To Tap or Not: Bacterial Meningitis & Complex Febrile Seizures


**PICO**

**Question:** Among young children who present to the emergency department with a complex febrile seizure, what is the rate of acute bacterial meningitis?

**Question type:** Diagnosis

**Study design:** Retrospective cohort study

To determine the rate of acute bacterial meningitis (ABM) among children presenting to the emergency department (ED) with a complex febrile seizure (CFS), investigators from the Children’s Hospital Boston conducted a retrospective cohort study. Medical records were reviewed for children ages 6 to 60 months who were evaluated in the ED after a first CFS from 1995 to 2008. A CFS was defined as a seizure with any of the following features: duration >15 minutes, focal motor activity, recurrence within 24 hours, or multiple consecutive seizures. ABM was defined as growth of a known bacterial pathogen from the cerebrospinal fluid (CSF) or CSF pleocytosis (white blood cell count >7/µL) associated with a growth of a bacterial pathogen from a blood culture. When a blood culture was positive without available CSF studies, the diagnosis of ABM was made in concordance with the treating provider.

The 650,993 ED visits occurring during the study period included 526 cases of healthy children presenting with a first CFS, with a median age of 17 months. Seizures stopped spontaneously in 300 patients (57%). Most children (88%) had an unremarkable physical examination. Approximately 14% of patients had one or more previous febrile seizures. Pretreatment with antibiotics had occurred in 29% of the study group. Of the 186 patients (36%) who did not undergo lumbar puncture, 87% received follow-up at the study facility and none experienced a clinical course consistent with ABM. Among patients with CSF studies, 14 (2.7%) had CSF pleocytosis, two of whom had ABM. Both of these patients had an abnormal physical examination and a CSF culture positive for *Streptococcus pneumoniae*. A third child was diagnosed with ABM despite a negative CSF culture. This child had a blood culture positive for *S. pneumoniae*; there was no available CSF cell count and the patient was treated for ABM. Only one patient with ABM presented after the introduction of the conjugated pneumococcal vaccine.

The authors report a rate of ABM among children presenting to the ED with a CFS of 0.9% (95% CI, 0.2-2.7), based upon those who underwent lumbar puncture. They conclude that few patients with CFS have ABM in the absence of other signs or symptoms and note that patients whose only feature of CFS is two brief nonfocal seizures in 24 hours may have a particularly low risk of ABM.

**Commentary by**

Michelle Stevenson, MD, MS, FAAP, Pediatric Emergency Medicine, University of Louisville, Louisville, KY

Dr. Stevenson has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

There is a strong association between seizure and acute bacterial meningitis.1 However, many children who present with a seizure and ABM also have other clinical features suggestive of serious infection (eg, nuchal rigidity, altered mental status, or petechiae). The decision to perform a lumbar puncture in children who experience a CFS is often challenging, since a large percentage of these patients have a normal physical examination. Although recommendations for the evaluation and management of children presenting with a simple febrile seizure were issued in 1996 by the AAP,2 no such guidelines exist for the management of CFSs.

The strengths of this study include a large number of patients with CFS in the era after introduction of the conjugated *Haemophilus influenzae* type b vaccine and a thorough medical record search to include all patients with CFS (many of whom were not diagnosed with CFS using billing codes). These data support the use of careful judgment, based upon both clinical as well as laboratory parameters, when considering the performance of a lumbar puncture in children with a first CFS.

**Editors’ Note**

An additional factor to weigh in deciding to tap or not is the patient’s immunization status. Two of the patients with ABM presented before routine infant pneumococcal conjugate vaccine was introduced. The authors report that 90% of their patients are now immunized. Notably, the third patient had *S. pneumoniae* type 19A, a type not included in PCV7 but which is in PCV13. Furthermore, querying parents about their child’s immunization status when evaluating a febrile infant reinforces the importance of timely infant immunization.

**References**


**Key words:** fever, bacterial meningitis, complex febrile seizure
Impact of Delayed High School Start Time

To assess the impact of delayed school start time on adolescents, researchers at the Hasbro Children’s Hospital in Providence, RI studied the effects of a 30-minute later start of classes on students in grades 9 through 12 attending a small college-preparatory boarding and day school. Sleep patterns, daytime sleepiness, and mood pre-and post-institution of a change in the start of classes from 8:00 AM to 8:30 AM were compared. Student self-reported mean sleep duration, bedtimes, and morning wake times were assessed with a retrospective survey before and two months after the change in start time. The survey included a Sleepiness Scale, a Sleep-Wake Behavior Problems Scale, and a Depressed Mood Scale, all adapted from the Sleep Habits Survey.

Of 357 eligible adolescents, parental consent for participation was received for 278; 225 students completed the survey before the change (survey 1) and 201 two months later (survey 2). The mean age was 16.4 years (57.3% girls) for survey 1 and 16.6 years (57.2% girls) for survey 2. There were no significant differences in participation rates across grades.

After changing to the later start time, average bedtime was 18 minutes earlier (P<.001), average wake time was 31 minutes later (P<.001), and mean school night sleep duration increased by 45 minutes (P<.001). School night sleep duration did not differ significantly between boarding and day students and no gender effect was identified. After delaying school start time, the percentages of students who reported rarely or never getting enough sleep, never being satisfied with their sleep, and never getting a good night’s sleep decreased significantly. Scores on the Sleepiness Scale were significantly higher in survey 1 than survey 2, indicating less sleepiness (P<.001). Mean scores on the Sleep-Wake Behavior Problems Scale also improved (P<.001). The number of students who required assistance with waking on school mornings decreased (P=.003). The percentage of students rating themselves as at least somewhat unhappy or depressed decreased from 65.8% to 45.1% (OR=0.43; P<.001); scores on the Depressed Mood Scale also improved significantly between survey 1 and survey 2.

The authors conclude that these results support adjusting school schedules, ie, delaying the typical “first bell” of high school, to better match adolescent circadian rhythms.

Commentary by
Mike Dubik, MD, FAAP, Norfolk, VA

Dr Dubik has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

One of the most important and underappreciated pubertal changes is the circadian-based delay in the “natural” fall-asleep time, typically leading to a pattern of progressive sleep deprivation during the week with catch-up sleep on weekends. This article adds to a growing body of literature showing beneficial effects of later high school start times.

