


The Child's Doctor

Journal of Children's Memorial Hospital, Chicago



In This Issue:

- Earn 2 CME Category 1 Credits
- Patient Safety in Pediatrics
- Minimally Invasive Surgery in Children
- Eosinophilic Esophagitis in Children
- Bipolar Disorder in Pediatrics
- Bacterial Rhinosinusitis in Children


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Physician Responsibilities in Patient Safety: A New Day

EDWARD S. OGATA, MD

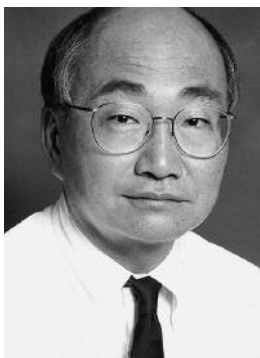
The overused term “do the right thing” does apply to the physician’s role and responsibility to assure the safety of every patient. Physicians should always meet certain key expectations, including being directly involved in a patient’s care, reporting issues that pose risk to a patient, and working to improve the practices and systems that affect patient care.

We must never forget to be cognizant of the privilege and burden of responsibility for the patient. In the inpatient teaching setting where residents, fellows, and other trainees care for patients, we must be ever mindful of our ultimate responsibility for the care of the patient. For this, the attending physician must be involved in the ongoing care of the patient, 24 hours a day, 7 days a week.

This responsibility poses a tension between educational goals and “doing the right thing.” The discipline and art of medical education is changing. Those of us who trained in earlier generations were allowed considerable independence in the care of patients – in retrospect, probably too much. I recall as a trainee seeing an attending faculty physician 3 times a week and almost never at night or off hours. Today’s approach to teaching mandates the constant involvement of attending physicians, engaging and challenging trainees, and always overseeing the care of the patient.

The pressures of medical malpractice costs are another imperative for the attending physician to be constantly involved with and responsible for the patient. Unexpected outcomes can occur despite the best possible care, and the possibility of unanticipated poor outcome is greatly increased when the attending physician is not involved with the patient. This problem is worsened by inadequate or missing documentation.

We physicians cannot by ourselves ensure the absolute safety of our patients. Health care systems are complex and have many potential risks. As hospitals have heightened their efforts to improve patient safety, many have realized that the means to get critical information concerning unexpected outcomes or “near misses” are not organized. Many, including Children’s Memorial Hospital, have invested in reporting systems and are encouraging physicians and staff to report occurrences and concerns to ensure that this important information gets to those who can assess trends, identify problems, and fix them. Every physician is responsible for participating in reporting and working to devise ways to reduce risk to patient safety. We all need to “do the right thing.”



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On the cover: Mary Beth Madonna, MD, with her patient
Olivia Rojas, treated with minimally invasive surgery for
Hirschsprung disease

Photo by Andrew Campbell

The Child's Doctor

Journal of Children's Memorial Hospital, Chicago

[3] CME: Patient Safety in Pediatrics

Jane Holl, MD, MPH, patient safety physician leader, Safety/Quality Learning Center

Educational Objectives: Recognize how flaws in clinical care systems can lead to medical errors; employ system evaluation methods to identify risk-prone steps within clinical processes; conduct process improvements to help prevent medical errors and improve patient safety

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Mary Beth Madonna, MD, attending physician, Pediatric Surgery

Marleta Reynolds, MD, interim head, Pediatric Surgery

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Patient Safety in Pediatrics

JANE HOLL, MD, MPH

An estimated 1% of hospitalized children¹³ in the US, or approximately 70 000 children, experience an adverse event each year, 60% of which may be preventable.¹ An adverse event here is defined as an injury caused by medical management, not the disease process that led to a prolonged hospital stay or disability at discharge. Adolescents experience the highest rate of adverse events.¹² Although only 10% of US children are hospitalized annually and most pediatric hospitalizations are for normal, healthy newborns (99.3% of US births take place in a hospital), nearly 20% of identified hospital-based preventable adverse events in children occur in the ambulatory care setting.¹ This article will review child-specific factors related to medical error risk and discuss strategies that could be applied in pediatrics to detect and prevent risks to patient safety.

The Institute of Medicine published landmark reports, “To Err Is Human: Building a Safer Health System,”⁵ and “Patient Safety, Achieving a New Standard of Care,”⁶ which identified the significant problem of medical errors and related injuries occurring in hospitalized patients and increased public awareness about patient safety. However, these reports and much of the subsequent literature about factors that contribute to increased patient safety risk,⁷ and the innovative processes and systems being developed to prevent patient safety problems, have focused primarily on medical care for adults, with limited information about medical care for children.^{8,9} Currently, the Pediatric Research in Office Settings (PROS) network supported by the American Academy of Pediatrics is engaged in a project called Learning from Errors in Ambulatory Pediatrics (LEAP) that seeks to develop a secure web-based tool for documenting and reporting errors and “near misses,” and to identify types of actual and potential errors that are occurring in pediatric ambulatory settings.¹⁰

Children are different from adults

Children experience different types and frequencies of risk for patient safety problems than adults.^{11,11} Birth related^{1,2} and diagnostic related¹ adverse events are the most frequent types of adverse events in children, whereas,

surgical and medication adverse events are the most frequent adverse events in adults.¹² While serious potential (near miss) medication errors were found to be 3 times more frequent in children compared with adults, children experience relatively low rates of medication adverse events.^{11,11} Very young children, however, are uniquely vulnerable to errors caused by giving medication doses that are 10 times greater than recommended.¹³⁻¹⁵

What are the underlying causes of differences between children and adults with regard to patient safety problems? A number of child-specific factors have been identified:¹⁶

- Child’s physical characteristics (small size, weight and morphology, varied physical characteristics)
- Child’s development (physiological, development and growth, cognitive-social-emotional)
- Child’s legal status as a minor (decision making and consent, parental responsibility, confidentiality, supervision)

All these child-specific factors are subject to significant variability, a principle known to increase the risk for error.¹⁷⁻¹⁹ For example, the range of normal values for blood, urine, or cerebrospinal fluid analyses is much wider for a

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Recognize how flaws in clinical care systems can lead to medical errors
- Employ system evaluation methods to identify risk-prone steps within clinical processes
- Conduct process improvements to help prevent medical errors and improve patient safety

pediatric population, which can make it more difficult for a clinician to interpret a result. Also, current Computer Physician Order Entry (CPOE) systems do not have the capability either to use weight, a key variable in pediatric medication dose calculation, or to consider age intervals of less than 1 year.

Children's immature physiology has been shown to increase error risk.²⁰ For example, the small size of young children can contribute to increased technical difficulties (eg, venipuncture). Conscious sedation also presents greater risk because of children's limited ability to regulate behavior and movement.²¹

Decreased communication is another principle related to error.^{22,23} In the medical care of children, information may be compromised because of a child's social-emotional-psychological immaturity, limited communication skills, or constrained ability to understand the impact or consequences of his or her medical care.

Strategies to learn about pediatric patient safety risk

Making mistakes is human nature and cannot be eradicated,²⁴ but "active failures" and "latent failures" contribute to mistakes. Active failures are unsafe acts committed by someone in direct contact with the patient or system, such as picking up the wrong syringe, forgetting to check a laboratory result, or not following a clinical protocol.²⁵ To prevent these failures, individuals and teams must be alert and trained to recognize error-prone situations (eg, 2 patients with the same name), but "system" design should also offer a safety-net (eg, consistent use of 2 patient identifiers). Failures to prevent or detect adverse events are often due to latent failures, or conditions within a system,²⁴ such as heavy workloads, inadequate supervision, or poor communication between clinicians. Reduction of latent failures requires a system approach that studies the conditions under which people work and invests in the redesign of processes to prevent adverse events, or mitigate their effects.

Consistent and comprehensive reporting of adverse events has been recognized as an important strategy to prevent adverse events, but there remains considerable discussion about mandatory versus voluntary reporting, organizational abilities to translate statistical reports into improvement plans, and the role of reporting near miss events.²⁶ The focus group methodology, used widely in business management and social science, is an efficient, effective, and economical means to elicit patient safety risk information within a health care system.²⁷

A widely adopted system approach aimed at reducing or eliminating latent failures is called the Root Cause Analysis (RCA). This approach to the analysis of a medical error was adapted by the Veterans Affairs Administration National Center

for Patient Safety²⁸ from the method used to investigate major industrial accidents through human factors engineering and industrial psychology.

Once an error occurs, the obvious goal is to develop a solution that will eliminate recurrence of the situation. A root cause is the most basic casual factor, or more likely, factors, which if corrected or removed will prevent recurrence of an error-prone situation. Through interviews with clinicians (nurses, physicians, technicians) who participated in the event and review of all relevant medical records, a timeline that defines each discreet action and significant thought that led up to the adverse event is constructed. The next step is to keep asking "why" for each action or thought to reach the root cause(s). In some cases, asking "how" repeatedly can reveal the deeper root causes that made it possible for an event to occur.

The RCA is usually conducted by a clinical team and can lead to cooperative relationships among the participants, provide an excellent patient safety learning opportunity, and improve the organizational culture of safety.²⁹ On the other hand, it takes place after an event has occurred, can be time consuming for the clinical participants, and lead to actual or theoretical attribution of blame that, in turn, leads to fear of and resistance to subsequent reporting of events by clinicians.

Punitive and blaming cultures have been shown to create disincentives for professionals to report adverse events and learn from their mistakes. However, the health care system cannot afford a totally blame-free approach and the concept of a "just" culture, in which the inevitability of human error is recognized but reckless acts are not tolerated, is widely promoted.³⁰ In this culture, workers are encouraged to report adverse events and to seek solutions.

Another approach borrowed from high-risk industries (eg, aerospace, nuclear, transportation) is a technique known as "hazard analysis." The Failure Mode and Effects Analysis (FMEA) is an engineering method that identifies weak points in products and processes. Industries using the FMEA technique take the viewpoint that human error is inevitable and address it by a prospective, systematic review of all steps and components of a process to predict how and where a process may fail and result in significant consequences, and then, design strategies to prevent the failure or mitigate the consequence.^{31,32}

FMEA can be a challenging process because it is often time consuming and costly, the terminology can be intimidating for clinicians, and, in order to be useful, may require significant changes in priorities, resource allocation, and organizational culture. However, compared to the RCA, it is a more open

approach, cannot lead to blame (because no event has occurred), and reviews an entire process rather than a single event.

Strategies to improve pediatric patient safety

Communication problems within a clinical team (eg, use of abbreviations, illegible handwriting, poor pronunciation, background noise, poor communication between clinicians) are known to contribute to adverse events. Current strategies to improve communication include “read back” of verbal orders,³³ team training, and use of debriefings.³⁴ Information technology systems, such as CPOE³⁵ and Personal Digital Assistants (PDAs), have also been evaluated.³⁶ The effectiveness of many of these technological solutions has not been fully established. For example, a recent study showed that a widely-used CPOE system facilitated medication error risks. Examples of medication safety problems with the CPOE system included inflexible ordering formats, fragmented display of patient’s medications, and pharmacy inventory displays that clinicians mistook for dosage guidelines.³⁷

A more recent approach to address latent failures that contribute to increased morbidity and mortality, such as lack of knowledge, failure to appreciate clinical urgency, lack of supervision, and failure to seek advice, is the use of Rapid Response Teams.³⁸ It is a new process that empowers nurses and other staff members to bypass the usual chain of command when a patient’s condition appears to be deteriorating and to obtain immediate assistance to assess and stabilize the patient.

