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Mission: To provide pediatricians with timely synopses and critiques of important new studies relevant to pediatric practice, reviewing methodology, significance, and practical impact, as part of ongoing CME activity.

UROLOGY

Better Diagnosis of Testicular Torsion

Source: *Barboso JA, Tiseo BC, Barayan GA, et al. Development and initial validation of a scoring system to diagnose testicular torsion in children. J Urol. 2013;189(5):1859-1864; doi:10.1016/j.juro.2012.10.056*

PICO

Question: Among boys with acute scrotal pain, is a scoring system to diagnose testicular torsion accurate?

Question type: Diagnosis

Study design: Prospective cohort

Investigators at Boston Children's Hospital and University of Sao Paulo sought to develop and validate a scoring system to diagnose testicular torsion (TT) based on presenting symptoms. The investigators first conducted a literature review to identify clinical variables associated with TT. Subsequently, they prospectively evaluated these variables in patients presenting to Boston Children's Hospital with acute scrotal pain between 2009 and 2012. Scrotal Doppler ultrasound, urinalysis, urine culture, and blood count were obtained in all patients. Using prediction models of the clinical variables that were independently associated with TT, the investigators created a scoring system that stratified patients into low, medium, and high risk categories. Lastly, this scoring system was retrospectively applied to patients presenting to Boston Children's with acute scrotum from 2007 to 2008 in order to validate its ability to predict TT.

In the prospective evaluation phase, 338 patients with acute scrotum were enrolled, of whom 51 were diagnosed with TT. The mean patient age was 11.6 years and all TT patients underwent surgery, with 36 testes being salvaged and 15 requiring orchiectomy. Clinical variables found to be independently associated with TT were nausea/vomiting, testicular swelling, high riding testis, transverse lie, hard testicle, thick spermatic cord, absent cremasteric reflex, and fixed scrotal skin to testis. The prediction model of choice featured testicular swelling (2 points), hard testis on palpation (2 points), nausea or emesis (1 point), high riding testis (1 point), and absent cremasteric reflex (1 point). Among the study population, use of a score distribution of ≤2 for low risk of TT (no need for ultrasound), a score of 3 or 4 for moderate risk (ultrasound indicated), and a score of ≥5 for high risk (ultrasound obviated by need for surgical exploration) placed no patients with torsions in the low risk category (negative predictive value [NPV] was 100%) and only patients with torsions in the high risk category (positive predictive value [PPV] was 100%). There were 65 patients (19.2%) who fell into the moderate risk category, 12 of whom had TT. In the retrospective validation phase, application of the scoring system also yielded a 100% PPV of TT for patients who scored as high risk (sensitivity 54%, specificity 100%) and 100% NPV for those who scored low risk (sensitivity 100%, specificity 97%).

The authors conclude that the proposed scoring system can reliably diagnose or exclude TT without a confirmatory ultrasound.

Commentary by

Aseem R. Shukla, MD, FAAP, Pediatric Urology, Children's Hospital of Philadelphia, Philadelphia, PA

Dr Shukla 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.

TT, usually due to a spontaneous rotation of the spermatic cord, causes acute ischemia to the testicle and is a true surgical emergency. While presenting symptoms such as acute pain with nausea, scrotal swelling, erythema, and high riding testis are associated with TT, scrotal ultrasound is nearly always utilized to confirm the need for surgical intervention and rule out more common causes of scrotal pain such as torsion of the appendix testis or epididymitis.[1] This study found that 80% of patients either scored ≤2 (suggesting no ultrasound is needed because the NPV for TT was 100%) or ≥5 (PPV for TT was 100%, obviating the need for an ultrasound) on a TT scoring tool. This tool therefore suggests that the number of ultrasounds for acute scrotum could be reduced by as much as 80%.

Doppler ultrasound of the scrotum may definitively diagnose TT, but hospital processes inhibit immediate access to this diagnostic modality. Even in many tertiary pediatric centers, ultrasound technicians may not be on-site during the night, prolonging the time to examination. And emergency room scrotal pain algorithms that demand absolute reliance on ultrasound often unnecessarily delay immediate surgical referral.

The scoring system introduced in the present study should discourage delays inherent in ordering an ultrasound when the symptom score is ≥5. Similarly, a score of 2 or less reliably predicts the absence of TT, but the desire to exclude other scrotal pathology, such as testicular mass or complex hydrocele, may still warrant imaging. The potential impact of medical cost savings and reduced testicular ischemia time by obviating ultrasound is significant, and mandates multicenter validation of this innovative approach to TT.

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Key words: testicular torsion, scrotal pain, scrotal ultrasound

Visit www.GrandRoundsBlog.org to read a post about this article appearing this month.

INSIDE

HPV Prevalence in the Postvaccine Era

Source: *Markowitz LE, Hariri S, Dunne EF, et al. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. J Infect Dis. 2013;208(3):385-393; doi:10.1093/infdis/jit192*

PICO

Question: Among females aged 14 to 59 years, what is the prevalence of human papillomavirus (HPV) infection in the post-HPV vaccine era compared to the prevaccine era?

Question type: Descriptive

Study design: Cross-sectional survey

Investigators from the Centers for Disease Control and Prevention (CDC) determined the prevalence of HPV infection among females aged 14 to 59 years during the pre-HPV vaccine era (2003-2006) and postvaccine era (2007-2010). These eras were delineated by the June 2006 recommendation for HPV vaccination, which was published in early 2007.[1] Data were collected as part of the National Health and Nutrition Examination Survey (NHANES), an ongoing national survey conducted by the CDC that includes a household interview and a physical examination. Demographic data, sexual history, and a self-collected cervicovaginal swab were obtained from all participants, and HPV vaccination history was obtained via self-report. Cervicovaginal swabs were analyzed for 37 HPV types, classified as vaccine types, high-risk (HR) vaccine types, and HR nonvaccine types (12 clinically relevant types). Investigators used logistic regression to determine prevalence ratios (PR) for the total participant population as well as for 6 age groups between 14 and 59 years. Adjusted prevalence ratios (aPR) among a subgroup of sexually active females aged 14 to 19 years were also calculated. Vaccine effectiveness among 14- to 19-year-old females who reported sexual activity was estimated.

