

PEDIATRIC Perspectives

MEDICAL PERSPECTIVES

FOR INDIANA'S CHILDREN

SPRING 2009



**Bassem I. Razzouk,
MD, FAAP**

Medical Director, Children's
Center for Cancer and
Blood Diseases
Peyton Manning Children's
Hospital at St.Vincent
(317) 338-6608
birazzou@stvincent.org

All patients at
Peyton Manning
Children's
Hospital at
St.Vincent are
eligible for treat-
ment protocols
developed by
the Children's
Oncology Group.

Acute lymphoblastic leukemia

| Novel protocols increase survival

by Bassem I. Razzouk, MD, FAAP

Children with acute lymphoblastic leukemia (ALL) benefit from enrollment in clinical trials; treatment provided in such settings has been shown to most effectively meet the individual's clinical needs and contribute to long-term survival. This common form of cancer in the pediatric population represents approximately 75% of all pediatric leukemia cases.

At Peyton Manning Children's Hospital at St.Vincent, these children receive the best possible care as a result of our team's clinical expertise; our participation in groundbreaking research in clinical trials; the multidisciplinary attention we give to patients' needs; and our collaborative relationship with patients' families and primary caregivers.

Importantly, the hospital is a member of the Children's Oncology Group (COG), a national research consortium comprised of more than 200 pediatric cancer centers. As a result, all patients at Peyton Manning Children's Hospital at St.Vincent are eligible for treatment protocols developed by COG. Typically, more than 50 active

treatment trials are available and include trials for ALL patients.

The value of pediatric clinical trials

Patients in clinical trials benefit from new and emerging treatments, including molecularly targeted therapies and cellular and immunotherapies. Other trials focus on relapse, treatment adherence, and developing protocols for disease classification. This facilitates risk-directed therapy, so that ultimately, no patient is overtreated or undertreated. Furthermore, in a clinical trial, overall management—including intensive supportive measures such as transfusions, antibiotics, and fluid replacement—is very exacting and timely.

ALL is diagnosed most often in children who are 3 to 5 years of age, and 90% of these children are treated in clinical trials. Cure or long-term remission generally is more difficult to achieve in patients who are 10 years of age or older at the time of disease onset. Overall survival for children between the ages of 1 and 9 years is 81%,

CONTINUED ON PAGE 6

IN THIS ISSUE

- 1 ACUTE LYMPHOBLASTIC LEUKEMIA by Bassem I. Razzouk, MD, FAAP
- 2 EDITOR'S LETTER by Joanne Hilden, MD
- 2 DIAGNOSTIC DILEMMA: RECURRENT EAR BLEEDING by Ronda A. Hamaker, MD
- 3 FAMILY-EXPERIENCE ENDOSCOPY by Susan Maisel, MD
- 4 PEDIATRIC INTENSIVE CARE WITH A DIFFERENCE by Thomas Williams, MD

**Peyton Manning
Children's Hospital**



at St.Vincent

ANNE COLEMAN, RN

Administrator
St. Vincent Women's Hospital
Peyton Manning Children's
Hospital at St. Vincent

JOANNE HILDEN, MD

Medical Director
Physician Editor

KAY SWANK-HERZOG

Editor-in-Chief

ELIZABETH CISCO

System Marketing Executive
St. Vincent Health

CONTRIBUTORS

**Bassem I. Razzouk, MD,
FAAP**

(317) 338-6608
birazzou@stvincent.org

Ronda A. Hamaker, MD

(317) 338-6815
rahamake@stvincent.org

Susan Maisel, MD

(317) 338-9450
skmaisel@stvincent.org

Thomas Williams, MD

(317) 338-5230
tmwillia@stvincent.org

Please send your comments,
questions, or suggestions
for future issues of
Pediatric Perspectives to
Kay Swank-Herzog at
KFSwankH@stvincent.org.

© 2009 by Peyton Manning
Children's Hospital at
St. Vincent.
All rights reserved.