Increasing patient involvement also should be a critical part of patient safety risk reduction, although factors such as disease complexity, language barriers, or educational level may mitigate the effect. Patient/family involvement to improve safety might include: providing a clear and complete medical history to clinicians, since inadequate or poor information is often an element in misdiagnosis; speaking up when the patient notices unexplained changes in medication, which may prevent a medication error; or reporting observed errors, such as a clinician consulting or writing in the wrong patient’s chart.³⁹ Health care institutions need to articulate the important role that patients/families play in promoting safety, provide easy mechanisms for patients/families to report errors and problems, and promote open, non-judgmental communication between clinicians and patients/families.

Development of clinical checklists, reminders, protocols, and guidelines is a useful way to reduce reliance on short-term memory, a form of cognition that should only be relied upon for essential tasks. Color coding medications, pre-printed orders, special packaging, or labels for high risk medications have been shown to reduce error.⁴⁰ There are hundreds of guidelines, best

practices, and protocols that have been developed,⁴¹ primarily for use by clinicians, but could be redesigned and adapted for use by patients (eg, to accommodate literacy level, language).

Conclusion

The number and complexity of medical treatments, procedures, and medications are increasing, and health care is delivered in high stress, often under-staffed environments leading to increased patient safety risk. Medical errors and adverse events have serious effects for patients and society. They can result in death or disability with significant pain and psychological trauma for both patients and health care workers. These events cost nations billions of dollars in direct health care costs, malpractice settlements, and indirect costs, such as loss of income and productivity, or increased costs of personal care.

Children are vulnerable in unique ways to medical errors and adverse events. Achieving improved patient safety will require input from all pediatric clinicians and staff and commitment by the leadership of health care institutions. Families and pediatric patients must also be engaged for the process to succeed. ■

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Minimally Invasive Surgery in Children

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For many years, pediatric surgeons did not feel there was an advantage to minimally invasive surgery in children, although it was introduced to the general surgery population in 1987¹ and became common for many abdominal and thoracic surgeries in adults. In the 1990s, the leaders in pediatric minimally invasive surgery began performing laparoscopic procedures, such as cholecystectomy and appendectomy. These procedures were first performed in older children due to limitations of equipment, but over time manufacturers began making shorter and smaller instruments so that minimally invasive surgery could be performed on even the smallest infants. The following discussion will focus on current uses of minimally invasive surgery for common conditions in pediatrics.

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Recognize the common pediatric conditions that may be treated with minimally invasive surgery
- Explain the advantages of minimally invasive surgery vs. open surgery
- Explain the basics of minimally invasive surgery to their patients and families

Principles of minimally invasive surgery

Minimally invasive surgery relies on access to the cavity of interest (eg, abdomen, chest) with the placement of ports that are long, thin valved tubular devices. Carbon dioxide is insufflated into the cavity through the ports to expand it, allowing adequate visualization and working space. A scope is attached to a camera so that the procedure is watched on a television monitor by the surgeons and all others in the room, or even at remote sites. Light is obtained with a halogen light source through fiber optics attached to the scope. Laparoscopic instruments are also long and thin and placed through additional ports (working ports). There are instruments available to retract, dissect, cauterize, and suture tissues. Hemostasis is obtained by a variety of techniques, including ligation, clips, stapling devices, cautery, and ultrasonic coagulation. Specimens are removed directly through the ports or after placement in a protective bag to avoid contamination. If needed, a port incision can be slightly enlarged to allow removal of the specimen. There are now 3 mm ports available with similarly sized instruments so that these procedures can be routinely performed in 2 kg to 3 kg babies.

Despite the advances in technology, there is still some controversy about the advantages of laparoscopy in children. The advantages described in the early reports of minimally invasive

surgery in adults included a shorter post-operative course, less pain and scarring, and no muscular damage from the standard open incisions. Resistance to this approach in children was mainly because open surgery requires small incisions in children as a rule, analgesic requirements are minimal for children, and they recover from major procedures and return to full activity quickly even with open procedures.²

In a paper by Rangel, et al,³ the 3 most common laparoscopic procedures performed in children were reviewed, namely appendectomy, fundoplication, and splenectomy. They found that due to the retrospective nature of the reports available, improvement in outcomes could not be proven in the pediatric population. They did note that the benefits have been definitely proven in adult patients through the use of randomized trials and meta-analysis. They felt that if these types of papers were available, the benefits in children might be proven as well.

Laparoscopic appendectomy

Appendicitis is the most common abdominal condition requiring surgery in children, accounting for over 320 000 operations per year in the United States.⁴ Despite improved access to medical care, a significant portion of these patients present with advanced disease and therefore incur increased morbidity. This is especially true of the youngest patients.



Photo by Steve Evans

Laparoscopy at Children's Memorial Hospital

In the past decade, over 870 laparoscopic procedures for a wide range of pediatric conditions have been performed at Children's Memorial, including:

- Laparoscopic appendectomy (approx. 200)
- Laparoscopic splenectomy (approx. 95)
- Laparoscopic Nissen fundoplication (approx. 75)
- Laparoscopic pyloromyotomy (approx. 55)
- Laparoscopic pull-through procedures for Hirschsprung disease (approx. 40)

Children's Memorial surgeons also have extensive experience with laparoscopic procedures for gynecological and urological disorders in children.

In the photo: Mary Beth Madonna, MD, and Srikumar Pillai, MD, perform laparoscopic Nissen fundoplication on an infant weighing less than 10 pounds.

Antibiotic therapy and appendectomy have been the mainstays of treatment for many decades. Ure⁵ reported the first laparoscopic appendectomy in a child in 1991. A decade later in a survey of North American pediatric surgeons,⁶ 31.3% of surgeons used the laparoscopic technique frequently or always and an additional 29.4% used it occasionally.

Open appendectomy is performed using a right lower quadrant incision and splitting the muscles of the abdomen. The appendix is then brought into the incision, the blood supply ligated, and the appendix removed. The laparoscopic approach generally uses 3 small incisions ranging from 5 mm to 12 mm with 1 of the small incisions being concealed in the umbilicus. The appendix and blood supply are separated, then ligated with a stapling device, clips or cautery. The appendix is then brought out through a port, usually in a protective bag to prevent contamination with bacteria.

In a study of 103 children,⁷ laparoscopic appendectomy was feasible in all stages of acute appendicitis, including perforation. The laparoscopic technique took slightly longer and there was an increased operative cost. There were fewer overall complications and infectious complications in the laparoscopic group. A single blinded randomized clinical trial comparing the 2 techniques for non-perforated appendicitis in 61 children found that pain scores were lower and the length of stay was shorter in the laparoscopic group.⁸

In another report comparing laparoscopic and open appendectomies in 391 children,⁹ there was no statistically significant difference in post-operative pain medication usage, operative, or post-operative complications. The length of hospitalization was significantly shorter in the laparoscopic group.

Most surgeons who perform minimally invasive surgery feel that it is an equal or better option for the patient and in most cases has been associated with shorter hospital stays, lower analgesic requirements, more rapid return to activity, and better cosmesis.

In the largest pediatric report to date including 1379 children treated laparoscopically, El Ghoneimi et al,¹⁰ found an incidence of 2.1% of intraoperative complications, such as insufflation of the omentum, visceral perforation, and appendiceal rupture. Post-operative complications were also very low (1.5%) and included bowel obstructions, wound infection and abscesses. When he further reviewed the data these complications occurred only in the group of patients with perforated appendicitis, and are comparable, if not lower, than with open appendectomy for perforated appendicitis.

Laparoscopic pyloromyotomy

Infantile hypertrophic pyloric stenosis is a common condition causing vomiting in infancy, with an incidence of 1 to 3 per 1000 live births.¹¹ The operation still used today was described by Ramstedt in the early 1900s.¹² The hypertrophic muscle is split leaving the mucosa intact and allowing gastric emptying. This operation has been performed countless times with a high rate of success, low rate of complications, and short operative time. In the early 1990s a laparoscopic alternative to this procedure was described by Alain.¹³ This approach uses the same principles as the Ramstedt procedure, but uses an arthroscopic knife to split the muscle and 2 additional 3 mm ports. The laparoscopic approach offers improved cosmesis.

Hall, et al,¹⁴ did a retrospective comparison of the open and laparoscopic approaches at their institution and concluded that there were similar complication rates and recovery times, but no clear benefit of either approach over the other. In a large series of 457 patients from a single institution,¹⁵ there was an equal overall complication rate with a higher degree of mucosal perforation (3.6% vs. 0.4%) in the open group and a higher incidence of incomplete pyloromyotomy in the laparoscopic group (0 vs. 2.2%). Hall, et al,¹⁶ also performed a meta-analysis of the literature available on the 2 approaches, which included 595 patients and showed no difference in mucosal perforation rates, but a higher incomplete pyloromyotomy

rate in the laparoscopic group (1.6% vs. 0.2%). There was a significantly shorter time to full feeds and length of stay in the laparoscopic group.

At present, the laparoscopic approach seems to be an option for treatment of this disease, but without a distinct advantage. This is in contrast to the next procedure described.

Laparoscopic splenectomy

Splenectomy is indicated in children with spherocytosis, refractile thrombocytopenia, storage diseases, hereditary anemias, and tumor. In the standard approach for splenectomy a midline or left upper abdominal incision is used in order to gain access to the blood supply to the spleen. This involves cutting the abdominal muscles. The anatomy of the spleen makes it quite amenable to the laparoscopic approach, thereby avoiding the more painful open incision. Four ports are routinely used and the blood supply is controlled most commonly using a stapling device. A protective bag is used to remove the spleen in piecemeal fashion to prevent spillage of the contents and possible splenosis. Accessory spleens are searched for in either approach to assure a complete operation.

In a comparison between the 2 approaches in 51 children who underwent splenectomy,¹⁷ 35 patients were treated laparoscopically and the remainder by the open technique. There was no difference in blood loss during the procedures or in hospital costs, but the laparoscopic group had a significantly shorter hospital stay.

In a case controlled study, Rescorla, et al,¹⁸ found that the laparoscopic group had less narcotic use and shorter length of stay with a comparable complication rate, and therefore in a subsequent study¹⁹ concluded that laparoscopic splenectomy is the gold standard in children.

Laparoscopic fundoplication for gastroesophageal reflux

Gastroesophageal reflux disease (GERD) is a common problem in the pediatric population. Carré²⁰ noted the natural history of GERD in children in a retrospective study. Most children are managed with medication and feeding

changes, but those who fail these therapies may be considered for surgical intervention. In addition, those with more serious sequelae, such as aspiration pneumonia, “near” sudden death episodes, wheezing, or choking may be considered for early surgical treatment.

To confirm reflux, the gold standard is the pH probe, which documents the reflux events. In addition, most surgeons would like an upper gastrointestinal study prior to any operative intervention to confirm normal anatomy. GERD must be differentiated from the normal “spitting up” that occurs in most infants. Endoscopy, esophageal manometry and gastric emptying studies may also be used to guide therapy.