There were 4,150 prevaccine era and 4,253 postvaccine era participants included in the analysis. In the postvaccine cohort, 34% reported receipt of ≥1 vaccine doses and 63% reported receipt of all 3 doses. There was no significant difference in HPV prevalence in the postvaccine era compared to the prevaccine era in all age groups except among those aged 14 to 19 years. In the 14 to 19 age group, the prevalence of any HPV type (PR 0.79; 95% CI, 0.66-0.95), vaccine types (PR 0.44; 95% CI, 0.31-0.62), and HR vaccine types (PR 0.50; 95% CI, 0.34-0.74) were all significantly lower in the postvaccine era. There were no differences in sexual activity, number of lifetime sex partners, or race/ethnicity between 14- to 19-year-old participants in the prevaccine and postvaccine cohorts.

Among the subset of sexually active 14- to 19-year-old participants, the prevalence of any HPV type (aPR 0.82; 95% CI, 0.69-0.98) and vaccine types (aPR 0.47; 95% CI, 0.33-0.67) was lower in the postvaccine cohort compared to the prevaccine cohort. Among those in this subset who received at least 1 vaccine dose, the adjusted prevalence of vaccine types was even lower (aPR 0.18; 95% CI, 0.07-0.47), resulting in an estimated vaccine effectiveness of 82%.

The authors conclude that after HPV vaccine recommendations, vaccine HPV types have decreased 56% among 14- to 19-year-old females despite low HPV vaccine uptake.

Commentary by

Robert W. Tolan, Jr, MD, FAAP,* The Children's Hospital at Saint Peter's University Hospital, New Brunswick, NJ and Drexel University College of Medicine, Philadelphia, PA

Dr Tolan 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.

This study is one of the first published to measure the impact of HPV vaccination on HPV prevalence. While the results suggest a significant impact on HPV prevalence despite relatively poor vaccine uptake, several potential limitations are notable. First, the investigators relied on self-report of vaccine receipt (rather than verification by review of provider records), likely resulting in misclassification of vaccine status. Second, although NHANES data are designed to be broadly representative, vaccine uptake from state to state varies widely (29%-73%),[2] compromising the validity of the sampling in this study. Third, adolescents were no longer oversampled in NHANES beginning in 2007, resulting in a lower number of postvaccine-era adolescent participants and reducing the strength of the study's results.

Hepatitis B virus and HPV together cause most of the infection-associated cancers worldwide.[3,4] Infections due to both viruses are now vaccine-preventable. The potential impact of the use of these vaccines worldwide is enormous. In terms of dollars alone, a 56% decrease in prevalence of HPV infection would save the United States more than $4,000,000,000.[5] These health and economic burdens should serve as cogent reminders to strongly recommend HPV vaccination to our patients.

Editors' Note

While we share, as always, Dr. Tolan's optimism, it is important to remember that receipt of HPV vaccine does not preclude the necessity of regular PAP screening. HPV vaccines do not prevent the progression of already established HPV infections, nor do they protect against all oncogenic HPV serotypes.

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Key words: human papillomavirus, HPV vaccine, vaccine effectiveness

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Declining Ingestions of OTC Cough and Cold Medications

Source: *Mazer-Amirshahi M, Reid N, van den Anker J, et al. Effect of cough and cold medication restriction and label changes on pediatric ingestions reported to United States Poison Centers [published online ahead of print June 12, 2013]. J Pediatr; doi:10.1016/j.jpeds.2013.04.054*

PICO

Question: Among children <6 years of age, have national initiatives to restrict the use of over-the-counter cough and cold medications reduced unintentional ingestions, therapeutic errors, and adverse medical outcomes?

Question type: Occurrence

Study design: Retrospective cohort

Investigators from multiple institutions in Washington, DC conducted a retrospective analysis to determine if changes in the labeling and age recommendations for over-the-counter (OTC) cough and cold medications were associated with a reduction in the occurrence of "unintentional ingestions," "therapeutic errors," and serious medical outcomes. The investigators utilized data from the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS) and poisonings reported to all US Poison Centers. They analyzed data on pediatric ingestions of OTC cough and cold medications coded as unintentional ingestions and therapeutic errors. Children were categorized into 3 age groups: <2 years, 2 to 5 years, and 6 to 12 years. For each age group, the frequency and severity of unintentional ingestions and therapeutic errors were compared between 2 time periods: 2005 to 2006 (pre-labeling and recommendation changes) and 2009 to 2010 (post-labeling and recommendation changes). Outcome severity was dichotomized as follows: (a) no effect or minor outcome (mild symptoms which rapidly resolve), or (b) moderate outcome (more pronounced or systemic symptoms), major outcome (life-threatening or resulted in permanent sequelae), or death.

In 2009 to 2010, the number of unintentional ingestions of OTC cough and cold medications was 9,170 for children <2 years of age, 42,503 for children 2 to 5 years of age, and 2,495 for children 6 to 12 years of age. Compared to 2005 to 2006, this represented declines of 40%, 33%, and 20%, respectively, in children aged <2 years, 2 to 5 years, and 6 to 12 years ($P < .0001$ for each comparison). Between these time periods, the frequency of therapeutic errors of OTC cough and cold medications also declined significantly by 75%, 46%, and 9% for children aged <2 years, 2 to 5 years, and 6 to 12 years, respectively. Moderate, severe, or fatal outcome after unintentional ingestions decreased 32% for children <2 years of age ($P < .001$) and 21% for children 2 to 5 years of age ($P < .001$). Moderate, severe, or fatal outcome after therapeutic errors did not change significantly between periods for any age group.

The authors conclude that restrictions on the use of OTC cough and cold medications has led to a reduction in unintentional ingestions, therapeutic errors, and adverse medical outcomes in children <6 years of age.

Commentary by

Adam Frymoyer, MD, FAAP, General Pediatrics & Neonatal and Developmental Medicine, Stanford University School of Medicine, Palo Alto, CA

Dr Frymoyer 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.

Prior to 2007 as many as 1 in 10 children in the United States received OTC cough and cold medications each week. However, OTC cough and cold medications have not been shown to be effective in children,[1] and in young children the potential for harm is clear.[2] This discordance resulted in several changes to the labeling and new recommendations for OTC cough and cold medications in children. The key changes occurred between the 2 time periods examined in the current study and included a voluntary withdrawal by manufacturers of products directed at children <2 years of age (2007), guidelines by the FDA recommending against their use in children <2 years of age (2008), and a subsequent voluntary label change by manufacturers noting "do not use" in children <4 years of age (2008). In addition, the American Academy of Pediatrics supported the position that OTC cough and cold medications are not effective for children <6 years of age.[3]

A limitation to the current study is that it does not address trends in the overall use of OTC cough and cold medications in children, but instead only self-reported poisonings. A recent survey of parents found that two thirds were unaware of the FDA guidelines on OTC cough and cold medications in children <2 years of age.[4] What are parents using as a guide for dosing since no information for children <4 years of age is available on the label? Additionally, direct causation of the decline in poisonings by OTC cough and cold medications cannot be established. Nonetheless, examination of medication misuse is informative. The temporal pattern of the large reduction of poisonings from OTC cough and cold medications in a national reporting system is highly suggestive of the impact that concerted efforts by the FDA, industry, and professional organizations had on improving the safety of medication use in children. Additionally, this study refutes concerns that OTC cough and cold medication poisonings would increase as parents turn to "off-label" use of formulations designed for older children and adults.

