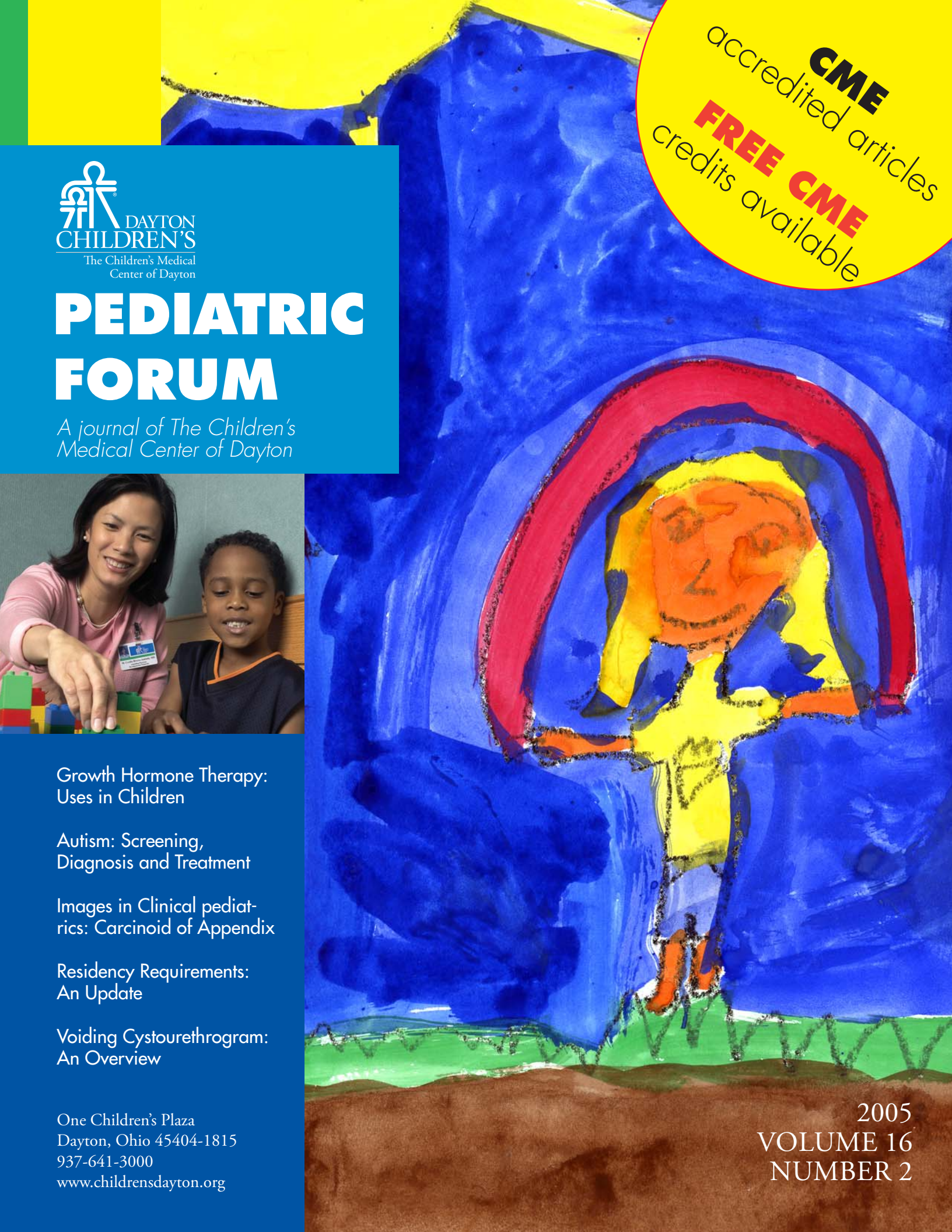

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Educational objectives

- Articles will review commonly encountered clinical conditions and provide updates in pediatric medical and surgical care.
- Each individual article will have activity-specific learning objectives.

