soon after admission, while on treatment. The age of onset for such patients almost always is ≤21 days of age, and in this study infants with nonspecific presentation were ≤14 days of age, or had CSF pleocytosis, or both. Of infants with fever and nonspecific symptoms admitted in Salt Lake City during this study, HSV was confirmed in 0.88% of all infants admitted to the hospital at ≤14 days of age, and in 1.6% of infants ≤14 days of age who also had CSF pleocytosis. In this narrowly defined age group, these rates of HSV infection equal or exceed rates of confirmation of serious bacterial infection (too old for early-onset sepsis, and young for late-onset serious infection), for which possibility empiric antibiotic therapy is administered routinely.

Does this study fall onto the “pro” or “con” side of a debate over empiric use of acyclovir in very young infants? After acknowledging the tyranny of small numbers, the most appropriate conclusion may be that it sheds light on important hypotheses to be tested, ie, the restricted characteristic of patients at risk. The authors justifiably posit that the practice of “creeping empiricism” of administering acyclovir to infants ≥30 days of age with nonspecific symptoms is not warranted. Hear! Hear!

Optimal glucose control is important for the prevention of the microvascular complications in type 1 and type 2 diabetes (T2D). Although hyperglycemia is associated with oxidative stress, studies in adults have demonstrated that increased blood glucose variability can magnify this effect and may be as important or potentially, even more important, than the degree of blood glucose control in increasing the risk of microvascular and macrovascular disease. As the TODAY study demonstrated, youth with T2D have earlier appearance and more rapid progression of complications than do adults with T2D; it is important to determine if adolescents have the same effect of glycemic variability on oxidative stress as do adults.

In this issue of The Journal, Dasari et al evaluated the mean amplitude of glycemic excursion (MAGE) using continuous glucose monitoring in normal weight (n = 12), normoglycemic obese (n = 10), and adolescents with T2D (n = 12). The authors quantified MAGE and counted the number of glucose excursions, calculating the mean and standard deviation for each set of glucose values. All subjects wore a continuous glucose monitor and step activity monitor for 5 days. Markers of oxidative stress were correlated with MAGE, with oxidized low density lipoprotein, an inflammatory marker of atherosclerotic risk, having the highest correlation. Traditional cardiovascular risk factors moderately to strongly associated with MAGE were body mass index, body fat, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, C-reactive protein, and nonesterified fatty acids. The vascular inflammatory biomarkers, E-selectin and intercellular adhesion molecule 1, also correlated with MAGE. This study demonstrates the significance of glycemic variability in inducing oxidative stress in youth with T2D. Although diabetologists typically have patients measure blood glucose values before meals, at bedtime, and occasionally at 2:00 a.m., glycemic variability is not assessed routinely. Pre- and postprandial blood glucose concentrations are usually measured only when adjusting insulin doses in an effort to improve glycemic control. Because this study indicates that glycemic variability is at least as important as blood glucose concentrations as a risk for endothelial dysfunction, clinicians should consider asking patients to monitor both pre- and postprandial blood glucose
levels routinely and to adjust bolus insulin doses to attempt to minimize pre- and postprandial glucose excursions.

**Does diabetes cause premature AGEing?**
— Janet H. Silverstein, MD

Chronic hyperglycemia in diabetes mellitus is associated with nonenzymatic binding of glucose to proteins, causing an unstable Schiff base that undergoes molecular reordering to form stable compounds called Amadori products. The most commonly used Amadori products are glycated hemoglobin and fructosamine. The Amadori products undergo glycoxidation, an irreversible process that generates advanced glycation end-products (AGEs). As this is an irreversible reaction, it is logical to think that the AGEs continuously accumulate, increasing in concentration over time. This is an important issue, as AGEs, just like Amadori products, are elevated in patients with both type 1 and type 2 diabetes and are associated with the development of long-term complications through their interaction with receptors for AGE (RAGE). Yet, there have been no studies looking at serum AGE concentrations at the onset of diabetes.

In this issue of *The Journal*, Jaisson et al measured AGE concentrations (carboxymethyllysine [CML], an “early” AGE rapidly formed by fructosamine oxidation, and pentosidine, a “late” AGE created by cross-linking reactions) in children with diabetes at the time of diagnosis (group 1, n = 36), at 5 years disease duration (group 2, n = 48), and at 10 years duration (group 3, n = 27), and controls without diabetes. The average age was 10 years, with the mean age of those in group 1 being 8.2 years and group 3, 13.7 years, respectively. Not surprisingly, those in group 1 had the highest hemoglobin A1c (HbA1c) (12.4%), whereas groups 2 and 3 had identical HbA1c concentrations of 8.2%. Similar results were found for fructosamine. Measurement of the AGEs revealed the concentrations of AGEs at the time of diabetes diagnosis were double the concentrations seen in the control group (CML 0.306 vs 0.155 mmol/mol, *P* < .001; pentosidine 492 vs 312) and higher than found in groups 2 and 3 (CML 0.306 vs 0.219 and 0.224, respectively; pentosidine 492 vs 365 and 403). The AGE concentrations correlated with HbA1c and glucose concentrations, especially at diagnosis of diabetes, and were not affected by age, sex, or pubertal stage.

The importance of this study lies in the fact that AGEs are present in the blood and likely in the tissues of patients with new-onset diabetes. As AGEs are associated with the vascular complications of diabetes, it is important to attempt to achieve the best glycemic control possible as quickly as possible at the time of diabetes diagnosis.

**Remember toxic exposures to antidementia drugs**
— Paul G. Fisher, MD

Is grandma or grandpa in the house? With our aging population, such will likely be true in the years ahead, more senior citizens will be on medications for dementia. In this issue of *The Journal*, Thornton et al report characteristics of accidental pediatric exposures to antidementia drugs, namely donepezil, rivastigmine, galantamine, and memantine. The first three carry cholinergic activity, and memantine is a N-methyl-D-aspartate antagonist.

The majority of children exposed, usually toddlers, had no symptoms. Among the 20% who did experience problems, gastrointestinal symptoms, such as nausea, vomiting, and diarrhea, were most common, followed closely by central nervous system depression, typically drowsiness. Oral rivastigmine was associated with a higher rate of symptoms, and that finding bears attention as that drug’s usage might increase.

We should pay attention to the findings of this study, as it may portend what we will see more often in the years ahead. The numbers of accidental exposure cases reported to the statewide poison control system increased from 4 in 2001 to 33 in 2011. We need to remember that antidementia drugs can be toxic exposures.