Continued guidance and education by pediatricians on the appropriate use (or nonuse) of OTC cough and cold medications in children, therefore, continues to be most important. Recent clinical studies supporting the use of honey for cough in children >1 year of age provide pediatricians a viable therapeutic alternative (see *AAP Grand Rounds*, March 2008;19[3]:28[5] and *AAP Grand Rounds*, February 2013;29[2]:14[6]).

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Key words: poisonings, cough medications, over-the-counter

Lack of Association of Vaccinations With Guillain-Barré Syndrome

***Source**: Baxter R, Bakshi N, Fireman B, et al. Lack of association of Guillain-Barré syndrome with vaccinations. Clin Infect Dis. 2013;57(2):197-204; doi:10.1093/cid/cit222*

PICO

Question: Among individuals with Guillain-Barré syndrome, is there an association with vaccination in the preceding 6 or 10 weeks?

Question type: Intervention

Study design: Case-centered

Investigators from the Kaiser Permanente Medical Group and Vaccine Study Center and the Centers for Disease Control and Prevention (CDC) retrospectively evaluated a cohort of individuals with documented Guillain-Barré syndrome (GBS) to see if there was an association with vaccination in the 6 or 10 weeks prior to onset. Cases were classified based on a review of medical records by a neurologist according to the Brighton Collaboration case definition criteria.[1] The study population was comprised of the >3 million individuals in Northern California insured by Kaiser Permanente. Cases included all individuals hospitalized with first occurrence of verified GBS between 1995 and 2006. Only those who received any vaccine dose within a year of onset of GBS (9 months for influenza vaccine to avoid confounding from the previous year's vaccine) were included. Odds ratios were calculated by comparing the observed odds that vaccination of cases occurred within the risk interval prior to GBS onset compared to the expected odds derived from the proportion of the vaccinated health plan population, matched for age and sex, who were vaccinated with that same vaccine within the same risk interval.

Electronic medical record review revealed 415 confirmed cases of GBS during the study follow-up period of over 32 million person-years, yielding an incidence of 1.27 cases/100,000 person-years. Two thirds of cases had a documented respiratory or gastrointestinal illness in the 90 days preceding onset of GBS. Cases peaked in March and were more common in winter compared to nonwinter months ($P = .003$). Among the 415 cases, 25 (6%) had received any vaccine in the 6 weeks prior to onset. The odds ratio for receipt of influenza vaccine (TIV) within 6 weeks of onset of GBS compared to the prior 9 months was 1.1 (95% CI, 0.4-3.1). The odds ratios of receipt of tetanus-diphtheria-containing vaccine, 23-valent pneumococcal vaccine, or all vaccines combined in the 6 weeks prior to onset of GBS compared to the prior 12 months were 1.4 (95% CI, 0.3-4.5), 0.7 (95% CI, 0.1-2.9), and 1.3 (95% CI, 0.8-2.3), respectively. Using the 10-week risk interval, 37 (9%) of the individuals with GBS had been vaccinated. However, only injectable typhoid vaccine had an elevated odds ratio (10.75; 95% CI, 1.14-285.04) for GBS. For childhood vaccines, there were no cases of GBS during the risk intervals, despite administration of >8 million doses. Of the 18 persons with onset of GBS within 6 weeks of receipt of TIV, 13 (72%) had a documented antecedent respiratory or gastrointestinal infection.

The authors conclude that there is no evidence for an association of GBS with antecedent vaccination, including influenza vaccination. They point out that a very small increased risk of GBS cannot be excluded, however, because of the rarity of the outcome (despite the large numbers included in the study).

Commentary by

Robert W. Tolan, Jr, MD, FAAP,* The Children's Hospital at Saint Peter's University Hospital, New Brunswick, NJ, and Drexel University College of Medicine, Philadelphia, PA

Dr Tolan 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 use of a case-centered approach and a large cohort of individuals renders this study a valuable addition to the evidence that vaccines are rarely, if at all, associated with GBS (since the 1976 A/New Jersey swine influenza vaccine was removed from the market).[2] As pointed out in the editorial commentary that accompanies this article,[3] the power of the study was insufficient to completely exclude any association between vaccines and GBS. Further, the reviewing neurologist was not blind to the diagnosis and possible vaccine triggers documented in the charts, although the criteria used to assign a GBS diagnosis were strict. Most important, however, is the potential that vaccine uptake was underestimated by relying solely on the electronic medical record. In fact, this population was 1 of 4 cohorts analyzed to ascertain the sensitivity of the electronic medical record for TIV receipt.[4] Although blinded to particular site, only 51% to 89% of TIV doses actually received were captured in the electronic record. Thus, an important number of TIV doses (11%-49%) were not identified in this study.

This important study addresses both influenza and other vaccines, and provides reassurance that childhood vaccines are not associated with GBS. Even if there is a risk on the order of 1 or 2 cases of GBS per million doses of TIV, this risk pales in comparison to the lives saved by influenza vaccination.

Editors' Note

GBS, an acute inflammatory polyneuropathy, has been associated with one universally administered vaccine, the 1976 Swine influenza vaccine – and, despite continuing concerns as underscored by this report, none since. Pediatricians might well be reminded that the most frequent antecedents of GBS are infectious. *Campylobacter jejuni*, the most commonly associated agent, is a preventable foodborne and zoonotic pathogen.

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Key words: Guillain-Barré syndrome, vaccination, influenza

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Effect of ADHD Treatment on Injury Rates

Source: *Raman SR, Marshall SW, Haynes K, et al. Stimulant treatment and injury among children with attention deficit hyperactivity disorder (ADHD): an application of the self-controlled case series study design. Inj Prev. 2013;19(3):164-170; doi:10.1136/injuryprev-2012-040483*

PICO

Question: Among children diagnosed with ADHD, does treatment with stimulant medication decrease the short-term risk of injury?