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GROWTH HORMONE THERAPY
CURRENT USES IN CHILDREN

by Paul Breyer, MD

Dr. Breyer is a pediatric endocrinologist at Dayton Children's and is assistant professor of pediatrics at Wright State University Boonshoft School of Medicine.

OBJECTIVES

After completing the article, the reader should be able to:

1. List the six indications for growth hormone therapy in children approved by the FDA.
2. Recognize which indications require a formal growth hormone stimulation test prior to treatment.
3. Describe the most common presenting signs of growth hormone deficiency.
4. Review the classic clinical features of Turner and Prader-Willi syndromes.

Recombinant growth hormone (GH) was first available in 1985 to treat growth hormone deficiency. There are now eight FDA-approved indications for GH therapy in the US (Table 1), six of them are directed at the pediatric population. These include childhood GH deficiency, growth failure secondary to chronic renal insufficiency, Turner syndrome, Prader-Willi syndrome, small for gestational age without growth recovery and idiopathic short stature. The different growth hormone preparations and their FDA approved indications are listed on Table 2.

Childhood GH deficiency: Children with classic GH deficiency (GHD) can present at different ages with different clinical signs. Infants with congenital GH deficiency either isolated or as hypopituitarism, can have micropenis, fasting hypoglycemia and jaundice. Infants and children usually present with proportional short stature, a slow growth rate and a delayed bone age. Due to the loss of the lipolytic action of GH, children may have a cherubic appearance due to a relative weight excess for height. The diagnosis of GHD is suggested by low IGF-I and IGFBP-3 levels, but is classically made using a growth hormone stimulation test. The GH response to secreatogues such arginine, L-Dopa, clonidine and glucagon are used to assess the GH production in children. A peak response of less than 10 ng/ml with two of these secreatogues is consistent with the diagnosis of GHD. A MRI scan of the brain and pituitary gland should be performed in all cases of confirmed GHD to rule out any CNS pathology. The efficacy of GH in promoting linear growth in these children is well established.[1] When started early, GH therapy can increase final adult height and restore full genetic height potential. With the availability of recombinant GH for the past 20 years, clinicians have been able to use higher doses of GH (average of 0.3 mg/kg/week up to 0.7 mg/kg/week in pubertal patients), more frequent dosing (daily instead of three times a week) and longer duration of therapy, leading to improved final height outcomes.

Growth failure secondary to chronic renal insufficiency: The etiology for growth failure seen in children with chronic renal insufficiency (CRI) is multifactorial. Younger onset, steroid use, severity of bone disease, inadequate nutrition, acidosis and other biochemical derangements are all contributing factors. These children are not truly growth hormone deficient but they appear to be partially GH-resistant with reduced levels of IGF-I due to increased binding to elevated IGFBP-3 secondary to decreased renal clearance. A formal GH stimulation test is not necessary in these children. The use of GH in these patients causes persistent catch-up growth with the majority of patients achieving a normal adult height.[2] Therapy (0.35 mg/kg/week) was not associated with an acceleration in the decline of the glomerular filtration or other toxicity.

Turner Syndrome: Turner syndrome or gonadal dysgenesis is a genetic condition that is associated with the absence of or a structural abnormality of one X chromosome. These girls typically demonstrate a 45 XO or a 46XX/45XO mosaic karyotype. The typical clinical features include growth failure/short stature, absent ovarian function, as well as other physical signs including edema of the hands and feet at birth, a webbed neck, high-arched palate, cubitus valgus, shield chest, short fourth metacarpals, hypoplastic nails, etc. They can also have

Continued

cardiac and renal abnormalities, scoliosis, frequent otitis media and autoimmune hypothyroidism. About 50% of affected girls have no stigmata except short stature and later ovarian failure, so a karyotype needs to be performed in all girls with short stature. The growth failure associated with Turner syndrome is not related to GHD but appears to be linked to a loss of function of the short stature homeobox (SHOX) gene normally located on the X chromosome.[3] However, these girls do respond to GH therapy (0.35 mg/kg/dl) with an additional 10 cm or 4 inches on average with long-term treatment. The final height outcomes are improved with earlier diagnosis and treatment as well as the later introduction of estrogen replacement (15 years).[4]