EDITOR'S LETTER

Novel treatments and management approaches = Improved outcomes

by Joanne Hilden, MD



**Joanne Hilden,
MD**

Medical Director
Physician Editor
Peyton Manning
Children's Hospital
at St. Vincent
(317) 338-3466
jmhilden@stvincent.org

With this edition of *Pediatric Perspectives*, we know that you—and, importantly, your patients and their families—are challenged during this time of widespread acute illness. In this issue, we focus on topics that include the improved outcomes of children in our care thanks to novel treatments and management approaches. First, we share with you the good news for children and young adults with leukemia, given the availability of unique clinical trials and our cancer center that provides supportive care in every aspect. Sometimes these children must stay in the Pediatric Intensive Care Unit. We review for you our PICU outcomes—specifically, decreased mortality—resulting from the physician staffing pattern and available technology. Take note of the cardiac surgery outcomes detailed there as well. We also describe a unique program in pediatric gastroenterology: family-experience endoscopy, during which parents stay with their child during the entire procedure, to comfort the child and to receive information and results in real time from the physician performing the procedure. Our diagnostic dilemma in this issue is that of a child with a draining ear; while the diagnosis was in question, the outcome was good. □

In this issue, we focus on topics that include the improved outcomes of children in our care.

DIAGNOSTIC DILEMMA

Unexplained recurrent bleeding from the ear

by Ronda A. Hamaker, MD



**Ronda A. Hamaker,
MD**

Medical Director
Pediatric Otolaryngology
Peyton Manning
Children's Hospital
at St. Vincent
(317) 338-6815
rahamake@stvincent.org

A 3-year-old girl was brought to the Ear, Nose & Throat Center at Peyton Manning Children's Hospital at St. Vincent because of mucous discharge and bloody otorrhea that occurred intermittently. Only her right ear was affected. The patient's primary physician used ciprofloxacin and dexamethasone otic drops without success. The child's medical history was pertinent for myringotomy tubes inserted by another ENT specialist 2 years earlier. The presence of tubes provides important diagnostic clues. In children without tubes, the likely causes are a ruptured tympanic membrane or a traumatized ear canal. When tubes are present, the differential diagnosis includes infection, tube extrusion, and myringotomy tube granuloma.

Examination of the child revealed a normal tympanic membrane in the left ear and a thickened, irregular, erythematous tympanic membrane in the right ear. A granuloma covered the right membrane.

The patient's history revealed that usual care of the granuloma had previously been initiated in the form of treatment with a steroid otic drop. This modality often helps shrink the granuloma and possibly make it disappear. Because the child's PCP

CONTINUED ON PAGE 5

Family-experience endoscopy

| A child- and parent-centered program

by Susan Maisel, MD

More than 15 years ago at Peyton Manning Children's Hospital at St. Vincent, we introduced family-experience endoscopy, in which parents and even siblings of a child undergoing an endoscopic procedure can stay with the patient throughout the procedure. Child comfort and parent education were the chief reasons for implementing this program. But other benefits have been realized as well.

Considering the child's perspective

Being separated from parents in the company of strangers wearing gowns and masks can be unnerving and even frightening for a child. Having family present to hold hands and talk reassuringly raises the comfort levels of patients and parents alike. Moreover, for children with chronic disorders that will necessitate repeated procedures—eg, Crohn's disease, eosinophilic esophagitis—we want the experience to become familiar and nonthreatening.

Other pre-procedure tactics lessen patient anxiety by demystifying the setting. Our anesthesiologists let children hold the mask and choose a flavor of lip balm they would like applied to it, to cover up the odor of the general anesthesia. We show them how the cameras work, and they watch themselves on the television screen. We also promise them pictures they can take to school and show their friends.

If lab work is needed, we never make patients endure venipuncture beforehand. We draw blood only after the child is under anesthesia. The same is true for inserting intravenous lines, if needed.