Question type: Treatment

Study design: Self-controlled case series

To understand whether injury risk is reduced during treatment of attention-deficit/hyperactivity disorder (ADHD), researchers from the University of North Carolina and the University of Pennsylvania retrospectively assessed data from general practices (GP) in the United Kingdom. Information was abstracted on children under 19 years of age with ADHD who had ever been treated with stimulant medication, applying a self-controlled design in which each child served as his/her own control. Every medically-attended injury that occurred in a study child was classified as having occurred either during a treated or an untreated period. A "treated period" was defined as starting on the day a stimulant was prescribed and extending through the end of the period for which medication was supplied, plus a 30-day grace period. The grace period was used to try to minimize misclassification of a period as untreated when a child was actually still using medication. Because injury risk for a given individual can vary with age and season, researchers controlled for these variables in the analysis. The incident rate ratio (IRR) for injuries occurring during a treated period was compared to injuries occurring during an untreated period.

Of 4,234 children diagnosed with ADHD and treated at least once with stimulant medication, 328 had an injury attended medically at the GP, emergency department, or hospital. Most (86.9%) were male, and the mean age of ADHD diagnosis was 9.7 years. The mean observation period was 5.9 years per child. Almost all study participants (98.5%) were treated with methylphenidate. The leading types of incident injuries were fractures, head injuries, sprains/strains, contusions, and superficial skin injuries. The adjusted IRR for injury during treated periods compared to injury during untreated periods was 0.68 (95% CI, 0.50-0.91). Subgroup analysis showed the effect of treatment was most statistically convincing among males and children aged 10 to 14 years.

The authors conclude that periods of stimulant medication use are associated with lower risk of injury among children treated for ADHD. They caution that other factors not measured for individuals in this study might provide alternative explanations for their findings.

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.

The prevalence of ADHD is believed to have risen to 8% among children aged 4 to 18 years.[1] The risk and severity of injury are reported to be increased among children with ADHD.[2] (See also *AAP Grand Rounds*, July 2009;22[1]:10.[3]) Treatment with stimulant medication is strongly recommended for children aged 6 and up, diagnosed appropriately after systematic evaluation, with the goal of reducing behaviors of inattention, hyperactivity, and impulsivity that can impair academic performance, family functioning, peer relations, and adaptation.[1] While treatment to reduce core ADHD behaviors would seem likely to lower injury risk,[4] most studies on ADHD have not focused on injury outcomes per se, although the results of a randomized controlled trial demonstrated that osmotic-release oral system methylphenidate improved adolescent driving performance as measured by driving simulators.[5]

The authors of the current study offer some fairly compelling evidence that stimulant treatment of ADHD is associated with decreased risk of injury. Strengths of the study include the well-defined case series drawn from a large GP database, examined over a long period of time. The self-controlled design is appealing as a means of eliminating some potential confounders that might affect the results of an observational comparison study. The authors take care to explain the strengths and limitations of this design, pointing out that factors other than medication could have influenced the risk of injury.

The study design is far from perfect, however, in part because the effects of stimulant treatment are time-limited, and the methods allow only a crude approximation of actual treatment exposure in relation to incidence of injury. Further, certain within-individual factors that vary in time might be especially important confounders. For example, periods of school attendance could have been associated with increased medication treatment *and* with decreased risk of medically-attended injury independent of the treatment. Still, the findings here suggest that prevention of injuries in children with ADHD may be considered an additional benefit of stimulant treatment.

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Key words: attention-deficit hyperactivity disorder, stimulant medication, risk of injury

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Mortality and ADHD in Adults With Childhood ADHD

Source: *Barbaresi WJ, Colligan RC, Weaver AL, et al. Mortality, ADHD, psychosocial adversity in adults with childhood ADHD: a prospective study. Pediatrics. 2013;131(4):637-644; doi:10.1542/peds.2012-2354*

Investigators from Harvard, Mayo Clinic, and Baylor College of Medicine sought to examine the long-term outcomes for adults diagnosed with attention-deficit/hyperactivity disorder (ADHD) in childhood. For the study, the investigators reviewed medical and school records on a cohort of adults who had been born in Rochester, Minnesota between 1976 and 1982 and who granted permission for the review of their records. Individuals in the cohort were classified as having a diagnosis of childhood ADHD or no ADHD based on predefined criteria. Vital statistic data including overall mortality, cause-specific mortality, and rates of incarceration were collected on study participants. Standardized mortality ratios (SMR) were compared in those with and without a childhood diagnosis of ADHD. In addition, all of those members of the cohort with a childhood diagnosis of ADHD and a random sample of those without ADHD were invited to participate in a prospective assessment consisting of a standardized neuropsychiatric interview to identify the presence of current psychiatric conditions, including persistent symptoms of ADHD. Rates of psychiatric conditions in participants with and without childhood ADHD were compared.

PICO

Question: Among adults diagnosed with ADHD during childhood, how do rates of mortality due to accidents and suicide, incarceration, persistence of ADHD into adulthood, and comorbid psychiatric conditions compare to those of adults without childhood ADHD?

Question type: Prognosis

Study design: Prospective cohort

A total of 5,718 individuals granted permission for the record review. Of these, 367 were identified with childhood ADHD; 1.9% of individuals with ADHD were deceased and 2.7% were incarcerated. The SMRs for individuals with childhood ADHD compared to adult controls for all causes of death was 1.88 (95% CI, 0.83-4.26; $P = .13$) and for death by accident was 1.70 (95% CI, 0.49-5.97; $P = .41$); neither reached statistical significance. However, the SMR for suicide was 4.83 (95% CI, 1.14-20.46; $P = .032$) in ADHD cases.

In the prospective assessments, 232 individuals with ADHD and 335 controls were enrolled; 29.3% of those with childhood ADHD met criteria for symptoms of ADHD as adults. Participants with childhood ADHD were significantly more likely than controls to have 1 or more comorbid psychiatric conditions (56.9% vs 34.9%; $P < .01$). The most common comorbid conditions were alcohol dependence and abuse, antisocial personality disorder, other substance abuse, and anxiety disorders. Participants with ADHD that persisted into adulthood were significantly more likely to have 1 or more comorbid psychiatric conditions than in those in whom ADHD did not persist (80.9% vs 47.0%; $P < .001$).

The authors conclude that childhood ADHD is a chronic health problem with significant long-term morbidity and mortality.