Reflux disease is caused by failure of the lower esophageal sphincter, a short intraabdominal esophagus and/or an abnormal angle of His. A fundoplication, which wraps a portion of the fundus of the stomach around the esophagus, creates an artificial anti-reflux valve. The Nissen fundoplication is a 360° wrap. The open technique requires either an upper midline incision, or a left upper transverse incision. The laparoscopic procedure uses 5 small incisions. The fundoplication is fashioned with sutures and intracorporeal knot tying. A diaphragmatic crural repair is also performed to prevent the wrap from migrating into the chest causing a hiatal hernia.

In a study by Ostlie and Holcomb,²¹ 154 children who had laparoscopic Nissen fundoplication were studied. Only 2 patients had recurrent symptoms and only 1 required reoperation. The adult literature reports satisfaction rates of 85% to 100% after laparoscopic Nissen fundoplication and only one-third of failures require a second operation. In a long-term follow-up study of children undergoing a laparoscopic Nissen fundoplication, 66% of patients had complete relief, 26% had considerable improvement and only 2% had documented recurrent reflux with a median follow-up of 3 years. In addition, 92% of parents surveyed were happy with the results and would have their child undergo the procedure again.²² In comparison, Subramaniam²³ studied the long term outcome in children undergoing the open fundoplication and found 3.5% early recurrence. Most families felt the results were good and some were delighted, but there was no follow-up on 40% of the patients.

Laparoscopic pull-through procedures for Hirschsprung disease

Hirschsprung disease is a functional distal bowel obstruction caused by aganglionosis in the rectum and a variable length of proximal bowel. Patients were previously treated with colostomy, as the etiology of the disease was unknown. In 1948, Swenson performed the first operation for definitive treatment of Hirschsprung disease and reported on 50 cases.²⁴ Two subsequent open procedures – the Soave and the Duhamel – are commonly performed today.

These procedures were initially staged (diverting colostomy first) and then performed as a 1-stage procedure through a left lower abdominal incision with a transanal anastomosis. To spare the lower abdominal incision, 3 or 4 ports (3 mm to 5 mm) may be used in the neonate to dissect the colon and ligate the blood supply to the aganglionic bowel that is to be removed. The transanal anastomosis is performed as before.

In 1995,²⁵ the first 1-stage laparoscopic pull-through procedure was reported. Raffensperger published the first report of a Swenson procedure performed laparoscopically at Children’s Memorial Hospital in 1996.²⁶ In this report 8 laparoscopic procedures were compared to 10 open procedures, and there was decreased time to oral intake and discharge in the laparoscopic group.

Georgeson, et al,²⁷ have the largest report of the laparoscopic endorectal (Soave) pull-through to date with 80 patients. There were 4 patients that required diversion at a later time for enterocolitis or anastomotic leak. Only 20 patients were old enough to assess continence and of those 18 were continent and 2 had overflow incontinence.

Summary

With advances in technology, minimally invasive surgery is a viable option for many procedures in our smallest patients. In addition to those procedures discussed here, laparoscopic options are available for lung resections, pancreas and adrenal surgery, esophageal and bowel surgery and almost limitless other areas. Most surgeons who perform minimally invasive surgery feel that it is an equal or better option for the patient and in most cases has been associated with shorter hospital stays, lower analgesic requirements, more rapid return to activity, and better cosmesis. ■

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Eosinophilic Esophagitis in Children

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Eosinophilic esophagitis (EE) is a newly recognized clinicopathological disorder. It is the fastest rising diagnosis in pediatric gastroenterology practice at Children's Memorial Hospital. This disorder is frequently misdiagnosed and treated as severe gastroesophageal reflux disease (GERD). Clinicians should suspect EE when GERD symptoms fail to respond to aggressive acid suppression treatment. Symptoms dramatically improve, however, with elimination diet or with corticosteroid treatment. Prompt referral by primary care physician is essential to establishing the correct diagnosis and instituting appropriate treatment expediently to relieve symptoms and prevent complications.

EE is a chronic inflammatory disorder that is characterized by dense infiltration of the esophageal epithelium. This condition is categorized as a food hypersensitivity disorder. Generally, food hypersensitivity disorders are subdivided into:

- Type 1 immediate or immunoglobulin E (IgE)-mediated disorders diagnosed with radioallergen sorbent (RAST) test or skin prick tests
- Type 4 delayed or cell-mediated disorders identified with skin patch test

EE may be classified either as IgE-mediated or cell-mediated condition, or both, depending on the operative mechanism.

The dramatic rise in the number of children diagnosed with this condition, all over the country, is partly explained by increased awareness and partly by a true increase in prevalence. At Children's Memorial the number of children newly diagnosed with EE has progressively risen from only 1 case in 2000 to more than 50 in 2004.

Etiology

Support for an allergic etiology of EE is provided by:

- Associated atopic manifestations, such as reactive airway disease, allergic rhinitis and eczema, which are present in 50% of children with this disorder
- Family history of atopic disease obtained in up to 45% of children with EE
- Environmental allergies suggested by animal experimental data

Genetic predisposition is supported by findings that 10% of patients have an immediate family member affected with EE.

Clinical characteristics

This disorder is seen in all races, with a male to female ratio of 4:1. Two peaks at 1 to 4 years of age and 10 to 14 years of age have been identified. In addition to other atopic conditions, history of food allergies and peripheral eosinophilia is often present.

In younger children, symptoms are similar to those seen with GERD and include vomiting, dysphagia, abdominal pain, chest pain, and failure to thrive. These symptoms do not completely resolve with acid suppression treatment and these patients are referred to gastroenterologist for refractory GERD or to a surgeon for fundoplication. We have also encountered toddlers with EE presenting with significant food aversion as the primary manifestation. In adolescents, intermittent episodes of distress causing food impaction that

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Recognize the differences between eosinophilic esophagitis (EE) and gastroesophageal reflux disease
- Identify cases that warrant an evaluation for EE
- Describe the diagnostic features of EE and different treatment approaches



FIGURE 1: *Normal Esophagus*



FIGURE 3: *White Plaques*



FIGURE 5: *Granular*

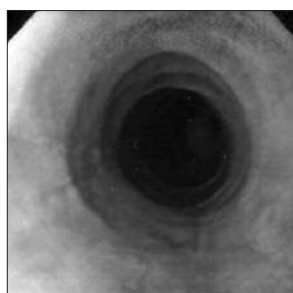


FIGURE 2: *GERD*

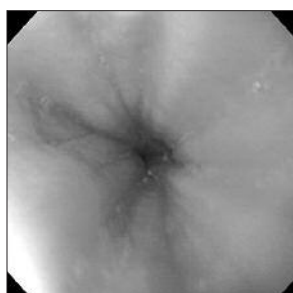


FIGURE 4: *Furrowing*

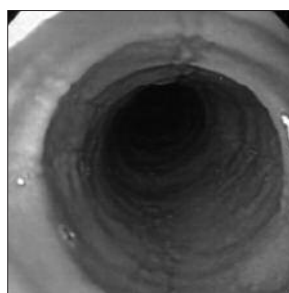


FIGURE 6: *Ringed*

leads to emergency room visits to have food dislodged is not an uncommon presentation.

Diagnosis

Endoscopy images of the normal esophagus and a case with GERD (Figures 1, 2) differ significantly from the several distinctive appearances of the esophagus that suggest EE (Figures 3-6):

- Multiple white plaques in the esophagus
- Furrowing: longitudinal linear creases or folds along the long axis of the esophagus
- Granular esophagus with multiple tiny nodules
- Trachealization or ringed esophagus, which is when the esophagus has the appearance of the trachea
- Tubular esophagus with a long mid-esophageal stricture

Ringed or tubular esophagus is commonly seen in adolescents and adults with EE. By contrast in GERD, erythema, erosions or ulcerations are seen.

Endoscopy findings are not diagnostic of EE, however. The gold standard for the diagnosis of EE is the dense infiltration of eosinophils, with at least 20 eosinophils per high power field

(hpf) in the esophageal biopsies. In GERD, eosinophilic inflammation is also present, but the eosinophil count rarely exceeds 7 to 10 eosinophils per hpf. Other findings, such as basal cell hyperplasia and increased papillary length are seen in both EE and GERD, but eosinophilic abscesses (4 or more eosinophils in superficial clusters) are typically seen only in EE and distinguish EE from GERD. The differences between EE and GERD are summarized in Table 1.

Complications

Since it is now only 10 years since the description of the first pediatric case series of EE, the natural history of this disorder in children is unknown and remains to be defined. Since 4% to 6% of children with EE present with stricture of the esophagus, it is felt to be a complication of persistent esophageal inflammation. Although links between EE and dysplasia have not been described, concerns about this possibility remain, since long term follow-up data is currently unavailable.

Investigations

A 24-hour pH probe study is helpful to exclude GERD, particularly in the younger children with reflux-type symptoms. A number of studies have utilized results of positive RAST, skin prick tests, and skin patch tests to eliminate the specific incriminating food allergen(s) from the diet. Elimination of food antigen based on the results of RAST and skin prick tests,

Table 1**CLINICAL AND DIAGNOSTIC FEATURES OF GERD VS. EE**

Features	GERD	EE
Vomiting and abdominal pain	Common	Common
Dysphagia and food impaction	Uncommon	Common
Atopy	No	Yes
Food allergies	No	Yes
Sex	Male and female	Male 4:1
pH probe study	Abnormal	Normal
Esophageal erythema	Yes	No
Esophageal furrowing	No	Yes
Esophageal mucosa	Erosion	Increase
Eosinophils in esophagus	0-7 eos/hpf	>20 eos/hpf
Eosinophilic abscess	No	Yes

however, has failed to improve symptoms, suggesting that the food allergy is not primarily IgE-mediated.

A recent study of food elimination based on positive response to a combination of skin prick and skin patch tests reported significant clinical and histological improvement in all EE patients. The mechanism responsible for causing allergen induced esophageal inflammation appears to be cell-mediated hypersensitivity from this study.

Management

Treatment of EE is challenging to the physician and difficult for the patient and family. The goals of treatment include resolution of symptoms and of the esophageal inflammation, and prevention of complications, such as strictures.

The most commonly utilized dietary approach eliminates all intact protein by administering an amino acid-based formula. This approach is highly effective, although compliance difficulties related to poor taste are overcome, in a majority of patients, with either nasogastric or gastrostomy tube feeding. Furthermore, these elemental

formulas are quite expensive, and the prospect of eliminating all solid foods from the child's diet is distressing to families.

At Children's Memorial, we have developed a new dietary approach that eliminates the 6 most common foods responsible for food allergies. These include milk protein, soy, wheat, egg, peanut (and all tree nuts), and all sea food. We have recently demonstrated that both symptom resolution and mucosal healing with elimination diet are comparable to that with amino acid-based elemental diet. The evident advantages include ability to eat solid foods, lack of tube feeding, and lower cost. The limitation of this approach is that it requires participation of an experienced dietitian to counsel families on proper diet implementation and prevention of repeated contamination due to the ubiquitous use of these food proteins in processed foods. Once the esophageal inflammation resolves, foods are re-introduced singly every 6 weeks until the offending food allergens are identified and excluded permanently. (Figures 7, 8 show the change in eosinophilic infiltration before and after the elimination diet.)

The gold standard for the diagnosis of EE is the dense infiltration of eosinophils, with at least 20 eosinophils per high power field (hpf) in the esophageal biopsies.