CONTINUED ON PAGE 7

Privacy, please

Occasionally, teens seen in the family-experience endoscopy center will request privacy during a procedure because their parents are unaware of tattoos they have acquired. We honor such requests.

One family's day at the center

As told by Becky Schnebly, Lafayette, Indiana

My 8-year-old daughter, Kaitlynn, had been complaining of stomach pain and diarrhea off and on for several years. I heard from my sister that Peyton Manning Children's Hospital had a special center that treated children for the same kinds of symptoms. When I called and spoke with one of the pediatric gastroenterologists, she agreed the symptoms should be investigated with a procedure called EGD, or esophagealgastrroduodenoscopy.

The night before the procedure, we told Kaitlynn she should not eat or drink anything the next morning because the doctor was going to "take special pictures of her tummy." She was happy to know she could stay in her pajamas for the drive to the center. When we arrived, the atmosphere was casual and low key. The anesthesiologist asked Kaitlynn what flavor of lip gloss she preferred and then lined the mask with that gloss. My husband and I stood on either side of Kaitlynn, holding her hands as she went to sleep.

Throughout the 20-minute procedure, the endoscopist, Dr Elizabeth Schaefer, explained everything she was doing. We watched the scope descend on the monitor, and Dr Schaefer took pictures now and then, as well as biopsy samples. My daughter hates needles, which she was spared because they took blood samples while she was asleep for lab studies, including a workup for allergies.

After the procedure, Dr Schaefer showed us photos and explained that, while waiting for lab results, she would start Kaitlynn on Prevacid to see if that would help. When Kaitlynn woke up, she felt so well that she wanted to stop at her favorite fast-food restaurant on the way home.

Dr Schaefer called us a week later to say the lab results showed that Kaitlynn had celiac disease. We started her immediately on a special gluten-free diet. Her symptoms began to resolve almost at once. We visited Dr Schaefer again 3 months later as part of the routine follow-up. Kaitlynn has been doing fine since the change in her diet. We are delighted to have learned about the family-experience endoscopy center at Peyton Manning Children's Hospital at St. Vincent.



Susan Maisel, MD

Medical Director, Pediatric Gastroenterology
Peyton Manning Children's Hospital at St. Vincent

(317) 338-9450
skmaisel@stvincent.org

For children with chronic disorders that will necessitate repeated procedures, we want the experience to become familiar and nonthreatening.



Thomas Williams, MD

Medical Director
Pediatric Intensive Care
Unit
Peyton Manning Children's
Hospital at St.Vincent
(317) 338-5230
tmwillia@stvincent.org

Pediatric intensive care with a difference

| Unique staffing and services yield impressive outcomes

by Thomas Williams, MD

The forward-looking Pediatric Intensive Care Unit (PICU) at Peyton Manning Children's Hospital at St.Vincent is demonstrably improving patient outcomes, chiefly due to an unusual 24/7 staffing arrangement and pioneering services.

Round-the-clock physician presence. Five attending physicians who are board certified in pediatric critical care share coverage in our 15-bed unit, which means one of them is in the PICU every hour of every day. The advantages of this arrangement are many.

First, the physician can manage nearly any urgent episode at bedside. With 24/7 physician coverage, critical decisions need not be put off until the next morning or after the weekend, as happens in other settings. Parents, too, have immediate access to the attending physician, who can answer their questions and speak with authority to their concerns.

Continuity of management is another advantage. The physician who is on duty during the day several days in a row is the one who makes regular rounds and modifies the plan to advance a child's care. The attending on duty at night makes sure the plan is followed. As decisions change, a physician is always present to implement the steps necessary to ensure efficient recovery and eventual discharge. In addition, a pediatric PharmD rounds routinely with the care team.

Personalized nursing care. Every family can expect an experienced nurse to be at their child's bedside continuously. Typically, nurses in the PICU care for 1 or 2 patients, depending on the individual child's needs. The PICU nursing staff gets to know both the child's and family's needs during the stay. We believe that caring for the entire family ultimately makes us better able to care for our patients. No one knows the child better than the family.