Prader-Willi Syndrome: Prader-Willi syndrome (PWS) is associated with hypotonia, mental retardation, obesity and short stature. These children can also have hypogonadism with cryptorchidism and micropenis. Genetic testing has led to the association of PWS with abnormalities of the long arm of chromosome 15. The short stature associated with PWS is due to GH deficiency due to hypothalamic dysfunction. GH and IGF-I deficiencies can lead to the abnormal body composition, since treatment with GH decreases fat mass, increases lean body mass, increases physical function and increases resting energy expenditure.[5] A growth hormone stimulation test is not required in these patients and a dose of 0.24 mg/kg/week is recommended. There have been several cases of sudden death in children with Prader-Willi on GH but this has also been the case with PWS patients not on GH. These deaths were respiratory related and thought to be due to insufficiency of respiratory muscles and pharyngeal narrowness in association with severe obesity. Therefore, before institution of GH therapy it is recommended for all children with PWS to have polysomnography, an otorhinolaryngologic examination and tonsillectomy in the case of enlarged tonsils. GH is contraindicated in PWS patients who are severely obese or have severe respiratory impairment.

Small for Gestational Age Without Growth Recovery by 2 Years of Age: The majority of healthy infants born small for gestational age (SGA) will achieve catch-up growth in length during the first two years of life. Unfortunately, a great number of the remaining children continue to grow poorly and will remain short as an adult. These children typically have normal or low normal IGF-I and IGFBP-3 levels and they have normal GH stimulation tests. Studies demonstrated that GH therapy was able to normalize stature and increase final height potential above predicted height.[6] The FDA-approved dose of GH is 0.48 mg/kg/week. The improved growth response is dose-dependent and with the higher GH dose, increased side effects were monitored. Studies on long-term use showed higher post-glucose insulin levels, but there have been no effects on the plasma glucose or HbA1C levels in these patients. Formal GH testing is not required in these children, however, if the patient does have an abnormal growth velocity, true GHD needs to be ruled out with a formal GH stimulation test.

FDA approved indications for GH therapy in US and date of registration

Childhood GH deficiency	*1985*
Growth failure secondary to chronic renal insufficiency	*1993*
Wasting syndrome associated with HIV infection in adults	*1996*
Turner syndrome	*1996*
Adult GH deficiency	*1997*
Prader-Willi syndrome	*2000*
SGA without growth recovery by 2 years of age	*2001*
Idiopathic short stature	*2003*

Table 1

GH preparations with their FDA-approved uses*

Medication	*Company*	*GHD*	*CRI*	*TS*	*PWS*	*SGA*	*ISS*
Genotropin	*Pfizer*	*yes*	*no*	*no*	*yes*	*yes*	*no*
Humatrope	*Lilly*	*yes*	*yes*	*yes*	*no*	*no*	*yes*
Norditropin	*Novo Nordisk*	*yes*	*no*	*no*	*no*	*no*	*no*
Nutropin	*Genentech*	*yes*	*yes*	*yes*	*no*	*no*	*yes*
Nutropin AQ	*Genentech*	*yes*	*yes*	*yes*	*no*	*no*	*yes*
Saizen	*Serono*	*yes*	*yes*	*yes*	*no*	*no*	*no*
Tev-Tropin	*Teva*	*yes*	*no*	*no*	*no*	*no*	*no*

**Status as of June 2005. GHD, growth hormone deficiency; CRI, chronic renal insufficiency; TS, Turner syndrome; PWS, Prader-Willi syndrome; SGA, small for gestational age; ISS, idiopathic short stature.*

Table 2

Continued

CME QUESTIONS

1. Which of the following is NOT an FDA-approved indication for growth hormone?
   a. Chronic renal insufficiency
   b. Cystic fibrosis
   c. Turner syndrome
   d. Prader-Willi syndrome

2. Which of the following requires a formal GH stimulation test prior to treatment?
   a. Chronic renal insufficiency
   b. Small for gestational age
   c. Turner syndrome
   d. Idiopathic short stature