Here, a modest (30-minute) delay in the start of high school classes was associated with a significant increase in self-reported sleep duration. Curiously, not only was wake-up time delayed, but teenagers reported going to bed earlier, suggesting their recognition of the benefits of additional sleep. Consistent with another article reviewed in these pages (AAP Grand Rounds, May 2010;23:59), earlier bedtime and increased sleep duration were associated with a decrease in self-reported depressive symptoms.

In the current study, there was no control group and most of the analysis was based on retrospective, subjective self-reported data. Further, the small prep school in this study differs from a typical large public high school and the results are not easily generalized, although they are consistent with a similar study involving Minnesota public high schools. When high school start times are aligned with adolescent circadian rhythms, students benefit. Why aren’t schools scrambling to adopt this seemingly straightforward change for the better? There are many vested interests in the status quo: transportation systems, after-school extracurricular activities, employers, etc. However, if there was ever a place for decisions driven by data and not politics, one would hope it would be where our children go to school.

Editors’ Note

While this study raises the possibility of important benefits by starting school later, readers should keep in mind that since there was no control group, the reported findings may be due to a Hawthorne effect (see AAP Grand Rounds, December 2009;22:72). That is, students’ behavior may change just because they know they are being studied, having nothing to do with the intervention. Stay tuned for future studies on this issue with comparison groups.

References

Key words: high school start time, sleep duration, mood
Prenatal Maternal Zinc Supplements Reduce Infant Diarrhea


Investigators from the US and Peru performed this double-blind randomized controlled trial in a peri-urban slum of Lima, Peru between 1995 and 1997 to assess the effect of zinc supplementation during pregnancy on subsequent infectious diseases through infancy. Researchers enrolled 1,295 women between 10 and 24 weeks gestation who were carrying a low-risk singleton pregnancy. These women were stratified by gestational age (less than or more than 17 weeks) and parity (nulliparous or multiparous) and then randomized to take a daily supplement of 60 mg of iron and 250 μg of folic acid either with or without 15 mg of zinc. The two tablets were otherwise indistinguishable, and were taken from 10 to 24 weeks gestation until one month postpartum. Socioeconomic and household characteristics and maternal anthropometric measurements were recorded. Infant weights were recorded at birth and then monthly for 12 months. Morbidity surveillance was done by field workers through weekly home visits.

Of the 421 infants who completed the 12-month study, 214 received zinc supplementation. There were no differences between the zinc-supplemented and control groups with regard to socioeconomic or household characteristics, gestational age at birth, or birth weight. Adjusting for the age of the infant, breastfeeding, season, and sanitation and hygiene covariates, prenatal zinc supplementation reduced the risk of a diarrheal episodes lasting more than seven days by 34% (OR 0.66; 95% CI, 0.43-0.99; *P*=.04) and decreased the presence of mucus in the stool (OR 0.65; 95% CI, 0.46-0.92; *P*=.01) as compared to controls. The mean observed days with diarrhea among infants prenatally treated with zinc (5.8%) was less than infants in the control group (7.7%; *P*=.01). There was a trend toward fewer diarrheal episodes (≥3 liquid or loose stools in 24-hour period) in the prenatal zinc-supplemented group. No effect was detected for respiratory illness and hygiene covariates, prenatal zinc supplementation reduced the risk of a diarrheal episodes lasting more than seven days by 34% (OR 0.66; 95% CI, 0.43-0.99; *P*=.04) and decreased the presence of mucus in the stool (OR 0.65; 95% CI, 0.46-0.92; *P*=.01) as compared to controls. The mean observed days with diarrhea among infants prenatally treated with zinc (5.8%) was less than infants in the control group (7.7%; *P*=.01). There was a trend toward fewer diarrheal episodes (≥3 liquid or loose stools in 24-hour period) in the prenatal zinc-supplemented group. No effect was detected for respiratory illnesses, fever, scabies, or impetigo.

The authors conclude that prenatal zinc supplementation decreased diarrhea-associated morbidity in offspring during the first 12 months of life.

**Commentary by**

**Michael B. Dinerman, MD, FAAP,** Emergency Medicine, Piedmont Healthcare, Children’s Healthcare of Atlanta, Atlanta, GA

Dr Dinerman has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

In 2009, the World Health Organization recommended that zinc be added to oral rehydration therapy in the treatment of acute diarrhea.1 The authors of this article propose an immunological basis to explain the beneficial effect from prenatal zinc supplementation.

Zinc deficiency in humans decreases the activity of serum thymulin (a thymic hormone), which is required for maturation of T-helper cells and plays an important role in cell-mediated immune function and also functions as an anti-inflammatory and antioxidant agent.2 Infectious diarrheal diseases are the second leading cause of morbidity and mortality worldwide.3 Zinc deficiency places children at increased risk of illness and death from diarrhea.4 Zinc deficiency is prevalent in low-income countries, as this micronutrient is mainly found in expensive red meat. Pooled analysis of studies that have assessed the effect of zinc supplementation report an 18% reduction in mortality in children 12 months to 5 years of age but not a reduction in infant mortality.5 This study from Peru suggests that prenatal zinc supplementation may benefit infants by reducing morbidity from prolonged and inflammatory diarrhea in economically underdeveloped countries.

**Editors’ Note**

Zinc remains a virtually untarnished, essential element whose beneficial effects have been reported in children with ADHD, pneumonia, and diarrhea. (See also AAP Grand Rounds, December 2005;14:644 and June 2008;19:64.) Although red meat and poultry are the major vehicles of zinc in the American diet, fish, beans, seeds, and dairy products are also excellent food sources. We would love to see this Peruvian study taken one step further with an assessment of continued supplementation of women throughout lactation.