Unsurpassed services. Among the children we care for are those with conditions that require mechanical ventilation, those in shock who need continuous intravenous medicine to sustain blood pressure, and those who must be observed closely following major surgery. We have particular

expertise in the minute-to-minute care of children who have undergone open heart surgery. Whether caring for a newborn after a Norwood procedure or a teenager recovering from coarctation repair, we notify the cardiovascular surgeon directly about any changes in a patient's condition and immediately revise the treatment plan if needed. Extubating cardiac surgery patients as soon as possible hastens their recovery, and our 24/7 attending coverage ensures that this happens without delay.

The PICU of Peyton Manning Children's Hospital at St.Vincent was also the first to offer extracorporeal membrane oxygenation (ECMO) to the adolescent population in Indiana, and we now provide it for adults as well. We have also accommodated referrals from out of state.

Outcomes better than national standards. The success of our program is measurable in many ways. The predicted PICU mortality rate nationwide, for example, is 2.82%. At Peyton Manning Children's Hospital at St.Vincent, the rate is 1.57%. Since our unit opened in 1988, we have consistently scored in the highest or next-highest quartile of pediatric risk of mortality (PRISM) ratings (*see sidebar on page 5*).

Our data echo the clear evidence in the literature that outcomes improve in adult ICUs with 24/7 attending coverage. Importantly, more facilities around the country, including university centers, are changing to this model in the Pediatric ICU. □

Extubating cardiac surgery patients as soon as possible hastens their recovery, and our 24/7 attending coverage ensures this happens without delay.

With 24/7 physician coverage, critical decisions need not be put off until the next morning or after the weekend, as happens in other settings.

Collaboration between the PICU and cardiothoracic surgery team pays off

Pediatric risk of mortality, or PRISM, compares clinical outcomes among PICUs nationwide in a way that disregards unit size or the complexity of cases handled. In the first 24 hours after admission, a patient is given a risk-of-mortality score, regardless of diagnosis, based on recorded physiologic data (eg, heart rate, blood pressure, level of acidosis). Over a 12-month period, a PICU's accumulated data would predict the loss of a given number of patients. Fewer deaths than predicted indicate superior care.

Peyton Manning Children's Hospital at St.Vincent

30-day cardiothoracic surgery survival data for typical procedures^a

PROCEDURE	SURVIVAL
Arterial switch for the great arteries/intact ventricular septum or ventricular septal defect	33/36 ^b
Norwood for hypoplastic left heart syndrome	32/43 ^c
Atrial septal defect	37/38
Ventricular septal defect	56/57
Tetralogy of Fallot	49/51
Atrioventricular canal defect	25/27

^aSource: V. Simon Abraham, MD, Pediatric Cardiothoracic Surgeon, Cardiothoracic Surgery, The Children's Heart Center at Peyton Manning Children's Hospital at St.Vincent.

^bThe 8% mortality at Peyton Manning Children's Hospital at St.Vincent compares favorably with the 6% reported by a major university center. (Qamar ZA, et al. Current risk factors and outcomes for the arterial switch operation. *Ann Thorac Surg.* 2007;84:871-878.)

^cMortality of 26% at Peyton Manning Children's Hospital at St.Vincent vs 37% and 15% at 2 major centers.

Overall mortality at Peyton Manning Children's Hospital at St.Vincent from 2000 to 2007: 1.5% to 3.5% per year.

Pediatric risk of mortality, or PRISM, compares clinical outcomes among PICUs nationwide in a way that disregards unit size or the complexity of cases handled.

CONTINUED FROM PAGE 2

DIAGNOSTIC DILEMMA

had tried this option, we surgically removed the granuloma and the tube. This was accomplished in an outpatient procedure lasting fewer than 15 minutes and requiring no postoperative pain management.