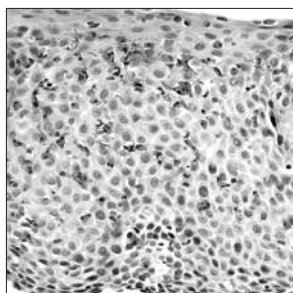


FIGURE 7:
Pre-elimination diet biopsy

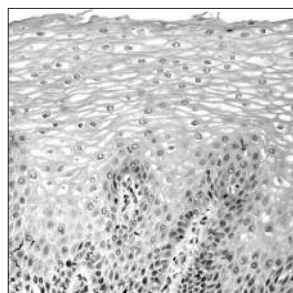


FIGURE 8:
Post-elimination diet biopsy

Images courtesy of Hector Melin-Aldano, MD, Pathology

Corticosteroids, swallowed or systemic, are also effective, but both symptoms and inflammation recur once treatment is discontinued. Since long term steroid use is associated with potential side effects, including candidiasis and suppressed linear growth, and because steroids are only palliative, at Children's Memorial we prefer the dietary approach, reserving corticosteroids for cases that are resistant to elimination of food allergens.

Resources for families of children with EE

For EE information and support resources, families can be referred to the American Partnership for Eosinophilic Disorders (www.apfed.org) and the Food Allergy Network (www.foodallergy.org).

Also, the Food Allergen and Consumer Protection Act, which goes into effect January 2006, will require manufacturers of all foods, flavorings and spices to identify on the label 8 food antigens – milk protein, egg, soy, peanut, tree nut, wheat, seafood, and shell fish. This law will make it extremely easy for patients with EE to know whether these allergens are present in products and avoid the restricted food antigens.

Summary

A high index of suspicion of EE is necessary to identify children with refractory GERD symptoms resistant to acid suppression treatment, male toddlers with food aversion, or adolescents presenting with food impaction. These children should be referred to pediatric gastroenterologist for endoscopy and esophageal biopsies. History of food allergies and atopic disease, such as asthma, allergic rhinitis, and eczema, as well as unexplained peripheral eosinophilia, are additional risk factors that should heighten suspicion of EE. GERD is the main differential diagnostic consideration and should be excluded. Treatment is challenging, and the dietary elimination/reintroduction approach is preferred. ■

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Bipolar Disorder in Pediatrics

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Bipolar disorder (formerly called manic-depressive disorder) has become increasingly recognized in children and adolescents. It occurs even in preschool-aged children, although this is very rare. Prior to mid-adolescence, bipolar disorder manifests differently from the adult-onset type, and it can be mistaken by pediatricians for attention-deficit/hyperactivity disorder (ADHD). Differentiating these conditions is complicated by very high comorbidity of ADHD with pediatric bipolar disorder.¹ Some symptoms of mania, such as hyperactivity and distractibility, overlap with ADHD, which contributes to misdiagnosis and inappropriate treatment. This review will discuss the presentation of mania in this age group, to help community physicians consider mania in the differential diagnosis of ADHD and in evaluation of children with poor response to ADHD medication. Children with suspected bipolar disorder will need child psychiatric referral for diagnosis, initial stabilization and treatment.

Clinical features

Recently issued consensus guidelines for diagnosis and treatment of pediatric bipolar disorder describe a presentation of the illness that is distinct from the manifestation in adults.¹ In children, the disorder typically appears as frequent, intense mood swings and irritability occurring daily for months to years, or as a chronic mixed state, with features of both mania and depression. To help identify the presence of mania in children, the guideline recommends the “FIND” framework for symptom thresholds:

- **Frequency:** symptoms occur most days in a week
- **Intensity:** symptoms are severe enough to cause extreme disturbance in 1 domain or moderate disturbance in 2 or more domains
- **Number:** symptoms occur 3 or 4 times a day
- **Duration:** symptoms occur 4 or more hours a day, total, not necessarily contiguous

It is useful to focus on recognizing 5 symptoms of pediatric mania that do not overlap with ADHD – euphoric mood, grandiosity, decreased need for sleep, racing thoughts, and

hypersexuality.² Most child psychiatrists believe that these symptoms should represent a change from the child’s previous condition. Descriptions of these manic symptoms below will also help to distinguish mania from normal childhood behaviors. The diagnosis of bipolar disorder requires an elevated, expansive or irritable mood plus several additional symptoms.

Euphoric mood: To differentiate pathologically elated mood from a child’s normal expression of excitement or giddiness, many examples that include context are needed to determine inappropriateness of behavior and associated impairment. For instance, a child’s exuberance on Christmas morning is appropriate to context, whereas extreme silliness with no apparent precipitant that does not respond to intervention by parent or teacher would be impairing and would be considered pathologically euphoric mood.

Grandiosity: Similarly, context must be considered in identifying pathological grandiosity. It is crucial to ascertain that a child can separate fantasy from reality. An example of age-appropriate play would be a 7-year-old boy pretending to be a firefighter directing other firefighters while playing with

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Differentiate symptoms of possible pediatric bipolar disorder from attention-deficit/hyperactivity disorder (ADHD)
- Recognize medical conditions that may mimic mania and medications that may increase mood cycling
- Identify cases that need referral for evaluation and initial stabilization and treatment

friends after school. If the boy believed himself to be a firefighter and kept calling the fire station to tell them what to do, this would exceed normal imaginative play. Grandiosity can lead children to dangerous activities, when they believe they cannot be harmed or are able to fly.

Decreased need for sleep: This is a symptom of mania when, for a period of time, a child sleeps much less than usual without any signs of fatigue or naps on the following day. In contrast to children with insomnia due to anxiety or depression, who are distressed by not being able to sleep, manic children will get up and energetically engage in pleasurable activities.

Racing thoughts: To establish this symptom, a child should be asked if his or her thoughts seem to be moving too fast. Children often will use concrete language to describe this experience, such as “I need a stoplight up there.”

Hypersexuality: With this symptom, sexual abuse or exposure to adult sexual activity needs to be ruled out first. Manic hypersexuality must be distinguished from normal age-appropriate curiosity, such as first graders playing doctor. Examples of excessive behavior would be a 7-year-old girl touching the teacher’s breasts and propositioning boys in her class, or a boy attempting to open-mouth kiss his mother.

Other less specific symptoms of mania include irritability, pressured speech, distractibility, increased goal-directed activity, psychosis, and suicidality. It is especially critical to screen all children with suspected bipolar disorder for suicidal ideation, intent, and plans, since these patients are at extremely high risk for suicide. It is also important to remember that irritability, mood lability, and low frustration tolerance can be present in more severe cases of ADHD, oppositional defiant disorder, post-traumatic stress disorder, anxiety disorders, autism spectrum disorders, or language delays. Dysregulated mood plus severe behavior problems do not automatically signal bipolar disorder.

Bipolar disorder is familial, and a family member diagnosed with bipolar disorder should raise the index of suspicion. It is important to keep in mind that prepubertal children with major depressive disorder are at risk for developing bipolar disorder, especially if they have a family history of mania.³ The role of antidepressant medication in triggering mania or unmasking latent bipolar disorder remains controversial. In any case, the possibility of switching to mania and a description of prepubertal manic symptoms should be made clear to parents of a depressed child, to aid early identification of children with bipolar disorder.

In addition to antidepressants, medications that may trigger symptoms of mania or increase mood cycling include stimulants

used to treat ADHD, some antibiotics (eg, clarithromycin, erythromycin, amoxicillin), sympathomimetic amines (eg, pseudoephedrine), corticosteroids, and aminophylline.¹ A washout period for up to 3 weeks will help clarify whether manic symptoms were related to medication.

Other medical conditions also may mimic a presentation of mania in children. These include temporal lobe epilepsy, hyperthyroidism, closed or open head injury, multiple sclerosis, systemic lupus erythematosus, alcohol-related neurodevelopmental disorder, and Wilson’s disease.¹ Substance abuse can either mimic bipolar disorder or precipitate mania or depression. In post-pubertal patients with suspected bipolar disorder, a careful history from parent and youth about possible substance use and a urine drug screen are indicated.

Referral

Since diagnosis and initial stabilization of bipolar disorder in children can be particularly challenging and often complicated by comorbid disorders, patients who present with manic symptoms should be referred to a child psychiatrist for definitive diagnosis and treatment. ADHD is the most common disorder comorbid with childhood bipolar disorder. Other common psychiatric comorbidities include oppositional defiant disorder, conduct disorder, anxiety disorder, and substance abuse. The differential diagnosis includes all these disorders, plus post-traumatic stress disorder and other forms of psychosis. Learning disorders, especially in expressive and receptive language, are common. Bipolar disorder symptoms will need to be stabilized before treatment for comorbid conditions is attempted.

If a child with ADHD treated with stimulants suddenly develops manic symptoms, stimulants should be discontinued and re-evaluation made in 7 to 10 days. If mania persists, an urgent referral is needed. Patients with a poor response to ADHD medication or a worsening course also need a referral. In depressed children or adolescents, pediatricians should suspend treatment with antidepressants if manic symptoms appear, and refer these patients immediately.

Children with suspected bipolar disorder may need urgent care, and if the problem is acute, hospitalization may be required. At Children’s Memorial Hospital, pediatric mental health professionals are available to the emergency department 24 hours, 7 days a week. An outpatient Urgent Care Program accommodates patients with acute symptoms who do not require hospitalization. The inpatient and day hospital programs admit youth with the most severe and disabling symptoms for acute stabilization and initiation of treatment.

Treatments

The primary treatment is medication. For bipolar disorder without psychosis, the new guidelines recommend as first-line treatment monotherapy with a traditional mood stabilizer (lithium, divalproex, or carbamazepine) or an atypical antipsychotic (olanzapine, quetiapine, or risperidone).¹ Lithium or divalproex were recommended as the first medication choice, and if no response is seen, another monotherapy agent is selected. An important potential advantage of lithium is its association with an eightfold decrease in suicide and reported attempts in adults with bipolar disorder.⁴ If there is partial response with a first choice monotherapy agent, augmentation with another mood stabilizer or atypical antipsychotic is suggested.

Far too little research has been done on the treatment of bipolar disorder in youth, and the detailed treatment algorithms in these guidelines represent a consensus based on existing research results (primarily in adults) and clinical experience with children and adolescents. At this stage, lithium is the only medication that is FDA-approved for pediatric bipolar disorder, for patients 12 years of age and older. Divalproex is approved for seizures in children aged 2 years and older, and carbamazepine is approved for seizures at any age. Olanzapine, quetiapine, and risperidone currently are not approved for use in patients less than 18 years of age.

Once the child has been stabilized, there is growing evidence of the usefulness of psychoeducational therapy for the patient and family, based on cognitive-behavioral and family intervention techniques and provision of information about the disorder.

Prognosis

Since recognition of pediatric-onset bipolar disorder and its distinct presentation are relatively recent, it is not certain at this point whether it will evolve into an adult type of bipolar disorder. The condition in children appears to be chronic, however, and these patients are at high risk of relapse. Optimal maintenance strategies have yet to be established by research. In the meantime, the guidelines suggest that medication may be tapered or discontinued after remission for 12 to 24 consecutive months. Many children with bipolar disorder, however, may require lifelong medication.

Potential side effects of medications

Weight gain is associated with many medications used to treat bipolar disorder in children. Given the medical consequences of childhood obesity, such as development of type 2 diabetes and changes in lipid levels, weight should be monitored closely and parents alerted to detect early symptoms of diabetes. Exercise and nutritional counseling may be helpful preventive measures.