**References**


**Key words:** zinc, diarrhea, infancy
Breastfeeding Duration and Exclusivity Decrease Infant Infections


To assess the association between duration of breastfeeding and infant infections, investigators from the Netherlands collected data from a population-based prospective cohort study of infants born in Rotterdam. Mothers of study children completed questionnaires at age 6 and 12 months regarding duration and exclusivity of breastfeeding and whether any infectious diseases occurred. Breastfeeding at different ages was categorized as exclusive or partial based on whether the infant received any formula or food in addition to breast milk prior to that time. Results were adjusted for important confounders such as maternal age, education, ethnicity, smoking, number of siblings, day care attendance, and family history of asthma and allergies. Infections were categorized as upper respiratory tract infection (URTI) for a serious cold, ear, or throat infection; lower respiratory tract infection (LRTI) for pneumonia, bronchitis or bronchiolitis; and gastrointestinal tract infection (GI).

Information on 4,164 infants was available. Compared to children who were never breastfed, in the first six months of life those who were breastfed exclusively until the age of 4 months and partially thereafter had a 35% lower risk of URTI, 50% lower risk of LRTI, and 59% lower risk of GI (all differences statistically significant). These children also had a 54% lower risk of LRTI between ages 7 and 12 months. Infants who were breastfed exclusively for six months also had significantly lower rates of URTI than those who were never breastfed. Overall, the length of exclusive breastfeeding was significantly associated with fewer URTI, LRTI, and GI in the first year of life. Partial breastfeeding, even for six months, did not significantly lower infection rates. Also, four months of exclusive breastfeeding without any later breastfeeding did not reduce rates of these infections.

The authors conclude that exclusive breastfeeding in developed countries should be recommended for at least four months, but preferably six months.

Commentary by
Lawrence M. Noble, MD, FAAP, Elmhurst, NY

Dr. Noble has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Previous studies have documented that breastfeeding results in improved infant and maternal health outcomes in both developed and developing countries. Although the World Health Organization has recommended that all children be exclusively breastfed for six months instead of four months, supporting studies have had methodological concerns such as varying duration and/or exclusivity of breastfeeding. Recent US breastfeeding initiation rates have approached the 2010 Healthy People Goals, but both duration of breastfeeding and exclusive breastfeeding fall short of the 2010 goals. The importance of duration and exclusivity are documented quite dramatically in the current study. Six months of partial breastfeeding or four months of exclusive breastfeeding without breastfeeding afterwards did not lower infection rates. However, significant reductions in rates of infection were obtained with exclusive breastfeeding for four months and partial thereafter. Exclusive breastfeeding for six months tended to be even more protective.

Several limitations of this study must be noted. Only 65% of eligible participants completed the breastfeeding questionnaires. Those who did not complete the questionnaire were more frequently younger, less educated, of non-Dutch origin, and had higher infection rates. These mothers tended to breastfeed less, which probably underestimated the effect of breastfeeding on infections. In addition, partial breastfeeding could be of any amount. Nor was any information gathered on the number of episodes of infections.

Despite these limitations, this is an important study of over 4,000 infants. In this large cohort, only 58 infants (1.4%) were breastfed exclusively for six months. Strategies need to be developed to increase the duration of exclusive breastfeeding. Only by increasing the six-month exclusive breastfeeding rate will such health outcomes be optimized.

Editors’ Note

The savvy reader may recall frequent reviews in these pages of studies that document the advantages of breast milk and breastfeeding to preterm (eg, decreased necrotizing enterocolitis) as well as term infants (eg, decreased procedural pain, decreased wheezing) (see AAP Grand Rounds, July 2010;24:37 and April 2003;9:41-42). Keep in mind that mothers and infants may achieve other substantial benefits by less than six months of breastfeeding.

Reference

Key words: breastfeeding, respiratory tract infection, gastrointestinal infection
INJURY, VIOLENCE AND POISON PREVENTION

Firearm Mortality Rates: Rural Versus Urban US Children


Researchers from the Children’s Hospital of Philadelphia and the University of Pennsylvania compared firearm mortality rates in children living in urban and rural counties. Using US vital statistics data from 1999-2006, they categorized all firearm injury deaths in youth, 0 to 19 years of age, both by intent (homicide, suicide, or unintentional) and according to the type classification of each county along a 10-point scale from most urban to most rural, based on both population and proximity to metropolitan areas. After controlling for several characteristics of individual counties, the odds ratios (OR) and 95% confidence intervals (CI) for different types of deaths in the most urban and most rural counties were calculated. The authors also compared deaths from causes other than firearms in urban and rural counties.

During the eight-year study period, 23,649 firearm-related deaths occurred in US youth, including 15,190 homicides and 7,082 suicides. Firearm homicides were significantly more common in the most urban than most rural counties (OR=3.69; 95% CI, 2.00-6.80). Conversely, increasing rates of both firearm suicide (OR 2.01; 95% CI, 1.43-2.83) and unintentional deaths (OR 2.19; 95% CI, 1.27-3.77) were observed in more rural counties. These variations produced overall firearm mortality rates that were statistically indistinguishable when comparing the most rural with the most urban counties (OR=0.91; 95% CI, 0.63-1.32). Whereas firearm death rates in rural and urban counties were similar, non-firearm injury death rates were much higher in rural than in urban counties.

The authors conclude that programs to reduce firearm-related deaths in children are needed in all locales, but that different approaches are needed in urban and rural areas.

Commentary by Eliot Nelson, MD, FAAP, University Pediatrics, Williston, VT

Dr Nelson has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Since the 1980s, firearm injury has shifted from being an epidemic condition to being endemic in the US. The statistics are staggering — during the years covered by the present study, firearm injury accounted for more than 11% of all deaths in those aged 1 to 19 years.

The present study offers convincing evidence that the overall burden of pediatric firearm death is shared by rural and urban communities, although the leading manner of death differs. The predominance of homicide deaths in urban counties, in contrast to the predominance of suicide deaths in rural ones, likely has fostered the mistaken impression that firearm injuries overall are chiefly an urban problem. This is in part because the total numbers (as opposed to rates) of homicides are higher, and in part because suicides are less likely to be publicized. The relatively higher rates of non-firearm injury deaths in rural counties may further obscure the importance of firearm injuries there.