Following treatment, the child did well. Her affected tympanic membrane healed, she experienced no further otorrhea, and her hearing thereafter was normal. □

Caveat

A granuloma in the ear also raises the possibility of a tumor (eg, benign, such as cholesteatoma, or cancerous) or an imbedded foreign body. This may prompt the health care provider to investigate further, as dictated by clinical findings.

but it is just 43% for young adults. However, outcomes even for young adults can improve by 15% to 20% in clinical trials. In a recent study, overall survival of young adults was 67% when treated on intensive pediatric ALL protocols versus just 46% when treated on adult ALL protocols.

The few young adults with ALL who are fortunate enough to be treated in a clinical trial usually find themselves in one that is not designed for their particular needs. At Peyton Manning Children's Hospital at St. Vincent, we have protocols for treating patients from 1 to 30 years of age. There are two advantages to having these young adults participate in our pediatric protocol instead of an adult protocol:

1. Most adult treatment protocols are designed—and therefore dosed—for those who are 60 years of age and older, who usually have comorbidities such as diabetes, heart failure, smoking-related lung impairment, and other chronic ailments. Young adults with ALL, however, are usually otherwise healthy. Moreover, most adult leukemia protocols are for acute myelogenous leukemia (AML) and not ALL.

2. We are equipped to deal with the complex, long-term aspects of the ALL protocol, eg, social issues, such as substandard performance in school or in the workplace; issues associated with side effects from medications or complications of the disease; and follow-up and monitoring for late

Case report

Frank (not the patient's real name) is a 19-year-old white man who noted lumps growing on both sides of his neck over a 2-month period. He also felt increasingly fatigued and took naps during the day. He had no fever or night sweats, but he lost 30 pounds over this time. The neck lumps grew harder and bigger, and new lumps developed over both inguinal areas.

Frank consulted his family physician, who ordered a CT scan of the chest and abdomen. Results showed diffuse mediastinal, hilar, axillary, and retroperitoneal adenopathy. His physician referred him to an adult hematologist-oncologist, who requested a cervical lymph node biopsy. Those results were compatible with T-cell lymphoblastic lymphoma. The complete blood count (CBC) and chemistry profile were normal.

Frank was then referred to the Children's Center for Cancer and Blood Diseases at Peyton Manning Children's Hospital at St. Vincent for further evaluation and treatment. A peripheral blood smear showed few abnormal white cells matching lymphoblasts. However, evaluation of bone marrow and spinal fluid revealed T-cell acute lymphoblastic leukemia (ALL). There was no central nervous system or testicular involvement.

We enrolled Frank in Children's Oncology Group (COG) front-line protocol AALL0434 for treatment of newly diagnosed T-cell ALL. During induction therapy, Frank was hospitalized several times for fever and neutropenia, and for pneumonia and cellulitis of his big toe. Despite his complicated treatment course, Frank achieved complete remission after induction chemotherapy. He is now receiving maintenance chemotherapy and is seen at the center once every 4 weeks. A local lab monitors his blood counts once weekly.

Periodic neurocognitive function testing monitors for side effects of disease and treatment. His chance for a cure is very good, with an estimated 5-year event-free survival between 75% and 80%.

Another benefit of our multidisciplinary team

Frank was medically uninsured when he came to the center. Our staff social worker helped him and his family successfully apply for Medicaid and Social Security assistance. She also identified several foundations that provided financial assistance to Frank and his family.

Frank will continue to receive treatment for his ALL for 18 more months. For at least 5 years after that, he will visit the center periodically so we can ensure he is leukemia-free and monitor him for long-term side effects of treatment.

Despite his complicated treatment course, Frank achieved complete remission after induction chemotherapy.