Pediatricians also should watch for possible hypothyroidism associated with lithium, and polycystic ovary syndrome in connection with divalproex. A rare, but serious pancreatitis in relation to divalproex also has been reported (almost completely restricted to children less than 5 years of age, on multiple anticonvulsants). Any of the atypical antipsychotic medications can cause prolactin elevation and intracardiac conduction changes can be seen with ziprasidone. All antipsychotics can cause abnormal involuntary movements or neuroleptic malignant syndrome.

Summary

It is important to remember that bipolar disorder does occur in children and adolescents and should be considered in complicated or severe cases of apparent ADHD or depression. A pediatrician could provide maintenance medication management, in collaboration with a psychologist or social worker who is expert in bipolar disorder. Initial diagnosis and initiation of treatment require a child and adolescent psychiatrist. Urgent consultation or even hospitalization may be needed. ■

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Bacterial Rhinosinusitis in Children

ILANA SELIGMAN, MD, FACS, FAAP

Rhinosinusitis (RS) in children can present a diagnostic dilemma for practitioners. Viral upper respiratory infection (URI) is the most common entity seen by primary care doctors, and recent data states that 5% to 10% of URIs in children are complicated by RS.¹ Proper diagnosis of bacterial RS is important in establishing the need for treatment. Viral URI and allergic inflammation need to be differentiated from a sinus infection to avoid unnecessary antibiotics and continued increases in community-wide bacterial resistance.

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Describe the pathophysiology of bacterial sinusitis in children
- Name the predominant organisms responsible for sinusitis and the antibiotics recommended for treatment
- List the orbital and intracranial complications of bacterial sinusitis in children

The peak incidence of bacterial RS occurs between the ages of 3 and 6 years, similar to the peak years for URIs.² Children average 6 to 8 colds a year (more in day care and with multiple siblings), and unless complicated by bacterial RS, these self-limited infections should resolve within 7 to 10 days.³

Allergic rhinitis is an inflammation of the mucous membranes of the nose, whereas RS is an inflammation of the mucous membranes of the nasal passages and sinuses. Nasal allergies cause itching and sneezing, clear rhinorrhea, stuffiness, and postnasal drainage. These symptoms are similar to those of RS and a common cold. Complete history and physical exam, and often accompanying imaging help make the correct diagnosis. Allergies also can contribute to swelling in the sinus and nasal mucous membranes. The swelling can lead to blockage of the natural openings, trapping bacteria and leading to infection.

There is controversy surrounding treatment, despite the fact that RS has a significant adverse effect on health related quality of life. Many practitioners feel that the disease process is self-limited, rarely needs antibiotic therapy and almost never requires surgical treatment. Others believe that these infections require aggressive medical therapy and surgical treatment when medical therapy fails. The answer is somewhere between these viewpoints, and it is essential to consider each case individually to avoid serious complications.

Definitions

Sinusitis is an infection of the mucosa of the paranasal sinuses. **Rhinosinusitis** is a better term than sinusitis alone, since inflammation and infection of the sinuses involves changes in the nasal epithelium with concurrent nasal airway inflammation. RS is generally divided into 3 varieties: **acute, chronic, and recurrent.**

Acute RS commonly presents as a URI that persists beyond 10 days with some combination of the following signs and symptoms: purulent rhinorrhea, persistent cough that is often worse at night, bad breath, fever, headache, and facial pain. Since most viral URIs resolve within 10 days, a worsening or persistence of these symptoms beyond this time has been empirically viewed as RS by practitioners for the purpose of prescribing antibiotics. Acute bacterial RS that is severe may present with the same symptoms, but is accompanied by greater toxicity, fever greater than 102.2° F, and the duration of symptoms observed may be less than 10 days. This is a less common presentation and can only be objectively differentiated from an acute viral URI with a CT scan or plain films.

Chronic RS is an infection of greater than 3 months duration, usually with a more benign course. Symptoms include nasal congestion, cough, bad breath, malaise, decreased energy, headache, behavioral problems, and nasal discharge. Exacerbation to acute RS is common in children with chronic RS.

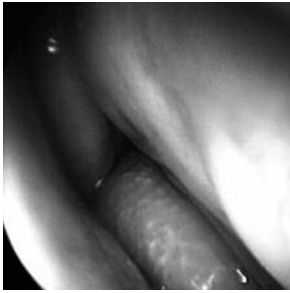


FIGURE 1: *Typical nasal polyp seen through a nasal telescope.*

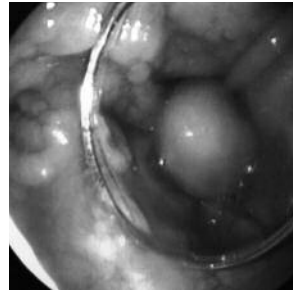


FIGURE 2: *Sphenoidal polyp in the nasopharynx visualized with a mirror in the oral cavity. This is an unusual presentation that can occur with chronic RS.*

Recurrent acute RS occurs when a child has complete resolution of an acute infection, but has repeated incidents. Some element of chronic RS is likely to be present between acute infections, but this cannot be determined without imaging.

Pathophysiology

Human beings have ethmoid sinuses on either side of the upper nose, bilateral maxillary sinuses in the face between the orbital rim and the upper teeth, and frontal sinuses above the eyes. The sphenoid sinus is in the back of the nose, at the base of the skull, and is divided by a septum. Because of its relative isolation, the sphenoid sinus is the least likely sinus to become infected.

The mucus membrane of each sinus has cilia that move the mucus to the sinus ostia for clearance through the nose. Maxillary drainage involves a cilia-dependent upward movement that joins the drainage of the anterior ethmoid air cells in a functional unit called the ostiomeatal complex. This area is believed to be the focus of edema during a viral illness, resulting in obstruction of the maxillary, frontal and anterior ethmoid drainage.

The failure of normal mucus transport (mucociliary transport) and decreased sinus ventilation are the major factors contributing to the development of RS. Obstruction of the sinus ostia occurs with mucosal edema or anatomic blockage, such as polyps, interfering with sinus drainage. Polyps are a common product of chronic allergic RS (Figures 1, 2). Noninfectious inflammation, such as allergic rhinitis can also block the ostia and lead to RS.

Cilia can beat only in a fluid medium. Alteration of cilia number, morphology and function may facilitate secondary bacterial invasion of the nose and sinuses. In addition to viral URI and

allergic inflammation, factors predisposing the formation of bacterial RS include, adenoid hypertrophy and infection, cystic fibrosis, immune disorders (especially IgG subclass deficiency), primary ciliary dyskinesia, trauma, swimming and diving, rhinitis medicamentosa, choanal atresia, deviated septum, nasal polyps, foreign body, tumor, dental infections, inhalation of irritants, mechanical ventilation, nasal dryness, nasotracheal and nasogastric tubes, and gastroesophageal reflux disease (GERD).

Diagnosis

On physical exam, the patient with acute bacterial RS may have mucopurulent discharge in the nose or posterior pharynx, with an erythematous nasal mucosa, but this can occur with acute viral rhinitis as well. Transillumination may be helpful in adolescents and adults, but does not tell much in children under 10 years of age, since frontal sinuses are not yet fully developed. In young children, the physical exam is generally not very helpful for making a specific diagnosis of acute bacterial RS. Although otolaryngologists may decongest the nose and use a telescope to view pus coming directly from the middle meatus, this is not practical for pediatricians.

One sign that does not predict acute bacterial RS is rhinorrhea that changes color from clear to cloudy or colored. This event coincides with migration of polymorphonuclear leukocytes into nasal secretions and occurs during the natural course of viral URIs.

All children with persistent RS should be evaluated for allergies to assess the role they play in the etiology. Therapy then can be directed towards decreasing the allergic response.

Getting culture from nasal discharge, the throat, or the sinus is not necessary for diagnosis of bacterial RS. Culture of nasal discharge or the nasopharynx lacks predictive reliability, both for establishing the diagnosis and for identifying the infective pathogen when acute bacterial RS is actually present. Organisms recovered from nasopharyngeal washing and throat culture do not reflect the organisms found in sinus aspirate.

Needle puncture of the maxillary sinus to get a culture is impractical and unnecessary in immunocompetent children with uncomplicated disease, and should be reserved for special circumstances. It is reasonable to get a culture of the sinus under controlled conditions in the operating room when a patient is not responding to antibiotics, is immune suppressed, or beginning to show signs of complications.

The radiographic finding most diagnostic of bacterial RS is an air-fluid level in, or complete opacification of the sinus cavities. Standard radiographic projections include anteroposterior, lateral



FIGURE 3: Moderate bilateral maxillary sinus mucosal thickening with blockage of both osteomeatal complexes in a coronal CT scan.

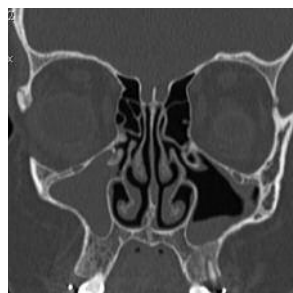


FIGURE 4: Complete opacification of the right maxillary sinus in a coronal CT scan.

and occipitomeatal (Waters projection) views. Complete opacification in a plain radiograph in a symptomatic patient has a specificity of 85%, and an air-fluid level has a specificity of 80% in establishing the diagnosis. When clinical signs and symptoms suggesting acute RS are accompanied by abnormal maxillary sinus films, bacteria in a sinus aspirate will be present 70% to 75% of the time.⁴

Computed tomography (CT) scans (Figures 3, 4) are the best way to view the extent of disease and are reserved for children with chronic RS, acute RS unresponsive to therapy or for evaluation of complications. Limited coronal views without contrast will provide information and use the least amount of radiation, however these studies may not be as sensitive in identifying the osteomeatal complex.

However, CT scans can overdiagnose RS. In a study of infants and children, 97% of patients who had a cold during the 2 weeks preceding cranial CT performed for other purposes had mucosal abnormalities suggesting bacterial RS.⁵ Abnormalities of the sinuses also are found frequently on conventional radiographs and CT scans in children without clinical evidence of sinusitis. MRI is not the best imaging modality for evaluation the bone/mucus membrane interface of the sinuses.

The American College of Radiology has taken the position that the diagnosis of acute uncomplicated RS in children, especially if they are less than 6 years of age, should be made on clinical grounds alone, since the films are technically difficult on young children, and images should be reserved for worsening clinical circumstance.⁶ Similarly, the Subcommittee on Management of

Sinusitis and Committee on Quality Improvement of the American Academy of Pediatrics stated that imaging studies are not necessary to confirm a diagnosis of clinical sinusitis in children less than 6 years of age.⁷ They did not make a recommendation for older children, leaving open the possibility that imaging may be necessary in this age group.

Microbiology

Children and adults have similar RS bacteriology. The predominant organisms include *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and *Hemophilus influenzae*, found in approximately 75% of maxillary sinus aspirates. Both *H influenzae* and *M catarrhalis* may produce beta-lactamase and are amoxicillin resistant.

The role of bacteria in chronic RS is controversial, since there may be disease in the absence of bacterial growth, as described below. Group A streptococci, *Staphylococcus aureus*, and enteric bacilli have been cultured in children with chronic RS, but 20% to 35% of sinus aspirates are sterile. Treatment with antibiotics in such cases most likely will not be effective. These patients are candidates for surgery to create better drainage, if medicines fail.