The strengths of this study lie in its use of nationwide statistics focused on the county level, with clearly defined criteria for designating counties as urban or rural. One might question the authors’ decision to designate the county where the fatal injury occurred as the county of interest; for example, if firearms used for urban homicide are actually acquired in rural counties (which might have more gun shops), part of the prevention effort might need to target the rural counties. On the other hand, the finding that many unintentional deaths occurred away from victims’ county of residence suggests that preventive measures at sites where children visit are critical.

Prevention of firearm deaths in urban areas must involve community-level interventions aimed at root causes of crime (poverty, drug abuse, etc.), as well as at reducing access to illegal guns. Recent research casts doubt on the notion that gun possession in urban settings protects from gun assault. In rural areas, where suicide and unintentional firearm deaths predominate, access to mental health care must be improved, but reducing access to firearms is also critical. Pediatricians should encourage gun owners to consider removing them from their homes, or at least to store them unloaded and locked away, apart from ammunition.

References

Key words: firearm, mortality, rural
Is Continuous Insulin Infusion 1st Line Rx for Diabetes Mellitus?


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vestigators from Reims, France studied the long-term metabolic outcomes of children with type 1 diabetes mellitus diagnosed prior to their 6th birthday with a treatment duration of at least five years. The participants fell into two groups: Group A consisted of 34 children who were initially treated with multiple daily subcutaneous insulin injections (MDI) and Group B consisted of 32 children who were treated by continuous subcutaneous insulin infusion (CSI) from the time of initial diagnosis. Children assigned to Group A received MDI treatment initially because they were diagnosed prior to 1999, when CSII became the first line treatment for all children under 6 years old (n=16), or because the children were started on MDI by other physicians prior to their referral to the Reims Hospital group (n=18). Data collected from participants’ medical records included basal and bolus insulin doses, height, weight, cutaneous reactions, severe hypo- or hyperglycemia, technical problems, illness, hospitalizations, treatment satisfaction, and the desire to continue the treatment. Thirty-one of 34 children in Group A switched to CSII because of elevated hemoglobin (Hb) A1c levels (>8%) at an average age of 7.6 (±3.3) years and after an average of 3.9 (±2.7) years of therapy. CSII dropout rates were similar in each group. Five boys and one girl (9.1%) abandoned CSII, four because of a refusal to wear the apparatus, one because of inability to manage constraints, and one due to infusion set intolerance.

During seven of the eight years of follow-up, HbA1c levels were significantly lower in children treated with CSII than those treated with MDI. During the first year, 37% of children receiving CSII had a mean HbA1c level <6.5% as compared to 11% in the MDI group (P=0.046). Children who switched from MDI to CSII tended to lower HbA1c levels and this became statistically significant in years 4, 5, and 7. Pump treatment was associated with lower rates of severe hypoglycemia. In Group A, the rate of severe hypoglycemia decreased from 22.3 events per 100 patient-years during the MDI period to 12 episodes per 100 patient-years after switching to CSII. The incidence of ketoacidosis was similar in the two groups, and remained comparable before and after pump therapy in Group A.

The authors conclude that among children under 6 years of age with type 1 diabetes, the use of CSII provides better long-term metabolic control and lowers the risk of hypoglycemia, particularly if initiated at the time of initial diagnosis.

Commentary by
Donald Schiff, MD, FAAP, University of Colorado School of Medicine and The Children’s Hospital, Denver, CO

Although pediatric diabetes mellitus centers have been using early forms of CSII cautiously for over a decade, the controversy over when and how to utilize this technological advance in very young children persists.1,2 This study demonstrates that with the exception of a few (9.1%), children and families accept the CSII approach and appreciate the improved control as measured by the HbA1c and the safety of a clearly lower incidence of severe hypoglycemia,3 despite experiencing technical problems and describing the pump as cumbersome and unsightly. In 1993, the Diabetes Control and Complications Trial4 demonstrated that intensive therapy lowered the time-averaged blood glucose levels (measured as HbA1c) and significantly reduced the development of microvascular complications in type 1 diabetes. Hirsch and Brownlee5 recently observed that several unknown factors may account for the preponderance (89%) of risk of complications related to diabetes. These include genetics, environmental toxins, and increased free fatty acid levels due to abnormal insulinization. These factors remain to be elucidated. Until then, keeping the HbA1c level at 6.5% or lower is a goal that we can strive for with the help of CSII.

References

Key words: diabetes, continuous subcutaneous insulin infusion, outcome

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Identification of Autism in Infants and Toddlers


Investigators from La Trobe University in Australia sought to determine if early behavioral markers of social attention and communication can be used to identify children at risk for autism (AD) and autism spectrum disorders (ASD) by 2 years of age. Children seen in community clinic sites in metropolitan Melbourne by maternal child health (MCH) nurses for routine well baby checks, including developmental surveillance, were prospectively enrolled in the study. The MCH nurses were trained to monitor specific behaviors at 8-, 12-, 18-, and 24-month routine visits. Children were considered “at risk” for an AD/ASD if they failed a specific number of key social and behavioral items at each age level — including pointing, eye contact, pretend play, social communication, turning to name, and gestures. Those with “at risk” behaviors were referred for thorough behavioral and developmental assessments every six months until age 24 months. A tentative diagnosis of AS/AD was made at 18 months in children who demonstrated “clear” signs of the disorder. At 24 months the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview-Revised were utilized for AD/ASD diagnosis.1,2

A total of 20,770 children seen at 170 MCH centers were followed. Among 216 children aged 12 to 24 months identified with “at risk” behaviors and referred for further evaluation, 110 were assessed. Of these children, 89 (81%) were classified as having AD/ASD. Among the remaining 106 children who were referred but not followed up, one typically developing child was later excluded, 20 children met criteria for developmental or language delay, and 10 children did not return for assessment at 24 months. Assuming that those children who were referred for a behavioral and developmental assessment but not evaluated would have the same rate of diagnosis as those who were evaluated, the researchers calculated an AD/ASD prevalence at 24 months of age of 1:119 using their screening protocol. They estimated an overall sensitivity of 69.0% to 83.8% and specificity of 99.8% to 99.9% based on varying estimates of prevalence of AS/AD in Australian children.