Doing more for infants, too

Acute lymphoblastic leukemia (ALL) accounts for just 2% to 5% of all cancers in infants. However, the cure rate is a disappointing 35% to 40%. Dr Joanne Hilden of Peyton Manning Children's Hospital at St. Vincent serves as co-chair of the COG AALL0631 study, which investigates the addition of a novel targeted agent, lestaurtinib. This small molecule targets the MLL gene, which is rearranged in more than two-thirds of infant ALL cases and is associated with poor prognosis. Lestaurtinib is combined with multi-agent intensive chemotherapy that is active both in ALL and acute myelogenous leukemia (AML), and is expected to increase overall survival in this vulnerable patient population.

cardiac, endocrine, and other possible consequences of treatment. We monitor the progress of long-term survivors for at least 10 years following treatment, starting at every month the first year and gradually increasing the intervals to once a year.

Current clinical trials of ALL in young patients

Among the trials currently active, 2 are studying the effects of combining the promising agent clofarabine with different medications in the treatment of relapsed leukemia.

- I serve as the institutional principal investigator for the CLO218 protocol for patients 1 to 21 years of age who have ALL; Peyton Manning Children's Hospital at St. Vincent is the only site in Indiana participating in this study. Etoposide and cyclophosphamide are the 2 agents combined with clofarabine.

- I serve as the study chair for the COG AAML0523 protocol, in which clofarabine is paired with cytarabine to treat relapses of either ALL or AML in patients 1 to 30 years of age.

- COG protocol AALL0434 is open to patients 1 to 30 years of age who have T-cell ALL, as determined by immunophenotyping. This type of ALL occurs more commonly among older patients. This study uses a novel chemotherapeutic agent, nelarabine, which has specific activity against pediatric and adult ALL and lymphoma. The protocol also employs systemic and intrathecal chemotherapy and cranial irradiation. □

Family-experience endoscopy

Optimizing parental education

An engaged mind is a receptive mind, and family-experience endoscopy offers a unique opportunity to teach parents. After being ushered into the endoscopy suite, parents stay with their child until anesthesia takes effect. They then sit on a nearby couch to view the procedure, to receive real-time information from the endoscopist, and to ask questions.

Following the procedure, parents are given key photos and an explanation of the preliminary findings. We have found these teaching moments to be especially effective. In fact, parents who are present at their child's procedure generally will be more compliant with follow-up medication instructions than those who are not. (Parents can also sit through a therapeutic procedure—eg, placement of a gastrostomy tube—if they wish.)

At the time of the procedure, a follow-up appointment has already been scheduled for 1 to 2 weeks later, when final outcomes are discussed with parents. We also send the patient's primary care provider copies of all reports, including lab and biopsy results.

Another benefit of family-experience endoscopy

Many of the problems we see in children have a familial component, and we often refer parents for endoscopy, especially when they volunteer that they experience symptoms similar to their child's. Such conditions include celiac disease, eosinophilic esophagitis, *Helicobacter pylori*, and Crohn's disease.

Acid reflux disease also falls in this category. In younger patients, dysphagia unresponsive to usual therapy may point to reflux affecting the esophagus or adjacent arytoids. Recurrent ear and sinus infections, chronic diarrhea, or evidence of malabsorption may also suggest this problem. Older patients often complain of epigastric or abdominal pain, nausea, diarrhea, or chronic airway disease.

Interestingly, dentists sometimes refer patients to us because of dental erosions that suggest reflux. Pulmonologists, too, will refer patients who have asthma unresponsive to medications. □

Parents who are present at their child's procedure generally will be more compliant with follow-up medication instructions than those who are not.

Peyton Manning Children's Hospital at St.Vincent

In conjunction with

St. Mary's Hospital for Women and Children

Present:

The Spring Pediatric Conference:

*Provider, Patient, Problems, and Profit:
Real Issues in Primary Care Pediatrics*



**This pediatric conference is designed for
MDs, NPs, PAs, and RNs from
pediatric and family practice settings.
CME and CNE credits are pending.**

June 12-14, 2009

French Lick Resort, French Lick, IN

For Information and Early Registration:

317-338-CARE (2273)