Fungi are normal flora of the upper airway, but can cause acute RS in immunocompromised and diabetic patients, with invasion that leads to life threatening disease. The noninvasive forms of fungal RS, mycetoma (fungus ball) and allergic fungal sinusitis, are likely caused by an IgE-mediated hypersensitivity to a fungus, and are not life threatening. *Aspergillus* is the most common organism cultured, but several other fungal species have been identified. Bacterial RS and noninvasive fungal infection can look alike and are difficult to distinguish radiographically, except when there is a distinct fungal ball or mycetoma. Noninvasive disease has an indolent, often asymptomatic and benign course. Invasive disease is accompanied by severe toxicity, and inflammation and necrosis in the nose, sinuses, and surrounding tissues.

Treatment

The treatment of acute RS is directed at the predominant organisms. Physicians should consider use of the most narrow spectrum antibiotic for the initial treatment. Risk factors to consider for penicillin-resistant *S pneumoniae* include day care, recent antimicrobial therapy (less than 30 days), age less than 2 years, and exposure to environmental tobacco smoke. In a child without these risk factors, standard dose amoxicillin or amoxicillin/clavulanate may be considered as initial therapy. In children with the above risk factors, high dosage amoxicillin (80-90mg/kg/day) or amoxicillin/clavulanate with a high dosage amoxicillin component may be used as first-line therapy.

Cefprozil, cefdinir, cefuroxime, and cefpodoxime are reasonable choices as second-line agents. Third-line agents with failure of above include clindamycin and cefixime. In penicillin allergic patients, second- or third-line agents, in addition to the macrolides and azilides may be considered. The efficacy of macrolides (erythromycin, clarithromycin), azilides (azithromycin) and sulfa containing agents has not been established.

The duration of therapy should be a minimum of 10 to 14 days and is often continued for several weeks depending on the clinical response. If no improvement occurs or there is worsening after 72 hours, a change in antibiotics should be considered. Optimum duration of therapy in acute disease has never been proven in scientific trials, although recommendations typically include 10 to 21 days, or until symptoms resolve, plus an additional 7 days.⁸ In patients with persistent or recurrent RS, it is important to consider an otolaryngology consultation after antibiotic therapy of at least 6 weeks duration or 3 separate courses of unsuccessful treatment.

Patients with severe acute RS who cannot take oral therapy may require initial parenteral therapy. Therapy by intravenous injection has not been shown to be superior to oral therapy for acute RS in the absence of complications.

Successful treatment of chronic RS with antibiotics is critical because failure will usually lead to surgical therapy. There are many conflicting studies regarding adjuvant therapy, and the efficacy of nasal steroids, saline spray, oxymetazone, mucolytics, and antihistamines has not been established. Saline spray may help clear nasal secretions, and antihistamines may be beneficial in children with RS where allergy is suspected as a causative factor. Control of causative factors, including allergy and GERD, is important in the prevention and treatment of recurrent or chronic infections.

Surgical therapy is indicated for children with chronic RS or recurrent acute RS who have failed maximum medical therapy, including treatment of any underlying disease.

Occasionally, it is necessary to drain an acute infection unresponsive to antibiotic therapy for relief of severe symptoms.

Adenoid tissue serves as a reservoir of bacterial pathogens. Adenoidectomy for enlarged adenoids is almost always the first-line intervention for preschoolers, with a 70% to 80% expected rate of improvement. The procedure is safe, has minimal morbidity, and no effect on long-term immune function.

For treatment of chronic disease, functional endoscopic sinus surgery (FESS) has replaced the creation of nasal antral windows in children. The technique is designed to alleviate the cause of RS, which is mechanical obstruction to drainage at the ostiomeatal complex, with a net effect of widening the outflow tract. The natural ostia are enlarged while preserving most or all of the sinus mucosa. Surgical outcome is dependent on the degree of mucosal disease present before the operation. With careful patient selection, the published results indicate 80% to 100% improvement with surgery.⁹ FESS should only be performed in children by an otolaryngologist experienced in pediatric sinus surgery. The incidence of major complications in experienced surgeons is less than 1%.¹⁰

Complications

In the era of antibiotic therapy and adequate access to primary care, major complications are uncommon. Complications of RS can be divided into orbital, intracranial, and local.

Orbital complications are the most common category, and include orbital cellulitis, orbital abscess, optic neuritis or retrobulbar neuritis, superior orbital fissure syndrome, and cavernous sinus thrombosis. Seventy five percent of orbital infections are a direct result of RS.

Intracranial complications are the second most common category, and include intracranial mucocoele, meningitis, epidural abscess, and subdural abscess. Finally, brain abscess, which has a high mortality rate, also is a possible complication of RS.

Control of causative factors, including allergy and GERD, is important in the prevention and treatment of recurrent or chronic infections. Surgical therapy is indicated for children with chronic RS or recurrent acute RS who have failed maximum medical therapy, including treatment of any underlying disease.

Local complications include the formation of mucocoeles and pyoceles, which may enlarge and cause bone erosion, pain, and swelling over the sinus. Other local manifestations include osteitis, especially of the maxillary sinus, with swelling and erythema of the cheek and osteomyelitis of the frontal or maxillary sinus, and rarely, the sphenoid bone.

What's new?

RS is complex and we are far from completely understanding all aspects of this disease. Clinical trials that target its various causes will help clinicians understand better how to prevent and treat RS.¹¹ Some of the more promising research directions are listed below:

- Aerosolized antimicrobials and steroids are widely prescribed now, but evidence of their effectiveness has not been established and is being evaluated.
- No studies have established the role of vaccines in prevention of acute RS and chronic RS, but it is reasonable to expect that severely affected children would benefit from the conjugated pneumococcal vaccine.
- Biofilms can develop in patients with chronic disease. A film of glycocalyx may protect bacteria from contact with antimicrobials, explaining the poor response to medical therapy in some patients.

Summary

RS is a common pediatric infection that usually responds well to medical therapy. The goal for clinicians is to prevent complications and improve quality of life for children with this disease. Treatment depends on accurate diagnosis, identification and correction of underlying contributing factors, as well as adequate antimicrobial therapy. Surgery, including adenoidectomy and functional endoscopic sinus surgery, is effective in selected patients who are refractory to more conservative measures, and in patients with complications of RS. ■

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What is the diagnostic approach to prolonged fever of unknown origin in children?

The evaluation of children with prolonged fever of unknown origin (FUO) provides pediatricians with a unique opportunity to use every ounce of their diagnostic skills. Clinical practice guidelines and complicated algorithms generally do not apply to the diagnostic approach to children with FUO. Rather, the art of medicine and a return to the basics learned in medical school – repeated detailed history-taking and physical examinations – are the keys to diagnostic success.

Definition of fever of unknown origin

While there is no universally accepted definition of FUO, 2 principles remain constant. First, the child should have had a daily fever, or near-daily fever, for a certain period of time. A reasonable time period would be 8 or more days of fever, which would serve to eliminate most self-limited viral illnesses. Second, the physician should have actively been looking for a source of the fever through careful and repeated history-taking, physical examinations, and judicious use of the laboratory. The correct diagnosis is most often made by diligent physicians who continue to ask questions and monitor changes in the patient's physical examination.

Implicit in the above definition are a number of common clinical scenarios that do not qualify for FUO status. The common discharge diagnosis "fever without localizing signs" should not be confused with FUO. The former diagnosis may be used for children with an acute presentation of fever of less than 8 days duration. Additionally, children 3 to 36 months of age who are being evaluated for occult bacteremia, usually pneumococcal in origin, do not have FUO. Finally, children who present with a history of periodic or cyclic fevers interspersed with periods of wellness should not be confused with those who have FUO. The differential diagnosis of these clinical conditions is decidedly different.

Differential diagnostic framework

Rather than listing an exhaustive litany of diagnoses, a general sense of the possibilities is necessary before a diagnostic approach to FUO can be outlined. Most studies that have looked at the outcome of children with FUO show that the most likely diagnoses are "unknown" and "viral," without a definite viral etiology found. These diagnoses account for approximately 20% of the cases. Of the remaining cases, approximately 50% of the diagnoses are an infectious disease, 20% a collagen-vascular disorder, and 5% to 10% a malignancy.

Any discussion of infections should start with tuberculosis (TB) and a search for TB risk factors, which will be outlined below. Common viral infections such as Epstein-Barr virus and cytomegalovirus are certainly known for causing prolonged fever. However, in my experience, children with such infections invariably have readily recognizable features, such as hepatosplenomegaly or atypical lymphocytosis; prolonged fever as the sole manifestation of disease is unusual. Finally, it is useful to divide the gamut of bacterial infections into pathophysiologic categories – focal bacterial infections (eg, abscesses, osteomyelitis, endocarditis) and disseminated bacterial infections (eg, typhoid fever, brucellosis, tularemia).

Systemic-onset juvenile rheumatoid arthritis (JRA), the leading rheumatologic cause of FUO in children, may be extremely difficult to diagnose, largely because arthritis is commonly absent and may not appear for 6 months to 2 years following diagnosis. In addition, the signs of systemic-onset JRA – lymphadenopathy, hepatosplenomegaly, and fever, are nonspecific and may be found in a variety of infectious and rheumatologic conditions. The astute clinician will look for more specific signs, such as the classic double quotidian fever curve, or an evanescent, macular rash that appears with fever. Other rheumatologic diagnoses to consider include lupus and inflammatory bowel

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Evaluate children with fever of unknown origin
- Initiate appropriate treatment



disease, although classic symptoms and signs of these diseases may be lacking.

Malignancies are an unusual cause of true pediatric cases of FUO. In my experience, a preliminary search for a cause of fever (eg, complete blood count, chest x-ray) usually will lead to the diagnosis of leukemia or lymphoma. However, leukemia specifically should be considered if a child presents with fever and diffuse bone pain, even if the CBC is normal. Abdominal and retroperitoneal lymphomas may be considered even if the child does not have any gastrointestinal symptoms. Finally, neuroblastoma and soft tissue sarcomas occasionally may present as FUO.

Repeated history-taking and physical examinations

With this differential diagnostic framework in mind, repeated history-taking and physical examinations by multiple care takers is often the key to making an accurate diagnosis. Aside from the usual historical questions, there are several important areas that need to be explored. It is helpful to know who measured the temperature and what method was used. For example, if an adolescent goes into the bathroom and comes back with a thermometer reading 111° F, something is definitely wrong!

The astute historian will attempt to discover any unusual exposures that may lead to the patient's diagnosis. First, a history of exposure to TB should be sought. This would include questions regarding family members or contacts who have chronic cough, a history of TB, or a history of incarceration. Other key questions include a history of travel and exposure to foreign travelers, unusual foods, or animals.

In addition to TB, common diseases acquired abroad that may present as FUO include typhoid fever and malaria. Thus, it is important to ask about the specific regions the patient has visited (eg, malaria-endemic areas), dietary indiscretions (eg, non-bottled water, raw meat, unpeeled fruit), recreational activities (eg, swimming in ponds), and sexual experiences, if an adolescent.

Improperly prepared food also may be the source of exotic infections that can cause FUO. Unpasteurized milk or cheese may be the source of brucellosis or tularemia. Other potential infectious cesspools in improperly cooked food include eggs (*Salmonella*), poultry (*Salmonella*), pork (trichinosis), and wild game (trichinosis, tularemia, toxoplasmosis, and brucellosis).