The authors conclude that developmental surveillance of social attention and communication behaviors during four routine well child consultations between 8 and 24 months of age allows for prospective identification of infants/toddlers with AD/ASD with high ascertainment rates and few false positives.

Commentary by Lisa Nalven, MD, MA, FAAP, Kireker Center for Child Development-Valley Hospital, Ridgewood, NJ

The ability to identify children with AD and ASD has improved greatly over the past few decades and age of identification has decreased significantly. Early identification of developmental risk allows for the initiation of early intervention during a “critical period” in brain development and has the potential to change developmental trajectories and outcomes. The Early Denver Start Program has demonstrated that intensive intervention combining applied behavior analysis and developmental interventions can improve the skills of young children diagnosed with an ASD.

The current study expands on the literature utilizing the Checklist for Autism in Toddlers (CHAT)/Modified-CHAT at one time point (18 months, with 98% specificity and 38% sensitivity) and demonstrates the potential for earlier and more accurate identification.6,7 In addition, the results indicate that developmental screening can be successfully employed in a public health setting. The recommendation for ongoing surveillance of social and communication skills is consistent with recommendations by the AAP.8 The AAP Autism Toolkit includes the Communication and Symbolic Behavior Profile, a screening instrument that can be administered from 6 to 24 months of age, as well as the CHAT/M-CHAT for use at 18 months.8

Although true sensitivity/specificity data cannot be determined in the current study as the entire cohort of children was not referred and followed longitudinally, the prevalence rate of AD/ASD established based on the study population is comparable to US (1:150) and international rates.3 In addition, the vast majority of children who were determined to be “at risk,” but who did not meet criteria for an ASD, were found to have other developmental delays.

Editors’ Note

This study is an impressive and laudable undertaking, but the results need to be taken with at least a grain of salt. How many of the children picked up through the specific screening techniques would have been “missed” with routine care? In other words, what was the value added by administering CHAT at 18 months? Perhaps more worrisome, without some evaluation of children classified as normal, the false negative rate is totally unknown. The investigators’ estimate of sensitivity and specificity of their instrument is so prone to error it seems to us akin to a back-of-the-envelope calculation.

References


Key words: autism, developmental surveillance, social communication
INFECTIONOUS DISEASES

Viral Coinfection and Invasive Pneumococcal Disease


Investigators from Southwestern Medical Center, Texas examined the records of all children treated for invasive pneumococcal disease (IPD) between 2005 and 2008. Children were divided into three groups based upon whether viral studies were performed and if the studies were positive or negative (+, -, not done or ND). Viral studies consisted of culture, direct fluorescent antibody staining, and rapid influenza and respiratory syncytial virus (RSV) tests. All available Streptococcus pneumoniae isolates from normally sterile sites were serotyped.

Records from 129 children with IPD were reviewed; the median age was 25 months (range 2 months to 18 years) and 43% were Hispanic. Fifty-eight children had underlying conditions, the most common being immunosuppression/immunocompromise, prematurity, and neurodevelopmental disorder. There were no differences among the three groups with regard to demographics, underlying conditions, or child care attendance.

S pneumoniae serotype 19A was the most frequent cause of IPD identified (41/126 cases). Viral studies were performed on 82/129 (63%) children and 28/82 (34%) were positive. Most viral isolates were identified in February and November, and coincided with peak numbers of IPD cases admitted. Influenza, rhinovirus, adenovirus, and RSV were the viruses most frequently identified. All IPD patients with influenza virus coinfection presented with pneumonia. Three isolates of adenovirus occurred in children with pneumococcal meningitis. Of six total cases with adenovirus coinfection, five (83%) were admitted to the PICU. No significant differences in clinical or laboratory characteristics among the three groups were identified. Comparing only those cases with viral studies performed, three deaths occurred in the + viral group (3/28, 10.7%) versus none in the - viral group (P = .037); two of the three deaths had adenovirus coinfection. Two additional deaths occurred in the ND group.

The authors conclude that viral coinfections in children with IPD are common and, in general, do not change the clinical or laboratory characteristics or outcome in these patients. Adenovirus coinfection may increase IPD severity.

Commentary by
Dennis L. Murray, MD, FAAP, Pediatric Infectious Diseases, Medical College of Georgia, Augusta, GA

Since the introduction of heptavalent S pneumoniae conjugate vaccine (PCV7), cases of IPD have dramatically decreased in both children and unvaccinated adults. However, increasing rates of IPD caused by non-PCV7-containing serotypes have been seen in many regions of the US. An association between influenza virus and S pneumoniae infection has been known for many years and is the most frequent combination represented in mixed community-acquired pneumonia in adults. Temporal associations of different respiratory viruses and IPD in children have also been previously demonstrated, including RSV, human metapneumovirus (hMPV), and adenovirus. Adenoviruses are known to increase attachment of S pneumoniae to the human respiratory tract. However, no correlation between adenovirus infection and IPD was found in a study of children with culture-confirmed IPD.

Approximately 41% (34/82) of the children in the current investigation who had viral studies performed had an underlying medical condition. Unfortunately for practitioners, no differences in clinical characteristics or laboratory data between viral + and viral - children were identified. Children with positive viral studies were more likely to be admitted to and stay longer in the PICU, but this difference was not statistically significant, possibly due to the small numbers of children evaluated.

Readers should recognize that Techasansiri, et al’s study was retrospective and that “sicker” children may have been more likely to have viral studies obtained. The viral studies performed, especially the direct fluorescent antibody and rapid influenza and RSV tests, are not 100% sensitive or specific. Finally, positive blood cultures in children with bacterial pneumonia are relatively uncommon; thus some cases of S pneumoniae pneumonia could have been missed in this review. The study does add to our understanding of viral bacterial coinfection in both healthy children and those with underlying medical conditions.