Commentary by

Richard M. Wardrop, III, MD, PhD, FAAP, Internal Medicine and Pediatrics, University of North Carolina School of Medicine, Chapel Hill, NC

Dr Wardrop 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 an era in which the prevalence of chronic conditions such as kidney disease, diabetes mellitus, cardiovascular disease, and obesity is increasing among younger persons, there is much consternation among adult health care providers regarding the impact these childhood diseases have on the well-being of those who are transitioning to adulthood. ADHD, the most commonly encountered neurodevelopmental disorder of childhood, can clearly be categorized as one of these diseases. In this regard, the current study is both important and timely, underscoring the need to better understand the long-term impact of childhood ADHD on adults.

As the authors indicate, "ADHD should no longer be viewed as a disorder primarily affecting the behavior and learning of children." This has long been suspected from past studies that have examined the impact of ADHD that persists in adulthood and the prevalence of comorbid psychiatric conditions in adults with ADHD.[1,2] The current study offers fresh insight into these areas using data from a large birth cohort. The results of this study show that a large proportion of children who suffer from ADHD (~30%) become adults with ADHD, and have an increased risk of comorbid psychiatric conditions and an increased risk of death by suicide. Thus, ADHD can be added to the ever-lengthening list of childhood disorders with important future health implications for adults, highlighting the need for improved treatment modalities for childhood ADHD.

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Key words: attention-deficit/hyperactivity disorder, mortality, suicide

See related article on page 29

Follow-up Skeletal Survey for Suspected Nonaccidental Trauma

Source: *Harper NS, Eddleman S, Lindberg DM, for the ExSTRA Investigators. The utility of follow-up skeletal surveys in child abuse. Pediatrics. 2013;131(3):e672-e678; doi:10.1542/peds.2012-2608*

PICO

Question: Among children evaluated for nonaccidental trauma, do follow-up skeletal surveys provide new and/or useful information?

Question type: Diagnosis

Study design: Prospective cohort

Investigators from Corpus Christi, Texas and Boston conducted a prospective secondary analysis of 2,890 children evaluated by the ExSTRA (Examination of Siblings To Recognize Abuse) study. The purpose of the current study was to evaluate rates of follow-up skeletal surveys (FUSS) in suspected cases of nonaccidental trauma and determine whether FUSS provides new information. Participants included children <10 years of age who underwent evaluation for possible physical abuse by one of 20 child abuse teams in the study network. Only evaluations of index cases were included. Initial skeletal surveys (SS) were obtained based on American College of Radiology or American Academy of Pediatrics guidelines. The primary outcome was whether FUSS provided new information, defined as new fractures, or that a concerning finding on the initial SS was, in fact, not a fracture. A secondary outcome was the change in perceived likelihood of abuse before and after FUSS as measured by a child abuse physician using a previously published 7-point scale.[1]

There were 2,049 children who had an initial SS, among whom a new injury was found in 23% (471 children). FUSS were recommended in 50.7% (n = 1,038) of those who had an initial SS, but the FUSS was only obtained in 76.7% of these children. New information was found in 21.9% (n = 174) of FUSS, most of which were new fractures (n = 124). Of those with new fractures on FUSS, the most common were of ribs, long bones, and metaphyseal lesions; 52.4% had multiple fractures. The perceived likelihood of abuse increased in 41 (33%) of these new fracture cases, while the likelihood remained at the maximum value in 51 cases (41%). Findings concerning for fractures on initial SS were determined by FUSS not to be fractures in 55 (6.9%) subjects. An initial negative SS followed by a positive FUSS occurred in 7.1% (n = 18) of cases.

The investigators conclude that FUSS are useful in children with suspected nonaccidental injury. They suggest that FUSS may be valuable in cases with a moderate level of concern for abuse.

Commentary by

Charles L. Snyder, MD, FAAP, University of Missouri at Kansas City School of Medicine, Kansas City, MO

Dr Snyder 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.

Skeletal surveys are useful to obtain in children for identifying occult injuries, since only approximately 10% of cases will present with bruising or signs of trauma at the fracture site.[2] This is particularly true in cases of suspected physical abuse. Specific recommendations regarding the indications for FUSS exist, but previously only a few retrospective studies have documented the results.[3-5]

The investigators of the current study offer interesting insight into the value of FUSS. However, this study has several weaknesses acknowledged by the authors: (1) it is observational and the indications for FUSS were variable between centers and physicians; (2) the rating scale for perceived likelihood of abuse has many subjective measurements and its reproducibility is questionable; (3) FUSS radiographs were not independently reviewed in the research protocol; (4) the time interval between the initial SS and FUSS was not determined, and thus some fractures could have healed and not been seen on FUSS; (5) approximately 25% of recommended FUSS were not obtained, introducing bias; and (6) the investigators did not determine which initial SS had findings that were concerning but inconclusive for abuse, and therefore some fractures identified by FUSS may have already been suspected.

The accurate identification of nonaccidental trauma is critical for appropriate medical treatment, protection of at-risk children, and medico-legal purposes. This report and prior studies document a significant incidence of new fractures found with FUSS and a conversion rate from negative SS to positive FUSS (and vice versa) of about 7% each.[2-4] The direction for future studies should be toward trying to determine the optimal timing of FUSS and which specific radiographs have the highest yield.

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Key words: abuse, fractures, skeletal survey

Visit www.GrandRoundsBlog.org to read a post about this article appearing this month.

Retinal Exams in Abused Children With Normal Neuroimaging

Source: *Greiner MV, Berger RP, Thackeray JD, et al. Dedicated retinal examination in children evaluated for physical abuse without radiographically identified traumatic brain injury. J Pediatr. 2013;163(2):527-531; doi:10.1016/j.jpeds.2013.01.063*

PICO

Question: Among children <10 years of age evaluated for physical abuse without traumatic brain injury, what is the rate of retinal hemorrhages?

Question type: Descriptive/Occurrence

Study design: Cross-sectional

Researchers from the multi-institutional Examining Siblings to Recognize Abuse (ExSTRA) research network sought to determine the prevalence of retinal hemorrhages (RH) in children <10 years of age who were being evaluated because of concerns for physical abuse and did not have evidence of traumatic brain injury (TBI). Additionally, the researchers aimed to evaluate the associations of RH in children who had no evidence of TBI, but who had abnormal mental status, facial bruising, and complex or occipital skull fracture. For the study, data collected at 20 participating US centers on all children <10 years of age who underwent subspecialty consultation for physical abuse between January 15, 2010 and April 30, 2011 were reviewed. TBI was defined as any radiological evidence of intracranial trauma, including subdural, subarachnoid, or epidural hemorrhages, brain contusions, and/or brain edema. The following information about RH was collected: presence, number, distribution, number of layers involved, and presence or absence of retinoschesis (splitting of the layers of the retina). RH that were numerous, multilayered, and extended to the periphery of the retina were considered to be "characteristic" for abuse.

