To evaluate the accuracy of history and physical examination in detecting heart disease, the authors compared the results of a complete physical examination against a reference standard of a complete two-dimensional and Doppler echocardiography for 357 apparently healthy adolescents participating in a longitudinal study of insulin resistance at the University of Minnesota. Although all participants were examined by a board-certified pediatrician and were found free from evidence of heart disease, 13 abnormal echocardiograms were recorded. The most common unappreciated cardiac conditions in these children were minor left-sided cardiac valve abnormalities such as mitral valve prolapse and bicuspid aortic valve. Seven subjects, however, had more serious conditions, including atrial septal defect (2), patent ductus arteriosus (1), coronary artery fistula (1), pulmonary artery stenosis (1), pulmonary hypertension (1), and dilated cardiomyopathy (1). Five of these 7, in the judgment of the authors, should have cardiac catheterization and/or surgery.

The pediatric cardiologist who interpreted the echocardiograms also examined the 13 abnormal subjects and concluded that, even with the advantage of knowing the diagnoses, only seven of the 13 had abnormal physical findings. These were the children with mitral valve disease (3), atrial septal defect (2), bicuspid aortic valve (1), and pulmonary artery stenosis (1). Some of the more serious conditions encountered, therefore, were not apparent on examination by a pediatric cardiologist. The authors conclude that prevalence of unappreciated heart disease in adolescents is unexpectedly high and improved methods for screening children with heart disease are needed.

Commentary by David A. Danford, MD

Pediatrics, University of Nebraska Medical Center, Omaha, NE

The commonly proposed strategies for cost containment in screening for congenital heart disease depend on the reliability of the history and physical examination. Echocardiography is considered unnecessary because the technologically less intense and less expensive clinical examination will suffice, in most instances, to exclude heart disease. A nagging doubt persists that the clinical examination may not be sufficiently reliable. Steinberger et al have provided a scientifically sound basis for this concern by demonstrating not only that cases of significant undiagnosed heart disease are present among apparently healthy teenagers, but that it may be impossible, even for a pediatric cardiologist, to diagnose some of them by clinical examination. Adult cardiologists have long appreciated that clinically significant cardiac valve disease may be present in the absence of auscultatory findings. In the ongoing audit of pediatric echocardiograms, we continue to observe occasional examples of congenital heart defects discovered in the absence of auscultatory findings typical for any heart disease. It is, therefore, not surprising that this report confirms that some teenagers
with structural heart disease go undetected on clinical examination. It is, however, astounding that the prevalence of disease is many times the generally accepted figure for prevalence of congenital heart disease at live birth.

Although 3.6% of the “healthy” teenagers studied had occult heart disease, the authors stop short of recommending echocardiography for all children, perhaps in part because of doubts that the benefits could justify the enormous effort and considerable expense involved, not to mention problems with lack of equipment and personnel. Close scrutiny of the cases reported raises questions about how much actual benefit accrues from discovering these conditions. About half are hemodynamically unimportant mitral valve and aortic valve abnormalities. Therefore, while it would be ideal to identify such individuals so that bacterial endocarditis prophylaxis could be prescribed, the magnitude of the benefits of doing so is unknown and possibly quite small. The merits of treatment of the silent patent ductus arteriosus or the silent coronary fistula are not well established, so the advantage of detection (and subsequent aggressive evaluation and treatment) of this type of disease is at best unproved. The benefit of detection of the cases of pulmonary artery stenosis, dilated cardiomyopathy, and pulmonary hypertension in this series is difficult to judge because definitive evaluation and subsequent clinical course is pending. This leaves the two subjects with atrial septal defect. There is good evidence to show that diagnosis and subsequent treatment of such individuals likely prolongs life and prevents symptoms. Classic physical findings were identified (at least in retrospect by the pediatric cardiologist) that should have prompted a referral for cardiac evaluation in both of these cases. Mangione, et al, recently tested the auscultatory skills of physicians in training and documented their poor performance in identifying cardiac murmurs. If such performance is allowed to continue when residents leave their training program and begin their careers in primary care, it is likely that many congenital heart defects will go clinically undetected. Whether this is a significant problem remains questionable since only 0.5% (2 ASD’s out of 357 patients) of the patients had lesions definitely known to benefit from prompt diagnosis.