References

Key words: coinfection, virus, S pneumoniae

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Extracorporeal Resuscitation in Childhood Cardiac Arrest


Cardiac arrest occurs in 2% to 6% of children in pediatric critical care units, and survival to discharge after resuscitation varies from 25% to 33% following in-hospital cardiac arrest. Investigators used data contributed by 285 hospitals to the American Heart Association's National Registry of CardioPulmonary Resuscitation (NRCPR) from January 2000 through December 2007 to assess patient outcome after extracorporeal cardiopulmonary resuscitation (E-CPR). The NRCPR registry uses a standardized form to report patient characteristics, details of the cardiac arrest event, processes of care, and outcomes. A cardiopulmonary arrest (CPA) was defined as an arrest requiring chest compressions and/or defibrillation. E-CPR was defined as a CPA treated with extracorporeal life support. This study included children under 18 years of age who had an in-hospital cardiac arrest, refractory CPR, and then rescue by E-CPR. The primary outcome was survival to discharge. The secondary outcome was neurologic status based on the Pediatric Cerebral Performance Category (PCPC).1

During the eight-year study period, 6,288 children suffered CPAs and 199 (3.2%) received E-CPR. Those who received E-CPR had a median age <2.5 months and 167 (84%) had underlying primary cardiac disease. Ninety-eight percent of the CPAs were witnessed and 95% (56/59) had favorable neurologic outcomes: 37 with normal function, 15 with mild neurologic disability, and 4 with moderate neurologic disabilities. The median duration of CPR was 46 minutes (range 28-68) in those who survived and 57 minutes (range 38-71; P=.28) in those who did not survive. In a multivariable model, primary cardiac disease was associated with a greater than five-fold increased odds of survival (OR=5.82; 95% CI, 2.08-16.29) compared to non-cardiac disease, while pre-arrest renal insufficiency and metabolic abnormalities were associated with decreased odds of survival (OR=0.16; 95% CI, 0.03-0.84 and OR=0.25; 95% CI, 0.07-0.91, respectively). The authors conclude that the selective use of E-CPR as an adjunct to conventional CPR is associated with an encouraging rate of survival to discharge and a mild degree of post-arrest morbidity.

Commentary by
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E-CPR as rescue therapy for refractory in-hospital pediatric cardiac arrest is recommended for “consideration” by the American Heart Association for unresponsive CPA in children with either a reversible condition or one that can be treated by cardiac transplantation.2 No guidelines regarding the use of E-CPR are yet widely accepted. As data regarding favorable survival associated with E-CPR accumulate, the technique is increasingly being employed as an adjunct to CPR. Survival to hospital discharge after E-CPR ranges from 33% to 44%.3,4 Although E-CPR has not been studied in a randomized fashion, survival compares favorably to that in a large series of pediatric in-hospital CPAs treated with conventional CPR (25%-33%).5

This is the first multicenter study to report disability among E-CPR survivors. The PCPC is a scale that has been validated in children.1 It is similar to the Glasgow Outcome Score utilized in adults. Thiagarajan, et al evaluated the Extracorporeal Life Support Organization (ELSO) registry data and found 38% survival in 682 patients treated with E-CPR.3 Although reports to ELSO do not include assessment of neurological function, the datasheets do include complications such as stroke and seizures (21%-25%).6 Patients treated with E-CPR have risk of brain injury from both the arrest event and from extracorporeal membrane oxygenation (ECMO).

E-CPR is an expensive support technique and appears to primarily benefit young children with cardiac disease. ECMO can support cardiopulmonary function for days to weeks until recovery of the child’s organ function. Patients with multi-organ dysfunction pre-arrest do not appear to benefit from E-CPR, while acute issues such as dysrhythmias are rapidly reversible and associated with survival from E-CPR. However, the high costs and need for expert personnel are barriers limiting widespread use of E-CPR. Future research should focus on developing consensus guidelines for patients likely to benefit from this invasive therapy.

References

Key words: extracorporeal cardiopulmonary resuscitation, cardiac arrest, extracorporeal membrane oxygenation
Allergy and Immunology

Predictors of Childhood Allergic Rhinitis


Investigators from Cincinnati Children’s Hospital and the University of Cincinnati sought to evaluate the combined effects of host factors and outdoor and indoor environmental exposures on the development of childhood allergic rhinitis (AR). Participants included a prospective cohort of children born to atopic parents from the greater Cincinnati area and followed annually until age 3 years. Infants were enrolled in the study if either parent had atopy and at least one positive skin prick test (SPT).

The families returned for a comprehensive study visit at ages 1 and 3 years. The infants underwent a physical examination and SPT for 15 aeroallergens, egg, and milk. Parents completed a medical history and home environmental questionnaire. Child respiratory symptoms were captured using items adapted from the validated International Study of Asthma and Allergies in Childhood questionnaire. Primary outcome was the presence of AR at age 3 years defined by parental report of no upper respiratory infection symptoms and a positive SPT to one or more aeroallergens. Children with AR were compared to children without symptoms and with a negative SPT.

Additional study evaluations included house dust endotoxin (HDE) at 8 months of age, outdoor traffic exposure estimation, elemental carbon counts attributable to traffic, and pollen counts. Additional variables included smoke exposure, breastfeeding duration, household income, dog exposure, and number of children in the home at 1 year of age.

At age 3 years, 606 children completed the evaluations and SPT (21.5% African American, 78.6% non-African American). A total of 116 (19%) children had AR and 245 (40%) were nonatopic and asymptomatic. These 361 children comprised the case and comparison groups. Of the remaining children, 151 were atopic and asymptomatic and 94 were nonatopic but symptomatic.

Univariate analysis of factors associated with AR at age 3 years included birth during the spring or summer months, a positive SPT to milk, egg, or both, and a positive SPT to any tree pollen in infancy. Prolonged breastfeeding duration (at least four months) was the only protective factor in African American subjects (Adjusted OR=0.8; 95% CI, 0.6-0.9). Development of AR was associated with HDE with concentrations between 36.6 and 244.7 EU/mg. No association with AR was found for elemental carbon attributable to traffic, environmental tobacco smoke exposure, cat allergen levels, number of dogs in the home, fungal spore, or ragweed, tree, or grass pollen counts. Multivariate analysis was similar to the univariate analysis except that more than one child in the home during infancy was found to be protective against AR (Adjusted OR=0.4; 95% CI, 0.2-0.8). The authors conclude that multiple risk factors exist for childhood AR, that SPT is valuable in assessing that risk, and that African American infants are protected by prolonged breastfeeding.