Of the 1,122 eligible patients without TBI, 352 (32%) had dedicated examinations for RH, including 198 with complex or occipital skull fracture, altered mental status, or facial bruising. The median age of the 352 study children was 8.5 months (range 2-92 months). Among the 352 children, only 2 (0.6%; 95% CI, 0.1-2.0) had any RH identified. Neither child had "characteristic" RH that were thought to be "forensically significant" or retinoschesis. The authors calculate that it would require approximately 176 dedicated retinal examinations to detect 1 child with RH in this population, and that the RH detected would not likely be forensically significant.

The authors conclude that children being evaluated for physical abuse without TBI on neuroimaging may not require dedicated retinal examinations.

Commentary by

James D. Anderst, MD, FAAP, Children's Mercy Hospital, Kansas City, MO

Dr Anderst 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.

This study adds to the existing literature suggesting that RH, particularly forensically significant RH, are exceedingly rare in children with essentially normal neuroimaging and an examination for such is generally not indicated in this population.[1,2] This research is the first multi-institutional, prospectively planned study to collect and analyze these types of data.

One previous case series identified 9 children with altered mental status in whom there was RH despite a normal initial head CT. However, that study included some children who had abnormalities on subsequent head imaging. Additionally, the cases were accrued via an international list serve, creating a potential selection bias.

A weakness of the current study is a lack of information on when the dedicated retinal examinations were done and who did them. In addition, the decision to obtain head imaging and/or dedicated examination for RH was left to the individual centers, potentially introducing selection bias. Nonetheless, this large series, taken in context with previous work, solidifies the notion that dedicated retinal examinations are usually not necessary in young children who may have been abused, but have normal neuroimaging studies.

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Key words: retinal hemorrhage, child abuse

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Linking Personal, Public Health Data via Electronic Health Records

Source: *Al-Samarria T, Wu W, Begier E, et al. Evaluation of a pilot respiratory virus surveillance system linking electronic health record and diagnostic data. J Public Health Manag Pract. 2013;19(4):322-329; doi:10.1097/PHH.0b013e3182602ef6*

PICO

Question: Can a system linking electronic health records, clinical decision support, and diagnostic test results in community clinics provide useful epidemiologic information on emerging influenza epidemics?

Question type: Diagnosis

Study design: Cohort

During the 2009 influenza A (H1N1) pandemic, investigators at the New York City (NYC) Department of Health and Mental Hygiene (DOHMH) piloted a respiratory virus surveillance system in 9 community health centers in Manhattan and the Bronx with a networked electronic health record system (EHR) and standardized electronic communication to DOHMH. Triggered by symptoms listed in the EHR meeting a predefined case definition of influenza-like illness (ILI), providers were alerted by the EHR to obtain confirmatory testing (rapid influenza diagnostic test [RIDT] and PCR assay for respiratory viruses). Demographic data, ordered tests, and test results were subsequently transmitted from the EHR to DOHMH. The primary goal of the study was to assess the effectiveness of using surveillance clinics with multisystem electronic linkages to develop real-time data on the epidemiology of respiratory virus outbreaks. The sensitivity and specificity of RIDT and symptom criteria for ILI as predictor of a PCR positive for H1N1 were also compared.

Of 9,375 adult and pediatric patient visits during the study period, 537 (6%) met criteria as ILI visits. Children accounted for 63% of all ILI visits, with 12% occurring in 0- to 2-year-old children, 22% in 3- to 5-year-olds, 20% in 6- to 12-year-olds, and 9% in 13- to 17-year-olds; 48% of H1N1 cases confirmed by PCR occurred in children <17 years old. Despite EHR alerts, respiratory virus testing was only performed in 17% of ILI cases; overall, 40% of specimens for testing ordered by clinicians were in patients who were not identified as having an ILI. In 132 cases with both RIDT and PCR results, the ILI case definition was more sensitive (70% vs 29%), but less specific (48% vs 94%) and had a lower positive predictive value (59% vs 83%) when compared to RIDT as a diagnostic test for H1N1.

The authors conclude that despite the low sensitivity of RIDT as a test for H1N1, the study results demonstrate the potential of linked data from EHRs to provide important epidemiologic data on emerging respiratory virus epidemics.

James A. Taylor, MD contributed to this summary.

Commentary by

George R. Kim, MD, FAAP, Baltimore, MD

Dr Kim 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 ideal of health information technology for community health practice is a combination of workflow and technology that automatically collects, links, and organizes data from patient encounters, communicates it in real time to organizations and agencies for timely surveillance-response, and uses knowledge to guide timely and optimal care of individual patients. This ideal connects providers to care networks and public health agencies as well as EHRs to health information exchanges (HIE)[1] and public health surveillance networks.

The authors of this study describe part of an ongoing NYC effort to realize this ideal in a community health network. Note that the "intervention" (coordinated data collection, structured data communication to the DOHMH, defined point-of-care case identification/alerts, and ongoing data analysis during a defined outbreak) is not the "system" (the networked clinics, the laboratory, the analysis team, the DOHMH) and it is also not the "information technology" (the networked EHR, the clinical decision support rules/alert, the standard queries and electronic communication protocol). Evaluation of clinical information technology's true impact on outcomes and its translation/dissemination (ie, the evidence for HIE) may be difficult. Deployment of this EHR within a different structure, workflow, and culture may well produce different outcomes.[2]

Qualitative observations may be of equal value in understanding the success or failure of systems. For example, it was noted that during data collection, DOHMH discouraged RIDT/PCR testing in mild cases (which may have contributed to the low completeness rate), and that ILI symptoms/findings that defined a case were broad and not specific to the diagnosis. As US EHR adoption increases,[3] more projects that use networked data from EHRs for surveillance, research, and practice improvement may help measure and address some of the more difficult problems in pediatric and adult primary care.

Editors' Note

The results of this study are disappointing. The RIDT was not as sensitive as an old-fashioned symptom checklist as a test for H1N1 during the pandemic. (It should be remembered, however, that RIDT is known to be a relatively insensitive test for pandemic influenza H1N1.) Perhaps more worrisome, even with electronic triggers to direct care, the RIDT was only ordered 17% of the time that it was indicated. As all clinicians frustrated by the inadequacies of current systems know, we have a long way to go in maximizing the clinical utility of EHRs.