Finally, virtually any animal may be the source of infection. Representative infections include leptospirosis or *Toxocara canis* from dogs, toxoplasmosis or cat scratch disease from cats, histoplasmosis, cryptococcosis or psittacosis from birds,

brucellosis from cattle, goats, or sheep, tularemia from wild rodents, and *Salmonella* from reptiles.

Diagnostic tests

The diagnostic evaluation should not be a "shotgun" approach in which dozens of tests are ordered indiscriminately. Rather, a logical, step-wise evaluation should be guided by repeated history-taking and physical examinations. The physician should also remember that uncommon presentations of common disorders are much more likely than common presentations of rare diseases. Admission to the hospital should be considered if there is a need to document the presence of fever (ie, cases of factitious fever), obtain expedited testing or urgent subspecialty consultation, or if the child appears ill.

The initial evaluation should include an outpatient fever diary or inpatient documentation of the fever curve, CBC with differential and platelet count, erythrocyte sedimentation rate (ESR), serum transaminase (SGPT), tuberculin skin test, and chest x-ray. A low ESR may be helpful in providing evidence against the presence of a systemic inflammatory condition. Cultures of all readily accessible body fluids, blood, urine, and stool, should be obtained. Viral culture of nasopharyngeal secretions may be warranted if viral infection is suspected. A commonly made mistake at this point is to forget to perform any of these simple tests that could be diagnostic, or at least could point the physician in the correct direction.

The results of the above tests should guide second and third tier diagnostic testing. If a rheumatologic condition is suspected, tests for antinuclear antibodies (ANA) and complement may be warranted. However, a positive ANA in the absence of clear evidence of inflammatory disease has a low degree of specificity. For example, an ANA titer of 1:320 in a child with vague arthralgias and abdominal pain is of little importance. Ophthalmologic examination in children with suspected JRA or sarcoidosis may detect occult uveitis.

Judicious use of second and third tier diagnostic imaging procedures can be fruitful. Abdominal ultrasonography, easily performed without sedation or ionizing radiation, may detect occult masses or appendiceal and hepatic abscesses. Computerized tomography, which requires sedation of younger children, as well as the potential use of intravenous, oral, and rectal contrast, is excellent for the detection of intraabdominal abscesses, intestinal wall pathology seen in inflammatory bowel disease, lymphadenopathy, and for better defining the type and extent of pulmonary disease. Finally, while the literature suggests the lack of utility of gallium scanning, particularly in the face of

its high cost and relatively large radiation exposure, I have found it helpful in selected cases in detecting occult areas of inflammation.

Occasionally, the question arises as to whether the child could have an occult malignancy, particularly leukemia. Unless the patient has a distinctly abnormal CBC (eg, thrombocytopenia, leukopenia), bone marrow examination has very low utility. However, when performed, the marrow should be cultured for bacteria, viruses, mycobacteria, and fungi, as the diagnostic yield generally will be higher than with histologic examination alone.

Finally, a few thoughts about echocardiography are in order. Approximately 5% to 10% of pediatric cases of infective endocarditis may be culture negative. Transthoracic echocardiography will identify vegetations in approximately 60% of cases of endocarditis, whereas transesophageal echocardiography will identify vegetations in 90% of cases. Unfortunately, concerns about Kawasaki disease often create diagnostic conundrums. While classic cases of Kawasaki disease are easily diagnosed, atypical or “incomplete” cases may be very problematic. In such cases many of the more readily appreciated features, such as mucous membrane involvement and non-exudative conjunctivitis, are absent. Thus, echocardiography with particular attention to the coronary arteries should be considered in young children with prolonged fever and no readily apparent diagnosis. ■

FOR FURTHER READING

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The physician should remember that uncommon presentations of common disorders are more likely than common presentations of rare diseases.

Diagnostic and Consultation Services

Consultations for any pediatric problem are available to community-based physicians through the Diagnostic and Consultation Program at Children's Memorial. Call 773.880.3832 from 8:30 am to 5 pm.

New Trial to Identify Best Medication for Childhood Absence Epilepsy

VITA LERMAN

Although childhood absence epilepsy (CAE) has been considered relatively benign, since up to 79% of affected children outgrow it by puberty, the cognitive, psychosocial, and physical effects of the syndrome and its treatment are significant. Compared to matched controls, children with CAE have lower percentiles for general cognitive functioning (25th vs. 55th), visual-spatial skills (32nd vs. 62nd), nonverbal memory (50th vs. 71st), and delayed recall (24th vs. 65th). About one-third of children with CAE show impaired functioning in school, behavior, and social relationships. Twenty percent of patients with CAE experience accidental injury during their staring episodes, or the 10 to 15 second interruptions of consciousness occurring up to 100 times a day, every day.



Children's Memorial's neurologist Kent R. Kelley, MD, is the principal site investigator of the CAE trial, and an assistant professor of pediatrics and neurology at Northwestern University's Feinberg School of Medicine.

Epilepsy affects about 1% of children. CAE is the most common form of childhood epilepsy requiring treatment in otherwise normal children, affecting about 10% to 15% of children with epilepsy in the US. And yet so far, the optimal medication for CAE has not been defined, nor have the individual factors that contribute to treatment failure or side effects.

These issues are the focus of the largest clinical trial for pediatric epilepsy to date, which is actively recruiting patients at more than 20 sites nationwide, including Nordstrom Epilepsy Center at Children's Memorial Hospital. The 5-year study is funded by a \$17 million grant from the National Institute of Neurologic Disorders and Stroke, a division of the National Institutes of Health.

In this randomized, double-blind study, the 3 commonly used anti-epileptic drugs – ethosuximide, lamotrigine, and valproate – will be compared, in order to identify the best initial monotherapy for CAE, or the drug with the highest rate of seizure control and lowest incidence of treatment-limiting toxicity, including neurocognitive effects.

“We will examine the effects of each drug on quality of life, behavior, and cognition, especially in relation to attention and learning,

and this is the most unique and important aspect of this trial,” says Kent R. Kelley, MD, principal site investigator at Children's Memorial. “Optimal therapy does not just mean seizure control and this is much more than a drug trial for efficacy. We will begin to unravel the relative contributions of the underlying condition and comorbid brain-based disorders of attention and behavior, the neurocognitive effects of seizures and those from treatment, all compounded by the impact of the social and economic background, labeling, and stigma.”

Seeking to understand the reasons for individual variations in treatment response, the study also will include pharmacokinetic and pharmacogenetic research. “This is the first step toward our goal of making it possible for physicians to predict patient response and tailor therapies for individual needs of children with CAE,” says Kelley.

The study plans to enroll a total of 439 children, ages 2 to 13 years, with previously untreated CAE. Each child will participate for approximately 2 years. At Children's Memorial, the goal is to enroll 4 children a year over the next 3 years. For more details or to schedule an evaluation of a child, please contact Clara Samaniego at 773.883.6158. ■



 Children's Memorial Hospital at CENTRAL DUPAGE HOSPITAL

Through the new Children's Memorial at Central DuPage Hospital partnership, pediatric patients in the far western suburbs of Chicago will have improved access to leading subspecialists, treatments, programs, state-of-the-art technologies, equipment and facilities. For primary care physicians, this partnership will provide a high-quality, comprehensive and coordinated program, located at the Central DuPage Hospital in Winfield, which allows easy VIP physician access to key pediatric resources from Children's Memorial.

On July 1, 2005, Children's Memorial physicians began covering on a 24/7 basis the Central DuPage Hospital pediatric unit, and the neonatal and pediatric intensive care units (NICU and PICU). Central DuPage Hospital now houses the only partner hospital PICU in the 7-county Chicago area staffed by Children's Memorial.

The Children's Memorial at Central DuPage Hospital telemedicine program with pediatric cardiologists started in September. Additional services to be implemented throughout 2006 include:

- Comprehensive center with specialty outpatient programs
- Enhanced pediatric diagnostics and testing
- Dedicated pediatric emergency department and urgent care program
- Inpatient and outpatient pediatric surgery

The Children's Memorial at Central DuPage Hospital outpatient center will have approximately 22 000 square feet dedicated to outpatient, diagnostic, and testing services.

Young honored with international award for work in cochlear implants

Nancy Young, MD, FACS, was honored by the International Center on Deafness and the Arts with the 2005 Helping Hands award, which is given annually to outstanding physicians in the field of cochlear implants. Young is head of the Section of Otolaryngology and Neurotology within the Division of Otolaryngology. She is associate professor of otolaryngology-head and neck surgery at Northwestern University's Feinberg School of Medicine.

Pediatric and neonatal coverage begins at Provena Saint Joseph Hospital, Elgin

Onsite coverage of the pediatric unit at Provena Saint Joseph Hospital in Elgin by Children's Memorial pediatric hospitalists began in June. NICU coverage started late July.

New hospitalist program at Children's Memorial

The new hospitalist program, launched in July at Children's Memorial's Lincoln Park campus, establishes a structure to ensure comprehensive and coordinated care essential to patient safety. One team of 7 hospitalists covers the PICU, transport, and sedation services. Another team of 4 hospitalists coordinates inpatient care of children with medically complex conditions and provides medical consultation for surgical and psychiatric inpatients.

Hospitalist programs are a growing trend throughout the country. Studies have shown improved patient survival when hospitalists, as opposed to residents, care for patients in the pediatric intensive care unit after hours. Furthermore, the *Wall Street Journal* recently reported that hospitalist programs at large academic hospitals shortened lengths of stay by 30% and cut costs by 20%.

Hendrix lab finds clues to stop deadly tumor progression

The laboratory group of **Mary J.C. Hendrix, PhD**, president and scientific director of Children's Memorial Research Center, and colleagues, found that human metastatic melanoma cells placed in a zebra fish embryo survive, but do not form tumors. Instead, these aggressive cancer cells keep their unspecified nature, similar to embryonic stem cells, and express genes of various normal cell types. These results may help identify signals that suppress tumor progression, helping researchers find ways to fight deadly cancers. The study is published in the August issue of *Developmental Dynamics*.

Research center recruits cancer program director

Marcelo Bento Soares, PhD, arrived in June to direct the newly created Cancer Biology and Epigenomics Program at the research center. Soares was a tenured professor of pediatrics, physiology and biophysics, biochemistry and orthopaedics at the Carver College of Medicine at the University of Iowa. His research has made major contributions to the human and rat genome projects. His present research focuses on identifying genes that contribute to metastasis. ■



FIGURE 1

Educational Objectives

At the conclusion of this activity, participants will be able to:

- Recognize the pigmentary skin disorder in the photograph
- Describe different clinical presentations
- Describe methods of diagnosis and treatment

A 6-year-old Hispanic male presents to the dermatology clinic with a 6-month history of a white spot on the forehead that has been slowly enlarging. The spot had been treated with an anti-fungal cream a month prior, without improvement. It is asymptomatic. Review of systems and medical history is unremarkable. Family history is negative for pigmentary skin diseases, but positive for Graves disease in the mother and maternal grandmother. Physical examination reveals a depigmented, well-demarcated patch involving the right eyelid and forehead, with depigmentation of eyelash and eyebrow hairs of the right eye (Figure 1). The remainder of the physical examination is unremarkable.

What is the most likely diagnosis?