3. Which cause for short stature is linked to a loss of function of the SHOX gene?
   a. Chronic renal insufficiency
   b. Hypopituitarism
   c. Turner syndrome
   d. Prader-Willi syndrome

Idiopathic Short Stature: This is the term used to describe proportional short children (< -2 S.D.) with normal GH responses to secretagogues, normal growth factors and have no other identifiable cause for their short size. A randomized, double-blinded, placebo-controlled trial showed that GH treatment increased final adult height in peripubertal children with marked idiopathic short stature.[7] Over 40% of the GH-treated patients reached a final height above the 5th percentile for height versus 0% in the placebo group. There were no severe adverse effects in these patients during this trial and the GH-related acute events were similar to those seen with GHD and Turner syndrome. The FDA approved the use of growth hormone (0.37 mg/kg/week) for idiopathic short stature, defined by height SDS $\leq$-2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range. A complete work-up including a formal GH stimulation test needs to be performed to exclude other causes for short stature. A special growth curve is available that highlights the 1.3 percentile for height (<-2.25 S.D.) (Available from Lilly and Genentech).

Our knowledge of growth hormone physiology and our ability to treat children with GH deficiency has grown dramatically over the past 20 years. With the advent of recombinant gene therapy, endless supplies of GH have become available to lead us to new questions, new indications and the need for continued surveillance and follow-up studies. New indications for growth hormone including cystic fibrosis, Crohns disease and Noonan syndrome are currently being studied but await FDA approval.

References

1. Root AW, Kemp SF, Rundle AC, Dana K, Attie KM, Effect of long-term recombinant growth hormone therapy in children—The National Cooperative Growth Study, USA 1985-1994. *J Pediatr Endocrinol Metab* 1998;11:403-12.
2. Fine RN, Kohaut E, Brown D, Perlman AJ. Growth after recombinant human growth hormone treatment in children with chronic renal failure: report of a multicenter randomized double-blind placebo-controlled study. Genentech Cooperative Study Group. *J Pediatr* 1994;124:374-82.
3. Rao E, Blaschke RJ, Marchini A, Niesler B, Burnett M, Rappold GA. The Leri-Weil and Turner syndrome homeobox gene SHOX encodes a cell-type specific transcriptional activator. *Hum Mol Genet* 2001; 3083-91.
4. Chernausek SD, Attie KM, Cara JF, Rosenfeld RG, Frane J. Growth hormone therapy of Turner syndrome: The impact of age of estrogen replacement on final height. Genentech, Inc., Collaborative study group. *J Clin Endocrinol Metab* 2000;85:2439-45.
5. Carrel Al, Myers SE, Whitman BY, Allen DB. Benefits of long-term GH therapy in Prader-Willi syndrome: a 4-year study. *J Clin Endocrinol Metab* 2002;87:1581-5.
6. Boguszewski M, Albertsson-Wikland K, Aronsson S et al. Growth hormone treatment of short children born small-for-gestational-age: the Nordic Multicentre Trial. *Acta Paediatr* 1998;87:257-63.
7. Leschek EW, Rose SR, Yanovski JA et al. Effect of Growth Hormone Treatment on Adult Height in Peripubertal Children with Idiopathic Short Stature: A Randomized, Double-Blind, Placebo-Controlled Trial. *J Clin Endocrinol Metab* 2004;89:3140-8.

AUTISM:
SCREENING, DIAGNOSIS AND TREATMENT

by Cecilia Amisola, MD

Dr. Amisola is a developmental pediatrician at Dayton Children's and is assistant professor of pediatrics at Wright State University Boonshoft School of Medicine.

OBJECTIVES

After completing the article, the reader should be able to:

1. Describe the process of screening for autistic disorders in the primary care setting.
2. Describe the process of diagnostic evaluations of autistic disorders.
3. Review the role of pharmacologic treatment in autistic disorder.
4. Emphasize the importance of behavioral interventions in the treatment of autistic disorder.