**Editors’ Note**

We echo Dr. Danford’s sentiments and believe his commentary gets right to the heart of the matter. Before we can consider universal echocardiography for all children, we should do a more thorough job teaching cardiac physical diagnosis so that future pediatricians become more skilled at identifying significant abnormalities.

**References**


**INFECTIOUS DISEASES**

**Utility of Enterovirus PCR Testing of CSF**


Ramers et al retrospectively reviewed the records of patients for whom an enterovirus-specific (EV) PCR of the cerebrospinal fluid (CSF) was performed at the Children’s Hospital, San Diego during 1998 in patients with suspected aseptic meningitis. The median age of the 276 patients tested was 5.5 months (range 0 to 201 months). Of the patients tested, 49.6% (137) had a positive result. The test was available 6 days per week June-December, 3 days per week January-May. Eighty-nine patients were discharged before their PCR result was available. Median PCR result turnaround time was longer (48 hours) for patients discharged before results were available than for patients who received the results before discharge (32 hrs, P<.001). Of the 187 results available before discharge, 95 were positive and 92 were negative. The 95 EV-positive patients showed a significant reduction in length of hospital stay (median, 42 vs 72 hours), PCR-result-to-discharge-time (median, 5 vs 27 hours), number of ancillary tests performed (37 vs 162), and antibiotic use (median 2.0 vs 3.5 days) compared to the 92 EV-negative patients (all P values <.001). Except in neonates younger than 1 month, CSF pleocytosis correlated well with positive EV-PCR. The authors conclude that the use of EV-PCR can be clinically useful and may result in significant cost savings by reducing hospitalization, diagnostic testing, and empiric antibiotic therapy.

**Commentary by Mike Dubik, MD, FAAP**

Pediatrics, Naval Medical Center, Portsmouth, VA

Enteroviruses cause an estimated 750,000 cases of meningitis per year in the United States and account for between 80% and 92% of all cases of aseptic meningitis. Although usually benign, differentiating these from bacterial meningitis based on clinical and CSF findings may be problematic, especially in very young infants. Previously, the diagnosis of EV meningitis depended on viral culture, which has a turnaround time (6.8 days, average) that is too long to have a
major impact on patient management. EV-PCR has a sensitivity and specificity of virtually 100%. Perhaps EV-PCR's greatest asset is that it helps the clinician identify those patients that do not need further medical interventions more rapidly than clinical judgement alone. This is especially true in the youngest infants who may not show CSF pleocytosis. To be most cost-effective, the EV-PCR should not be ordered until the CSF data are available. Although it was not prospective and it did not include a detailed economic analysis, this study certainly suggests that enteroviral PCR can yield substantial clinical and financial benefits and that PCR will likely supplant viral culture for the diagnosis of viral meningitis.

Editors’ Note
These authors studied all patients for whom a PCR test was ordered and note that some of the tests appear to have been unwarranted (eg, for patients who did not have clinical criteria suggestive of EV central nervous system disease.) Only 4 of 98 patients older than 1 month had a positive EV-PCR without pleocytosis, whereas 11 of 24 neonates had a positive CSF EV-PCR in the absence of pleocytosis. To fully understand the utility of EV-PCR testing, a prospective study is needed in order to derive optimal criteria for testing.

References

GASTROENTEROLOGY AND NUTRITION

Nonalcoholic Steatohepatitis Associated with Childhood Obesity


Non-alcoholic steatohepatitis (NASH) occurs commonly in adults in association with obesity, hyperlipidemia, and adult onset diabetes mellitus and is known to be a cause of hepatic fibrosis and cirrhosis. The natural history and clinical presentation of NASH in children and adolescents is unknown. Rashid and Roberts report their 10-year experience of 36 children (21 male, 15 female) diagnosed with NASH. The median age was 12 years with a range of 4-16 years of age. Thirty patients (83%) were obese, with a mean weight of 147% of ideal body weight. Two patients had diabetes mellitus at the time of diagnosis, while 2 more later developed diabetes mellitus. Thirteen of 36 (36%) had acanthosis nigricans (all but one was obese). Thirty-three of 36 patients (92%) had elevated ALT values (mean 179 +/- 31 U/L with normal <40 U/L) although none of the 36 patients had signs or symptoms of chronic liver disease. Hypercholesterolemia (7/36) and hypertriglycerideremia (11/36) were relatively common features of NASH. Hepatic ultrasound was obtained in 31 patients, and 24 (77%) showed abnormalities including hepatomegaly and increased echogenicity suggestive of fatty infiltration. Liver biopsy was performed in 24 patients and all patients had significant macrovesicular lipid deposition. Inflammation was present in 88%, and fibrosis/cirrhosis in 75%. One 10-year-old patient had significant cirrhosis noted at biopsy. There were no predictive indicators separating the fibrosis/cirrhosis group from those children who did not have fibrosis at time of biopsy. In the follow-up of 21 patients it was noted that 6 patients lost weight and all of these patients had improvements in the AST level with normalization of values in 2 patients.