Commentary by
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Dr Nimmagadda has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

The increased prevalence of allergic diseases has stimulated research to identify potential disease-modifying measures. Studies have been inconclusive in identifying effective preventative measures such as avoidance of cat and dog allergens, gradual introduction of solid foods, and avoidance of maternal smoking.

The belief that breastfeeding should be recommended for primary prevention of allergic disease is widespread. Exclusive breastfeeding beyond four months of age reduces the development of atopic disease in early life, but the long-term benefits are in question. One study has suggested that breastfeeding increases both asthma and allergy sensitization in adult life, but weighing the study’s findings is difficult because the breastfeeding was not always exclusive. Another breastfeeding study demonstrated a protective effect on infantile wheezing of breastfeeding in early life but increased asthma incidence in older atopic children. There is evidence that food allergies in infancy are a risk factor for the development of both allergic rhinitis and asthma.

Most breastfeeding studies do not take into account additional environmental and host factors in the development of allergic diseases. The current study is the first to suggest that prolonged breastfeeding in African American subjects may have a protective effect on the development of allergic rhinitis. Follow-up studies of this birth cohort to determine what proportion eventually develop asthma or other atopic diseases will of interest.

References

Key words: breastfeeding, allergic rhinitis, environmental exposure

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CME OBJECTIVES

• Understand the risk of bacterial meningitis in children presenting with a first-time complex febrile seizure.
• Understand the impact of delayed high school start time on adolescents’ sleep patterns and mood.
• Contrast firearm-related deaths in youth from urban versus rural counties.

CME QUESTIONS

The following continuing medical education questions cover the content of the October 2010 issue of AAP Grand Rounds. Please keep this issue. Each year’s material is worth up to 18 AMA PRA Category 1 Credit(s)™.

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1. A previously healthy 18-month-old girl is brought by her parents to the emergency department with a one-day history of fever and rhythmic twitching of her left arm that lasted for three minutes, twenty minutes before her arrival at the ED. She has no prior history of seizures and her immunizations are up-to-date. She is now awake and alert, her temperature is 100.8°F, and her exam reveals no abnormalities. Which of the following is the most accurate statement?
   a. *Haemophilus influenzae* type B would be the most likely etiology of meningitis for this girl
   b. Her history is consistent with a simple febrile seizure
   c. Her risk for acute bacterial meningitis is 10%-15%
   d. Her risk for acute bacterial meningitis is 20%-25%
   e. She had a complex febrile seizure

2. A 15-year-old boy is brought in to see you for a routine health care supervision appointment. The parents report that their son can’t seem to settle down at night and stays up later than he did before high school. He is hard to wake up in the morning and, in fact, he has been late for his first class at 7:50 AM three times over the past two months. On the weekends he sleeps until nearly midday. You sense that dad is angry, mom feels guilty, and the young man is frustrated. Which of the following is the most appropriate next step?
   a. Explain that teenagers have a natural tendency to stay up later
   b. The boy should start drinking coffee in the morning
   c. The boy should try OTC sleeping pills
   d. The entire family should set a rigid, unified bedtime and wake-up time
   e. The parents need to force him to go to sleep earlier

3. A 25-year-old woman gives birth to a healthy 39-week gestation girl. During pregnancy the mother received iron, folic acid, and zinc oral supplementation. Which of the following is the most likely outcome for this girl at 12 months of age compared to a similar girl whose mother did not take any zinc supplementation?
   a. Decreased number of days with fever
   b. Decreased number of respiratory illnesses
   c. Increased number of respiratory illnesses
   d. Increased risk of bloody diarrhea
   e. Reduction of diarrheal episodes lasting longer than seven days

4. A healthy 2-month-old girl is brought to the pediatrician’s office by her mother for a well baby exam. The girl’s diet has consisted of only breast milk. The mother is considering stopping breastfeeding and switching the girl to cow’s milk-based formula. Which of the following is the most appropriate advice to give to the mother concerning breastfeeding and lowering the risk for the girl developing pneumonia in the first year of life?
   a. Exclusive breastfeeding until at least 6 months of life
   b. Partially breastfeed and supplement with formula
   c. Partially breastfeed, supplement with formula, and begin cereal
   d. Stop breastfeeding now and switch to formula as the baby has already significantly lowered her risk for pneumonia
   e. Stop breastfeeding, switch to formula, and begin pureed meats and fruits

5. Which of the following statements about pediatric and adolescent firearm-related deaths is the most accurate?
   a. Child and adolescent firearm deaths are rare (<2% of injury-related deaths up to 19 years of age) in US rural counties
   b. In rural counties public health efforts should emphasize improving access to mental health care and reducing access to firearms
   c. Of all firearm deaths, homicides are the primary concern in rural counties
   d. Of all firearm deaths, suicides are the primary concern in urban counties
   e. Since overall firearm injury death rates are similar in urban and rural counties, public health policies regarding firearm injuries should be identical everywhere

6. A 6-year-old boy with a 15-month history of type 1 diabetes mellitus is brought by his parents to his pediatric endocrinologist for routine follow-up. Since diagnosis his insulin treatment has consisted of multiple daily insulin injections. He has had HbA1c levels ranging from 7.3% to 9.6%. He has had four severe hypoglycemic episodes and was hospitalized once for ketoacidosis. The pediatric endocrinologist recommends that he switch to continuous subcutaneous insulin infusion, to which the parents agree. Over the next five years, which of the following is most likely?
   a. A 50% probability that he will switch back to multiple daily insulin injections
   b. Decreased incidence of ketoacidosis
   c. Increased incidence of ketoacidosis
   d. Increased incidence of severe hypoglycemic episodes
   e. Lower HbA1c levels

7. A 12-month-old boy is brought to a physician’s assistant by his parents for a health maintenance visit. The parents are concerned because he does not babble and does not respond when his name is called. On examination he does not point to objects, gesture, or smile. A blood lead level and formal audiologic evaluation are normal. Which of the following is the most appropriate next step in management?
   a. Advise the parents that he has a diagnosis of autism
   b. EEG
   c. Hair analysis for trace elements
   d. MRI of the brain
   e. Referral for thorough developmental assessment