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Key words: electronic health records, influenza, polymerase chain reaction

The Acute Management of Prolonged Febrile Seizures

Source: *Bassan H, Barzilay M, Shinnar S, et al. Prolonged febrile seizures, clinical characteristics, and acute management. Epilepsia. 2013;54(6):1092-1098; doi:10.1111/epi.12164*

PICO

Question: Among children who presented to the ED with a febrile seizure lasting >15 minutes, what prehospital treatments did they receive and how did these impact seizure duration?

Question type: Descriptive

Study design: Case series

Investigators at 4 Israeli medical centers and Albert Einstein College of Medicine in New York sought to determine the clinical characteristics and acute management of children with prolonged febrile seizures (PFS). From January 2008 to March 2010, investigators prospectively collected data on all children who presented to the emergency departments (ED) with PFS, defined as a febrile seizure (FS) lasting >15 minutes. FS was defined as a seizure provoked by a temperature ≥101.0°F, no history of afebrile seizures, and no evidence of acute CNS infection or insult. Data obtained included demographic and past medical history; prehospital and ED management, such as type of medication used; and clinical course, including seizure type, duration, and outcome. Investigators also constructed a logistic regression model to determine predictors of having a PFS >30 minutes.

A total of 60 children with PFS were enrolled, of whom 10% had a history of perinatal complications, 25% had a prior FS, and 18% had a significant neurodevelopmental disorder. The median age was 18.5 months, the median seizure duration was 35 minutes, and the PFS had a focal onset in 57%.

Of the 54 children who were transported to the ED by ambulance, 41 were actively seizing in the ambulance and 33 (61%) were treated in the ambulance (8 were not recognized as actively seizing); 15 (45%) of those treated stopped seizing prior to arrival at the ED. For the children treated in the ambulance, 19 were given IV diazepam or midazolam (median dose 0.16 mg/kg per dose), 9 received rectal diazepam (median dose 0.5 mg/kg per dose) either alone or followed by IV diazepam or midazolam, and 5 were given intramuscular or intranasal midazolam. Children receiving rectal diazepam first were less likely to stop seizing (n=1 of 9) compared with those who received IV diazepam or midazolam first (n=11 of 19; $P = .02$).

Upon arrival in the ED, 31 (52%) children were still seizing. Lumbar puncture was performed in 12 patients (20%). EEG was performed in 37 children and was abnormal in 17. A total of 38 (63%) children were admitted. Independent predictors of a PFS lasting >30 minutes included intermittent seizure type ($P = .02$) and failure to respond to initial treatment with rectal diazepam ($P = .001$).

The investigators conclude that although most children with PFS received anti-epileptic treatment in the prehospital setting, this treatment was effective in ending the seizure prior to arrival in the ED in only a minority of cases.

Commentary by

J. Gordon Millichap, MD, FAAP, Neurology, Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL

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/device.

A PFS, as defined in this study, is a subtype of the complex FS lasting >15 minutes. Recent data suggest that 10 minutes may be a more appropriate cutoff between the simple and complex FS.[1] A PFS lasting >30 minutes is classified as febrile status epilepticus (FSE), accounting for 5% to 9% of FS patients.[2] PFS and FSE may be associated with hippocampal injury, subsequent mesial temporal sclerosis, and temporal lobe epilepsy.[3,4] In light of the increased risk of subsequent epilepsy, the acute management and prevention of PFS and FSE become highly important.

The ineffectiveness of rectal diazepam in management of PFS reported in this study is consistent with findings in a United Kingdom study, in which investigators found that the control of status epilepticus with intravenous lorazepam was significantly superior to that with rectal diazepam.[5] In contrast, a retrospective analysis of ambulance-transported children in a large urban emergency medical service in San Francisco found rectal diazepam to be a simple, effective, and safe method of prehospital management of pediatric status epilepticus.[6] Compared with IV diazepam, rectal diazepam is easier to administer, especially in infants and toddlers, and is less likely to produce respiratory depression. Short duration of action is an important limitation of both treatments. In the San Francisco study, seizures were controlled in 13 of 16 children (81%) who received rectal diazepam in a single dose ranging from 0.16 to 0.57 mg/kg and in all of 15 treated with IV diazepam, 0.04 to 0.33 mg/kg. Convulsions recurred before arrival at the ED in 4 of the 13 (30.8%) treated with rectal diazepam in the ambulance and in 9 of 15 (60%) who received IV diazepam. Prehospital endotracheal intubation for profound respiratory depression was required in 2 children treated with IV diazepam and in none treated with rectal diazepam. As such, the optimal prehospital management of PFS remains incompletely determined.

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Key words: febrile seizures, status epilepticus, benzodiazepines

Visit www.GrandRoundsBlog.org to read a post about this article appearing this month.

CME QUESTIONS

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CME OBJECTIVES

- Delineate the utility of a clinical scoring system for the diagnosis of testicular torsion
- Understand the association of vaccinations with Guillain-Barré syndrome
- Describe the usefulness of follow-up skeletal surveys of children with suspected nonaccidental trauma

1. A 13-year-old boy presents to the emergency department with left scrotal pain that began 2 hours ago. He denies nausea or vomiting. He is found to have testicular swelling and the testis is hard to palpation. The cremasteric reflex is absent and the testis is high riding. Based on the study by Barbosa et al, which of the following is the most appropriate next step in management?

a. Admit for observation and obtain a scrotal ultrasound if his pain persists for over 8 hours
b. Discharge without ultrasound for presumed epididymitis
c. Discharge without ultrasound with diagnosis of torsion of appendix testis
d. Immediate surgical detorsion
e. Obtain a scrotal ultrasound

2. A 13-year-old girl and her mother are in your office for a well-child visit and you are discussing HPV vaccine. They ask how effective the HPV vaccine is and you cite the study by Markowitz et al. Which of the following is the most accurate conclusion from that study concerning the effect of HPV vaccine on HPV prevalence?

a. Decreased prevalence of HPV among female adolescents (aged 14-19 years)
b. Decreased prevalence of HPV among female young adults (aged 20-24 years)
c. Decreased prevalence of HPV among male and female adolescents (aged 14-19 years)
d. Decreased prevalence of HPV among male and female young adults (aged 20-24 years)
e. No significant impact on the prevalence of HPV infection

3. Which age group in the United States has seen a decline in moderate, severe, or fatal outcomes from unintentional ingestions of over-the-counter cough and cold medicines following changes in the labeling and age recommendations, according to the article by Mazer-Amirshahi et al?

a. Children <2 years of age
b. Children 2 to 5 years of age
c. Children 6 to 12 years of age
d. Children 12 to 18 years of age
e. None of the above as unintentional ingestions of over-the-counter cough and cold medicines have been unchanged