Editors’ Note
Although only a small number of NASH cases are reported in this study, we can’t ignore the possibility that we may miss this problem in the growing number of obese adolescents with type 2 non-insulin dependent diabetes mellitus. We will, however, continue to gnash our teeth until we have a better understanding of who should be screened for NASH and how that screening might be most cost-effective.

References
Nieminen and colleagues at the Oulu University Hospital in Finland prospectively evaluated children whose chief complaint was snoring in order to assess the utility of polysomnography (PSG) in diagnosing obstructive sleep apnea syndrome (OSAS), and record the natural history of OSAS and primary snoring. Children with abnormal facial morphologic characteristics were excluded. Fifty-eight children (31 males, mean age 5.7 years) were compared to 30 non-snoring normal children (17 males, mean age 7.1 years). All children underwent a PSG which included leads for an oronasal thermistor for air movement, thoracoabdominal strain gauge for respiratory effort, pulse oximeter, body-position sensor, leg electromyograph for restlessness, and static charge-sensitive bed for position and movement. All recordings were “manually checked” by one of the authors. Of the 58 children with snoring, 27 had PSG consistent with obstructive sleep apnea syndrome (OSAS) and 31 were diagnosed with primary snoring. No abnormal PSG results were found in the control group. All subjects were examined and evaluated for a history of snoring, apnea, nighttime mouth breathing, and restless sleep, and were each given a score of 1 to 3 for a maximum possible score of 15. Patients with probable OSAS, as diagnosed by PSG, had an average symptom score of 12 (range 4-14) while the primary snoring group's average symptom score was 9 (2-14) and the controls 1 (0-7). (No statistics given.)

The authors applied the Obstructive Sleep Apnea score developed by Brouilette, et al, in which a score of 0 is predictive of normality, a score of greater than 0 is predictive of OSAS, and a score of greater than 3.5 is diagnostic of OSAS. The presumed OSAS group mean score was 3.1, the primary snoring group 2.1, and the control group –3.7 (for all comparisons P<.03). Clinical evaluations included an evaluation of the oropharynx and tonsillar size. Among the patients with OSAS, 93% had enlarged tonsils, while in the primary snoring group only 68% had enlarged tonsils. The patients in the OSAS group all underwent adenotonsillectomy. The primary snoring group did not have surgical intervention. After six months, all patients in the primary snoring and OSAS groups underwent repeat clinical evaluations and PSG testing. There was a marked change in both clinical symptoms and PSG testing in patients undergoing an adenotonsillectomy. The average symptom scores in the OSAS group dropped from 12 to 1 (P<.01). Obstructive Sleep Apnea score in the operated group improved from 3.4 to -3.1 (P=.01). The Obstructive Sleep Apnea testing in the primary snoring group did not change significantly nor did their symptom scoring.

This study demonstrates that adenotonsillectomy in otherwise healthy children with OSAS is curative, bringing dramatic improvement in symptoms and in PSG results. However, the authors do not state what would be the most appropriate diagnostic evaluation and treatment for children with primary snoring. Some children who snore have increased upper airway resistance during sleep, which results in increased respiratory effort and sleep fragmentation without the clearly evident apnea/hypopneas or intermittently decreased blood oxygen levels of OSAS. This Upper Airway Resistance Syndrome (UARS) is thought to be more common than OSAS in children. UARS is diagnosed by esophageal pressure monitoring during sleep, a test not commonly performed in pediatric PSG. Despite normal PSG, children with UARS frequently benefit from an adenotonsillectomy. The second dilemma not addressed is the clinical utility of PSG in children with snoring and suspected sleep-disordered breathing. Currently, PSG is regarded as unnecessary in the preoperative evaluation of otherwise healthy children with sleep-disordered breathing due to adenotonsillar hypertrophy, because the test is costly and there are no universally accepted diagnostic criteria for pediatric OSAS. Recent studies have documented the overall benefits experienced by children with sleep-disordered breathing who undergo adenotonsillectomy, including improved quality of life factors, which must be considered along with the more objective clinical parameters when making treatment decisions.