8. A 5-year-old boy with egg allergy and asthma is hospitalized in mid-January because of fevers to 103°F, chills, cough, and nausea for 24 hours. Chest x-ray reveals a bilateral perihilar infiltrate. Several family members have “flu-like” illness. The most likely etiology of this child’s illness is:
   a. adenovirus
   b. influenza virus
   c. *Haemophilus influenzae* type b
   d. MRSA; methicillin-resistant *Staphylococcus aureus*
   e. *Streptococcus pneumoniae*

9. A 5-year-old boy with pneumonia and multi-organ failure, including renal insufficiency and metabolic acidosis, suffers a cardiac arrest in the ICU while receiving mechanical ventilation. CPR after 40 minutes has failed to reestablish a perfusing rhythm. The ICU initiates the ECMO team to start E-CPR. Which of the following factors is most strongly associated with a patient such as this dying prior to discharge?
   a. Age of the patient
   b. Duration of CPR
   c. Gender
   d. Multi-organ failure
   e. Pneumonia

10. A healthy 12-month-old African-American girl is brought by her parents to her pediatrician in May for a health maintenance visit. She has been breastfed and has not received cow’s milk-based formula. Both parents have allergic rhinitis and her father has a history of atopic dermatitis. She has three older siblings. A maternal grandfather lives in the home and smokes cigars. There is a pet cat and two pet dogs in the home. The parents ask about her developing allergic rhinitis. Which of the following factors increases her risk for being diagnosed with allergic rhinitis by three years of age?
    a. Breastfeeding
    b. Number of siblings
    c. Pet cat
    d. Pet dogs
    e. Smoke exposure
    f. Spring birth month
CASE REPORT:
Acute Necrotizing Encephalitis Complicating H1N1 Infection


A case of acute necrotizing encephalopathy (ANE) associated with novel H1N1 influenza A virus infection in a unimmunized 2-year-old girl is reported by investigators from Italy. The child was admitted with a two-day history of recurrent seizures, fever, sore throat, and altered mental status. On physical examination she had nuchal rigidity and severe opisthotonus. The patient's nasal swab specimen was positive for the novel H1N1 influenza A virus. There was no CSF pleocytosis and PCR testing was negative for influenza A, cytomegalovirus, Epstein-Barr virus, varicella zoster, and enterovirus. An EEG showed generalized medium-high voltage theta-delta waves. MRI showed lesions in the midbrain, brainstem meninges, and cervical cord, and swelling of subcortical white matter of thalami and pons tegmentum.

The diagnosis of H1N1/ANE was based upon the results of clinical, imaging, EEG, and metabolic studies. The child received antivirals, and, after exclusion of herpes virus infection, methylprednisolone was added and definite clinical improvement was noted. A repeat MRI with contrast eight days after the onset of symptoms showed ring-enhancement with central necrosis of lesions and extension of spinal cord involvement to thoracic and lumbar regions. By 20 days after the onset of the illness, there was substantial improvement in the child's mental status. However, she had divergent strabismus of the left eye, visual field abnormalities, and an unsteady gait.

The authors conclude that, although ANE is an uncommon complication of H1N1 infection in children, clinicians should consider this diagnosis in patients with clinical influenza and altered mental status.

Commentary by
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Dr Millichap has disclosed no financial relationship relevant to this commentary. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/service.

ANE is a potentially fatal subtype of influenza-associated encephalopathy, characterized by altered mental status and behavior, with or without seizures, and rapid progression to coma within 24 to 72 hours from onset of fever and respiratory symptoms. In contrast to the findings in acute encephalitis, there is no CSF pleocytosis in ANE. MRI reveals multiple, symmetrically distributed lesions involving thalami, brainstem tegmentum, and cerebral white matter.

The majority of children with pandemic H1N1 influenza A virus infection have an uncomplicated illness, but some have symptoms that require hospitalization. Of 75 children hospitalized with H1N1 in Milwaukee, WI between April and August 2009, neurological disorders included seizures in 5 (6.6%), febrile seizure in 1 (1.3%), cognitive dysfunction in 6 (8%), and a neuromuscular disorder in 7 (9.3%). None of these patients had encephalopathy.1 The first report of H1N1 influenza A virus encephalopathy in the US was in May 2009. Four pediatric cases were reported.2 All four had seizures and altered mental status and all recovered fully without neurological sequelae. Altered mental status and behavior abnormalities were reported with the 2004 through 2007 influenza seasons in Japan, leading to a Japanese guideline to prescribe oseltamivir (Tamiflu) at onset of infection as prophylactic therapy for encephalopathy. The suggestion that oseltamivir might have triggered abnormal behavior was ruled out by the results of a recent study, but the value of antiviral therapy in prevention of encephalopathy was undetermined.3

In addition to the current case report, sporadic cases of ANE in children have previously been reported. Among three reports of neurological complications of novel H1N1 influenza A virus infection, two cases of fatal ANE were included: one in a 12-year-old child, and another in a 7-year-old girl who developed increased intracranial pressure, herniation, and brain death within four days of onset of fever and respiratory symptoms.4,5 Another case of H1N1-associated ANE in a 3-year-old girl was complicated by tonsillar herniation and hydrocephalus. Consciousness improved after shunting and treatment with acyclovir and oseltamivir, but voluntary movements and speech were impaired. A MRI at 40 days showed residual evidence of cavitation in cerebellar hemispheres, thalami, corpus callosum, and frontal white matter.6 None of these patients had received the H1N1 vaccine.

Potentially fatal encephalopathy is a rare complication of H1N1 influenza A virus infection that presents abruptly within hours of onset of fever and respiratory symptoms. Although the pathogenesis of ANE still needs to be defined, any child admitted to the emergency department with influenza viral symptoms should be observed for altered mental status that may herald the onset of encephalopathy. Pediatricians and other physicians caring for children must recognize that H1N1 influenza A may cause ANE and may involve the meninges and spinal cord.

References