- A. Nevus depigmentosus
- B. Vitiligo
- C. Tinea versicolor
- D. Piebaldism

Answer: B

Discussion:

Vitiligo is an acquired pigmentary disorder caused by a loss of functional melanocytes in the skin. It affects 0.5% to 4% of the world population, and 50% of patients have an onset of disease before the age of 20 years. In the pediatric population, the mean age of onset is approximately 5 years. While gender differences are not seen in adult vitiligo, childhood vitiligo (vitiligo with an onset before age 12 years) is more commonly seen in girls than boys. Other differentiating features of childhood and adult vitiligo are: the higher incidence of segmental presentation in childhood vitiligo; the relatively decreased effectiveness of PUVA (psoralen and

ultraviolet A) as treatment (although rarely used in children); and the lower patient incidence of associated autoimmune and/or endocrine diseases.

The most common presentation is of a depigmented, enlarging macule or patch with discrete margins, surrounded by normal skin. It tends to localize most commonly on the face, dorsal aspect of hands, inguinal and anogenital regions, and is frequently classified based on the distribution of lesions. Segmental vitiligo, as exhibited by the presented case, is a localized form of vitiligo that occurs in a dermatomal or quasidermatomal distribution. Segmental vitiligo is seen more commonly in children than in adults. It tends to spread rapidly on the affected area, although activity usually ceases after a short period and involvement of other body sites is unusual. Other types of localized vitiligo include focal (1 or more macules in same area, but not segmental) and mucosal (affecting only mucous membranes). Generalized vitiligo (also called vitiligo vulgaris),

is the most common type in both children and adults, and consists of scattered patches that are widely distributed over the body. Acrofacial (affecting the face and distal extremities) and universal (a complete or nearly complete depigmentation of the body) are other types of vitiligo.

Diagnosis is based on the patient's history and clinical presentation. While vitiligo patches may be difficult to visualize in lighter skinned individuals, Wood's lamp examination identifies the depigmented (versus hypopigmented) patches and confirms the diagnosis. Laboratory studies are not helpful in diagnosis. The differential diagnosis of depigmented or hypopigmented lesions in children include nevus depigmentosus, pigment mosaicism (including what has formerly been termed hypomelanosis of Ito), tinea versicolor, seborrheic dermatitis, pityriasis alba, albinism, piebaldism, postinflammatory hypopigmentation, lichen sclerosis et atrophicus, and the white spots of tuberous sclerosis. These disorders can be distinguished from vitiligo by history, physical exam, or laboratory studies.

Although vitiligo is not considered a life-threatening disease, the psychological impact of the disease can be tremendous. Children and adolescents, particularly those with darker skin and more widespread disease, may suffer from anxiety and low self-esteem as a result of their disease. For this reason, family support and early, consistent treatment are recommended.

Topical steroids and calcineurin inhibitors (especially tacrolimus 0.1% ointment) have been used successfully in localized cases of vitiligo, including segmental forms. Ultraviolet light therapy is a major stimulant for repigmentation, and is often used in combination with topical anti-inflammatory agents. Exposure to sunlight is useful, although care must be taken to avoid sunburns. Treatment with ultraviolet light, especially narrow band ultraviolet light, can be performed in the dermatology office or by home units under physician supervision. PUVA therapy has been particularly successful in adults with vitiligo, but the risks of PUVA therapy and difficulty in protecting against UV-induced damage during the 24 hours after psoralen ingestion diminish the value of this therapy for the pediatric population. Camouflage makeup does not treat the disease, but may help in minimizing the visibility of the depigmented lesions.

The pathogenesis of vitiligo is poorly understood, although the frequent occurrence of familial cases and associations with various genetic loci suggest that vitiligo is a complex genetic disorder. An autoimmune explanation for the destruction of melanocytes also exists, and is supported by the association of vitiligo with other autoimmune diseases, such as thyroiditis, pernicious anemia, and systemic lupus erythematosus,

particularly in adults. A third multifactorial "convergence" theory suggests that genetic and autoimmune factors, in combination with stress, toxic compounds, and impaired melanocyte function, can all contribute to the development of disease. ■

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PATIENT SAFETY

1. Root Cause Analysis includes:

- Interviews with clinicians involved in an adverse event
- Review of medical records and a timeline of each action and decision leading to the adverse event
- Evaluation of each step in the clinical process to identify causes that made an error possible, to prevent recurrence of an error-prone situation
- All of the above

2. Failure Mode and Effects Analysis is:

- System used to discover who is to blame for a medical error
- Prospective review of a process to identify error-prone steps
- Retrospective review of steps within a process that resulted in a medical error
- Not useful for preventing safety risks in health care

3. Strategies to improve patient safety include:

- Read back of verbal orders, team training, debriefings, clinical checklists
- Rapid Response Teams
- Involving patients and families
- All of the above

MINIMALLY INVASIVE SURGERY

1. Minimally invasive surgery uses the follow equipment:

- Long thin instruments
- Halogen light sources with fiberoptic scopes
- Carbon dioxide insufflation
- All of the above

2. The 3 most common laparoscopic procedures performed in children are:

- Small bowel resection, colon resection, and gastrectomy
- Fundoplication, hepatectomy, and splenectomy

- Appendectomy, splenectomy, and fundoplication
- Appendectomy, colectomy, and fundoplication

3. Patients undergoing laparoscopic appendectomy have:

- Fewer overall complications
- Lower pain scores
- Shorter length of stay
- All of the above

EE

1. What percentage of children with EE are males?

- 75%
- 50%
- 25%
- 40%

2. Single most important test that establishes the diagnosis of EE is:

- UGI x-ray series
- 24 hour pH probe study
- Esophageal histology
- CBC with differential

3. Current accepted treatment options for treating EE in children include all of the following except:

- Systemic or oral steroids
- Elimination diet
- Mepoluzimab
- Elemental diet

BIPOLAR DISORDER

1. The 5 symptoms of pediatric bipolar disorder that do not overlap with ADHD are:

- Euphoric mood, grandiosity, decreased need for sleep, racing thoughts, hypersexuality
- Irritability, pressured speech, distractibility, grandiosity, decreased need for sleep
- Euphoric mood, irritability, pressured speech, distractibility, grandiosity
- Distractibility, racing thoughts, pressured speech, irritability, hyperactivity

2. Medications that may trigger symptoms of mania include:

- Antidepressants
- Stimulants
- Corticosteroids
- All of the above

3. If a child with ADHD treated with stimulants develops manic symptoms:

- Lithium should be immediately added to the treatment with stimulants
- Stimulants should be discontinued and re-evaluation made in 7 to 10 days, followed by urgent referral to a child psychiatrist if mania persists
- The dose of stimulants should be increased
- The child should receive immediate treatment for a conduct disorder

RHINOSINUSITIS

1. Factors predisposing formation of bacterial rhinosinusitis include:

- Nasal polyps
- Dental infections
- GERD
- All of the above

2. The most common organisms causing acute rhinosinusitis are:

- Staphylococcus aureus*, *Moraxella catarhalis*, *Hemophilus influenzae*
- Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Hemophilus influenzae*
- Streptococcus pneumoniae*, *Hemophilus influenzae*, *Moraxella catarhalis*
- Hemophilus influenzae*, *Moraxella catarhalis*, *Streptococcus pyogenes*

3. The most common complication of acute rhinosinusitis in children is:

- Subdural abscess
- Subperiosteal abscess
- Meningitis
- Orbital abscess

FEVER OF UNKNOWN ORIGIN**1. The keys to a successful diagnostic evaluation of children with FUO include:**

- Repeated history-taking by multiple examiners
- Repeated physical examinations over time
- Thorough assessment of all exposures, including animals, travel, and exotic foods
- All of the above

2. Which statement is true?

- Malignancies most commonly cause FUO in children.
- A child with 5 days of fever without obvious source has FUO.
- A positive ANA absolutely establishes the diagnosis of a collagen-vascular disease.
- Ingestion of unpasteurized milk may cause brucellosis.

DERMATOLOGY**1. Segmental vitiligo is:**

- A localized vitiligo that occurs in a dermatomal or quasidermatomal distribution
- A localized vitiligo that affects only the mucous membranes
- Consists of scattered patches that are widely distributed over the body
- Is more common in adults than children

2. Treatment for vitiligo in children may include:

- Topical steroids
- Calcineurin inhibitors
- Ultraviolet light therapy
- All of the above

REGISTRATION FORM**Please print:**

Last Name	First Name	Degree

Mailing Address		

City	State	Zip Code

Phone Number		

Email Address		

Date of Participation	Time to Complete Activity	

EVALUATION

- Were the activities' objectives met? Yes No
- Do you feel the activity was fair, balanced and free of commercial bias? Yes No
- What topic areas would you like to see covered in future educational activities?

The Child's Doctor, Fall 2005

Please circle the correct answers for every article.

Patient Safety

- a b c d
- a b c d
- a b c d

EE

- a b c d
- a b c d
- a b c d

Rhinosinusitis

- a b c d
- a b c d
- a b c d

Minimally Invasive Surgery

- a b c d
- a b c d
- a b c d

Bipolar Disorder

- a b c d
- a b c d
- a b c d

Fever of Unknown Origin

- a b c d
- a b c d

Dermatology

- a b c d
- a b c d

Register and take CME quiz **online** at <http://www.childrensmemorial.org/cme/> • Or **mail** completed Registration Form to: Children's Memorial Hospital, *The Child's Doctor* CME Program, 2300 Children's Plaza, Box 40, Chicago, IL 60614-3394. • **Questions?** Please contact *The Child's Doctor* CME Program at: 773.880.6855 • **Deadline for registration:** For credit to be received, the Registration Form must be received (online or via mail) no later than October 21, 2006.

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Chicago Locations

Children's Memorial Hospital
Fullerton and Lincoln

Children's Memorial Outpatient Center
Clark and Deming

Children's Memorial Pediatrics – Uptown Teen Health Center
Broadway and Lawrence

Suburban Locations

Children's Memorial Outpatient Center in Arlington Heights
Northwest Community Hospital

Children's Memorial Outpatient Center in Glenview
Glenview Hospital

Children's Memorial Outpatient Center in Tinley Park
Ingalls Family Care Center

Children's Memorial Outpatient Center in Westchester
Westchester

Outreach Partner Locations

Central DuPage Hospital | *Winfield*

Ingalls Memorial Hospital | *Harvey*

Lake Forest Hospital | *Lake Forest*

Northwest Community Hospital | *Arlington Heights*

Prentice Women's Hospital | *Chicago*

Provena Saint Joseph Hospital | *Elgin*

Silver Cross Hospital | *Joliet*

Swedish Covenant Hospital | *Chicago*

West Suburban Hospital Medical Center | *Oak Park*

Inpatient Pediatric Services Ranked #1

- Asthma
- Cardiology
- Cardiovascular surgery
- Dentistry
- Dermatology
- Gastroenterology
- General medicine
- General surgery
- Genetics
- Hematology/oncology
- Immunology/rheumatology
- Infectious diseases
- Kidney diseases
- Neonatology tertiary care (0-60 days)
- Neurology
- Neurosurgery
- Ophthalmology
- Orthopaedics
- Otolaryngology
- Plastic surgery
- Psychiatry
- Pulmonary medicine
- Transplantation (liver, kidney, stem cell)
- Urology

Sources: IHA Compdata, CY2002; UNOS, CY2002.
Based on volume in 7-county Chicago metropolitan area.



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