References
Laser Therapy for Hemangiomas


In this prospective, uncontrolled study, these German investigators evaluated the effectiveness of the flashlamp-pumped pulsed dye laser (FPDL) in treating superficial and mixed hemangiomas. Subjects aged 2 days to 7 years were divided into 3 groups: 100 patients with 153 flat cutaneous hemangiomas, 47 with 54 mixed cutaneous-subcutaneous lesions, and 18 with 18 superficial involuting hemangiomas. Eighty-seven lesions were located on the head and neck, 60 on the extremities, 59 on the trunk and 19 in the anogenital region. Lesions were treated until nearly resolved or until there was no response. Outcome was assessed using pre- and post-treatment photographs; results were considered “excellent” when the hemangioma cleared completely, “good” when involution was slower or lightening incomplete, and a “failure” when the lesion remained unchanged or enlarged. In addition, blood flow and vessel thickness were assessed before, during and after therapy with color-coded duplex sonography.

Among the 153 flat hemangiomas, the response was excellent in 34% and good in 52%. Early hemangiomas lightened more than actively proliferating lesions (41% vs 21%). Sonography of flat lesions showed no abnormal blood flow in the subcutis. In contrast, although the cutaneous portion of mixed lesions responded in 39% of patients, no lesions cleared completely and proliferation of the subcutaneous component continued in 61%. At presentation, sonographic evaluation demonstrated that all mixed lesions involved the subcutis to a depth of 4 mm. Of 18 superficial hemangiomas in the involution phase, 67% had an excellent outcome and 33% had good results. The authors conclude that FPDL is effective and may be the treatment of choice for superficial, mixed hemangiomas involving the face or sites that may cause functional impairment.

Parental Presence During The Preoperative Period


The authors studied effectiveness of parental presence at the induction of general anesthesia as an anxiolytic and evaluated parental satisfaction. The study group consisted of 103 generally healthy children, 2 to 8 years old, scheduled for elective, outpatient surgery at Yale-New Haven Hospital. All children were pre-medicated with 0.5 mg/kg midazolam syrup at least 20 minutes prior to the induction of anesthesia. Patients were randomized to 2 groups: parents present or not present at induction. The 2 groups did not differ in age, gender distribution, parental anxiety, visits to the preadmission center or prior surgery. Measurements of the children’s emotional state included the following validated instruments: State-Trait Anxiety Inventory (STAI), Modified Yale Preoperative Anxiety scale (mYPAS), and Induction Compliance Checklist (ICC). In addition, the parents were asked to complete a satisfaction questionnaire.

The children's observed anxiety increased significantly in the trip from the holding area to the operating room (OR) and at the induction of anesthesia. The observed anxiety was not different between the two groups. Parents who accompanied their children into the OR were significantly less anxious than those who did not while post-operative excitement did not differ between the two groups of children. Sixty-eight percent of the parental questionnaires were returned and the authors found that satisfaction with the overall care pro-
vided and the separation process was higher in the parents who accompanied their children into the OR.

**Commentary by Thomas Mancuso, MD, FAAP**

Anesthesiology, Children's Hospital, Boston, MA

As a pediatrician, I am sympathetic to the wishes of parents to participate as fully as possible in the care of their children, including during inhalation induction of general anesthesia. The results of this investigation support the practice of parental presence during induction of anesthesia in children, since the family’s experience is significantly improved. However, the results of this paper indicate that parental presence during anesthetic inductions offers no benefit to the child as far as lessened observed anxiety, more cooperation with the induction process or less post-operative excitement.