4. Parents bring their 6-month-old baby boy to the office for a well-child check. He is due to receive trivalent inactivated influenza vaccination (TIV). From reading information on the internet, they ask whether this vaccine is associated with Guillain-Barré syndrome (GBS). Based on the study by Baxter et al, which of the following is the most accurate response?

a. Only the intranasal live attenuated influenza vaccine is associated with an increased risk of GBS
b. There is no evidence for an association of GBS with influenza vaccination
c. TIV is associated with an additional one case of GBS for every 500 doses given
d. TIV is only associated with an increased risk of GBS in children above 8 years of age
e. TIV is only associated with an increased risk of GBS when given with conjugated pneumococcal vaccine

5. In the study by Raman et al assessing the association of stimulant treatment in children with ADHD and medically-attended injury risk, which of the following is the most accurate conclusion?

a. Periods of time during which stimulants were prescribed were associated with reduced risk of medically-attended injury
b. Stimulant treatment significantly reduced the injury risk for females with ADHD but not males
c. Stimulant treatment was associated with the greatest decrease in injuries in children 5 to 9 years of age
d. The study design showed stimulant medication prevents injuries since all relevant confounders were controlled for
e. There is a residual beneficial effect of stimulant medication as there were decreased injuries in the 2-year time period following the discontinuation of stimulant medication compared to the time period prior to starting stimulant medication

6. Which of the following most accurately describes the relationship of childhood ADHD and adults with ADHD based on the study by Barbaresi et al?

a. Adults diagnosed with ADHD as children have the same risk of psychiatric comorbidity as the general population
b. Adults diagnosed with ADHD in childhood are more likely to die by suicide than the general population
c. Adults diagnosed with ADHD in childhood are much more likely to die by way of accident than the general population
d. Incarceration rates of adults with ADHD from childhood is 20%
e. Less than 5% of children with ADHD have a persistence of symptoms into adulthood

7. A 15-month-old girl is admitted to the hospital for suspected nonaccidental trauma due to bruising noted on her exam. The child abuse team evaluates her and they are very concerned she had inflicted injury. A skeletal survey is done and is normal. A follow-up skeletal survey is recommended. A fracture at which of the following locations is most likely to be noted on the follow-up skeletal survey that was not noted on the initial skeletal survey based on the study by Harper et al?

a. clavicle
b. humerus
c. pelvis
d. rib
e. skull

8. What is the probability of finding any retinal hemorrhages in a child who may be a victim of physical abuse, but has normal neuroimaging?

a. 50%-60%
b. 20%-30%
c. 10%-15%
d. 5%-10%
e. <3%

9. Which of the following is the most accurate conclusion of the study by Al-Samarrai et al on the use of linking electronic health record (EHR) data to monitor influenza-like illness (ILI) in the community?

a. Less than 10% of specimens submitted for influenza testing as ordered by clinicians were in patients who did not meet the ILI case definition
b. Less than 25% of H1N1 cases confirmed by PCR occurred in children <17 years of age
c. The ILI case definition had a higher positive predictive value compared to rapid influenza diagnostic testing (RIDT)
d. The ILI case definition was more sensitive but less specific than RIDT
e. With EHR alerts respiratory virus testing was performed in >70% of patients who met the ILI case definition

10. A 38-month-old girl develops a generalized tonic-clonic seizure at home associated with a febrile viral upper respiratory infection. After 5 minutes the ambulance is called and arrives 8 minutes later. She receives rectal diazepam by the paramedics as soon as they arrive. The seizure continues for a total duration of 35 minutes. Based on the Bassan et al study findings, which of the following would be the strongest reason associated with development of a prolonged febrile seizure in this child?

a. Family history of febrile seizures
b. Female sex
c. Generalized seizure
d. Initial treatment with rectal diazepam rather than IV diazepam
e. No prior history of seizures

Answers:
1. d 3. a 5. a 7. d 9. d
2. a 4. b 6. b 8. e 10. d

Back Page

***Objective**: To promote dialogue among readers and between readers and editors, we offer here brief reports and observations on topics of interest authored by members of the AAP Grand Rounds editorial team.*

New Guidelines on Genetic Testing and Screening in Children

by **Rizwan Hamid MD, PhD, FAAP**, Nashville, TN

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

Recent advances in genetics and genomics have led to a tremendous increase in the availability and use of genetic testing and screening in children, including genetic assays marketed directly to consumers. Accompanying this trend are significant ethical issues. The American Academy of Pediatrics (AAP) and the American College of Medical Genetics and Genomics (ACMG) recently updated their policy statements regarding genetic testing in children to inform best practices.[1,2] These are comprehensive guidelines that address many commonly encountered clinical scenarios. A summary of the major guideline recommendations are provided below:

1. Newborn screening: The AAP and ACMG support the mandatory offering of newborn screening for all children but advise that parental permission be sought. In 2002, the ACMG recommended universal screening for a panel of 29 primary targets, which has since been endorsed by the US Department of Health and Human Services and adopted by all states.

2. Diagnostic genetic testing: Genetic testing for children with symptoms of a genetic condition is akin to any other medical diagnostic test. Parental permission should be obtained and the benefits and harms of the test considered (including discovery of misattributed parentage). When the medical benefit-burden ratio of a genetic test is unfavorable or uncertain, or the benefits won't accrue until a later time, there is less justification for performing the genetic test.

3. Carrier testing: The AAP and ACMG do not recommend routine carrier testing of children for autosomal recessive disorders except in the circumstances when carrier status has potential medical implications during childhood. For example, carrier screening may be appropriate for adolescents who are pregnant.

4. Predictive genetic testing: The AAP and ACMG recommend deferring predictive genetic testing for late-onset disorders until adulthood. However, predictive genetic testing may be appropriate in limited circumstances but ought to be guided by the child's best interests.

5. Direct-to-consumer genetic testing: The AAP and ACMG strongly discourage the use of this type of genetic testing in children given concerns about inaccurate results and unreliable interpretation.

6. Disclosure of genetic test results: The AAP and ACMG recommend giving priority to mature adolescents' requests for genetic test results over requests by parents to conceal this information. For nondisclosure requests by parents of young children, the provider should work with the parents to develop a plan for disclosing the existence of the test (and its results) when the child reaches adulthood.

References

1. Ross LF, et al. *Genet Med.* 2013;15(3):234-245; doi:10.1038/gim.2012.176
2. Committee on Bioethics. *Pediatrics.* 2013;131(3):620-622; doi:10.1542/peds.2012-3680

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