As an anesthesiologist, this paper gives me pause. Induction of anesthetic and emergence from anesthesia are the most dangerous times for children, and I wish to devote my full attention to the child during these times. Parental presence is always, to some degree, a distraction, which might be justified if the presence of a parent improves the child’s experience. The paper does not show this. Other studies offer no support for a helpful role for parental presence during the induction of anesthesia in children.1,2 Lerman, in an editorial in the same journal issue discussing parent-present inductions comments, “Parental presence during induction of anesthesia is not an inalienable right, but a therapeutic option...”3 In my view, a parent present during induction can only be justified if it benefits the child.

**Editors’ Note**

No anesthetic complications occurred in either group during induction and no parent was disruptive or refused to leave the OR when asked. Not all children underwent similar preoperative preparation programs and some children had prior surgery, a situation which may confound these results. Despite such limitations, our anxiety level remains high when it comes to recommending that all parents accompany their child through induction of their anesthesia.

**References**


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**The Next Conjugate Vaccine: Meningococcus C**

**Source:** MacLennan JM, Shackley F, Heath PT, et al. Safety, immunogenicity, and induction of immunologic memory by a serogroup C meningococcal conjugate vaccine in infants: a randomized controlled trial. JAMA. 2000;283:2795-2801.

This British group assessed the safety and immunogenicity of a group C meningococcal conjugate vaccine in young infants. In Oxfordshire, 182 healthy infants were randomized into 2 groups that received meningococcal C conjugate vaccine or to a third control group that received hepatitis B vaccine, each at 2, 3, and 4 months of age as specified in the UK immunization schedule. All three groups concurrently received oral polio vaccine, DTP and Hib which were administered in the child’s other leg. At 12 months, half of each group received a booster dose of the conjugate vaccine and the other half received unconjugated meningococcal group A and C polysaccharide vaccine. Local and systemic reactions were recorded for 6 days after each vaccine dose, and serum antibodies to meningococcal group C polysaccharide were assessed by ELISA (enzyme-linked immuno-absorbant assay) and by a serum bactericidal assay.

No significant difference in systemic reactions was noted between the vaccine groups. The rates of local reactions to meningococcal C conjugate and hepatitis B vaccines were quite similar and were lower than those to the whole cell DPT vaccine that was given simultaneously in the opposite leg.

Prior to the first dose of vaccine there were no differences in the meningococcal group C antibody titer (ELISA) among the three study groups. By both ELISA and the serum bactericidal assay, prompt antibody responses were observed in the two conjugate meningococcal C vaccine groups but not in the control vaccine group. These responses declined somewhat by 12 months of age, but remained significantly higher in the meningococcal C vaccine groups compared to those in the control group. The 12-month booster with the conjugate meningococcal C vaccine stimulated higher ELISA and serum bactericidal assay responses compared to the unconjugated meningococcal polysaccharide vaccine, reflecting immunologic memory. The authors conclude that the meningococcal conjugate vaccine is safe and immunogenic and results in immunologic memory when given with other vaccines to 2-, 3-, and 4-month-old infants.

**Commentary by Stanford T. Shulman, MD, FAAP**

Pediatric Infectious Diseases, Children’s Memorial Hospital, Northwestern University Medical Center, Chicago, IL

Hib conjugates virtually eliminated meningitis and other serious infections caused by *H influenzae* type b.
Conjugated polyvalent pneumococcal and conjugated meningococcal C vaccines provide hope for a similar success against infections due to the other encapsulated bacterial pathogens. Conjugation of bacterial capsular polysaccharides to a protein carrier renders the poorly immunogenic polysaccharides more immunogenic, especially in young infants. Data such as that of MacLennan et al, establish that the conjugate meningococcal C vaccine, which is not yet licensed in the US, is safe and well-tolerated in infants, stimulates production of antibody, can be assayed in several ways including a functional assay that reflects bactericidal activity and, more importantly, stimulates immunologic memory. Additional studies will be needed to establish the efficacy of the conjugated meningococcal C vaccine as well as how often boosters are needed.

In the United States, current efforts are focused on incorporating the new heptavalent conjugate pneumococcal vaccine into routine pediatric care. Serogroup C meningococcus accounts for about 30% of meningococcal infections, particularly in older children and adolescents, and for the majority of identified meningococcal outbreaks. The currently available quadrivalent (group A, C, Y, and W-135) conjugate vaccine would, theoretically, provide protection against almost 70% of meningococcal infections. The polysaccharide of group B meningococcus is poorly immunogenic and remains a stumbling block to developing an effective vaccine against this serogroup. Given the very crowded vaccine schedule for infants, routine utilization of a conjugate meningococcal vaccine will probably be deferred until combination vaccines become available that substantially reduce the number of injections. However, the current quadrivalent (unconjugated) meningococcal polysaccharide vaccine should be offered to entering college students as they are at moderately increased risk, particularly those who live in college dormitories.

References

CME Questions

The following continuing medical education questions cover the content of the August 2000 issue of AAP Grand Rounds. Please keep this issue. Each semester of material is worth 8 hours of AMA PRA Category 1 CME credit (16 hours per year).

CME Objectives: AAP Grand Rounds presents important new studies from the medical literature, selected by a panel of expert clinicians and editors. Selection criteria include clinical significance, methodological quality, and the importance of the research question. The CME activity is designed to introduce new knowledge, reinforce the critical assessment of the evidence, and provide insights into the clinical application of new research. The activity is also designed to help clinicians hone their critical assessment skills, increase awareness of the current research environment, and stimulate further learning and investigation. Participants in this month’s activity should be able to, upon completion:
• Discuss commonly proposed strategies for cost containment in screening for congenital heart disease;
• Evaluate records of patients for whom an enterovirus-specific (EV) PCR of the cerebrospinal fluid (CSF) was performed; and
• Assess whether obesity in children may be associated with the potentially life-threatening consequences of NASH.

1. The most common abnormality discovered by echocardiography in the “healthy” adolescent population in the study by Steinberger et al is:
   a. cardiomyopathies.
   b. coronary anomalies.
   c. patent ductus arteriosus.
   d. septal defects.
   e. valve disease.

2. The use of EV-PCR might be expected to lead to:
   a. delays in discharge.
   b. longer duration of antibiotic therapy.
   c. more diagnostic confusion for clinicians.
   d. shorter hospital stays for those with positive results.

3. The following statements are true about non-alcoholic steatohepatitis (NASH), except:
   a. Acanthosis nigricans is associated with an increased risk of NASH.
   b. ALT values can predict which NASH patients have fibrosis.
   c. An ultrasound cannot distinguish fibrotic/cirrhotic from non-fibrotic changes in NASH.
   d. NASH may occur in normal weight children, but is more prevalent in obese patients.
   e. Weight loss can improve obesity-associated NASH.

4. Based on Nieminen et al’s study of children with obstructive sleep apnea syndrome, adenotonsillectomy improved all of the following parameters EXCEPT:
   a. polysomnography results
   b. restless sleep
   c. rhinorrhea
   d. snoring

How AAP Grand Rounds Works

The writing team for AAP Grand Rounds is composed of physician representatives from each of the more than 40 specialty sections of the Academy. Every month, our physician experts from each section scan more than 75 journals for the most recent advances in pediatrics, summarize them, and add their expert commentary. Editorial Board members then make the final selections. Criteria for selection include methodologic soundness as well as relevance to practicing pediatricians.
5. Of the following, the type of hemangioma MOST likely to respond to flashlamp-pumped pulsed dye laser treatment is:
   a. early flat (superficial) lesion
   b. early mixed (superficial and subcutaneous) lesion
   c. proliferating flat (superficial) lesion
   d. proliferating mixed (superficial and subcutaneous) lesion
   e. subcutaneous lesion

6. Parental presence at the induction of anesthesia for his/her premedicated (0.5 mg/kg PO midazolam) 6-year-old undergoing a herniorrhaphy will likely
   a. cause the child to become uncooperative during the induction.
   b. have little effect on the child’s level of anxiety.
   c. help the anesthesiologist with the induction.
   d. make the parent much more uncomfortable with the hospital experience.

7. According to the study by MacLennan, et al, all of the following statements about meningococcal C conjugate vaccine are true EXCEPT:
   a. It does not result in immunologic memory when given with other routinely administered vaccines.
   b. It is safe and well tolerated.
   c. It results in increased antibody titers to serogroup C meningococcus at 12 months
   d. It results in increased serum bactericidal activity against serogroup C meningococcus at 12 months.

Correction
In the May 2000 issue, the correct answer to question 9 is e: Bicarbonate therapy in patients with severe DKA (pH<7.1) has been shown to lower serum potassium. (The answer was incorrectly stated as response “c” in that issue.)