Autism is a neurobiological and complex developmental disorder that typically manifests itself during the first three years. Leo Kanner first described autism in 1943. His study discussed 11 children with "autistic disturbance of affective contact" exhibiting three major symptoms: social isolation, insistence on sameness and abnormal language. In the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) autism is classified as one of five pervasive developmental disorders (PDDs), now more commonly referred to as autism spectrum disorders (ASDs). While numerous studies have shown that laboratory and anatomical differences exist in individuals with ASDs, the diagnosis continues to be based on behavioral criteria. Children with ASD demonstrate delays and/or deficits in social interaction, verbal and nonverbal communication, and manifest repetitive behaviors or interests.

The most common presentation is speech and language delay. This delay also may present as echolalia or hyperlexias precocious language with a large vocabulary yet inability to sustain a conversation. Often times disruptive behaviors are reported: frequent temper tantrums; unusual attachment to toys; odd movement patterns (eg, peripheral gazing, hand flapping, finger play); oversensitivity to sounds, textures, sensations; and inappropriate play with objects (eg, spinning objects not meant for spinning). Typically caregivers have difficulty competing with the objects on which the autistic child focuses. The restricted range of interest interferes additionally with the ability to socialize and carry on a conversation. No single pathognomonic behavior can be attributed to all children on the spectrum; furthermore, atypical behaviors may not be prominent in the very young child with autism. The delays/deficits in language and atypical socialization skills vary in degree among these children (Table 2).

With a documented increase in the incidence of ASDs, primary care physicians are likely to encounter more patients exhibiting ASDs. Because studies are showing that early and intensive behavioral and educational intervention leads to improved outcome in autistic children, early diagnosis is critical. Several screening tools are available to aid primary care physicians in detecting ASD. The M-CHAT (Modified Checklist for Autism in Toddlers) is a parent-completed questionnaire designed for use with 18-month-old children in primary care settings. It consists of 23 yes/no questions, is easy to score and readily available. The M-CHAT can be downloaded from the website www.firstsigns.org. The Pervasive Developmental Disorder Screening Test-Stage 1 (PDDST-II) is a parent-completed survey for children from birth to 3 years. It is one of a three-stage tool. The next two stages are applicable for use in more specialty settings.

When autism-specific screening tools are not available, the physician should ask specifically about aspects of language and social emotional development, joint attention skills and pretend play. The absolute indications for the immediate evaluation for autism are no babbling and/or no pointing by 12 months, no single words by 16 months, no two-word spontaneous (non-echolalic) phrases by 24 months, and any loss of language or social skills at any age (Table 1). Siblings of children already diagnosed with autism should be carefully monitored.

Continued

Absolute indications for immediate evaluation of autism:

By 12 months:
- *No babbling*
- *No pointing or other gestures*

By 16 months:
- *No single words*

By 24 months:
- *No two-word spontaneous phrases*

At any age:
- *Any loss of language or social skills*

Table 1

Diagnostic Criteria for Autistic Disorder:

Impaired social interaction (at least two of the following):
- *Marked impairment in the use of nonverbal behaviors to regulate social interaction (eye contact, gestures, facial expression)*
- *Failure to establish developmentally appropriate peer relationships*
- *Lack of spontaneous sharing of enjoyment/interests*
- *Lack of social or emotional reciprocity*

Impairment in communication (at least two of the following):
- *Delayed or absent speech, not accompanied by compensatory nonverbal communication*
- *Inability to initiate or sustain a conversation (if speech is present)*
- *Stereotyped and repetitive language, echolalia or idiosyncratic language*
- *Lack of developmental appropriate imaginary play or social imitative play*

Restricted range of interests or behavior (at least one of the following):
- *Restricted pattern of interest that is abnormal in focus/intensity*
- *Rigid adherence to nonfunctional routines or rituals*
- *Repetitive and stereotyped motor movements*
- *Preoccupation with parts of objects, often overlooking the function/purpose of the whole object*

Table 2

Initial laboratory investigation should include lead screening in any child with developmental delay and pica. Periodic lead screening should be done if pica persists. The child should have formal assessments of hearing and vision. A formal audiological assessment by a pediatric audiologist is preferred over office-based hearing screening, since the audiologist's assessment includes behavioral audiometric measures, middle ear function and electrophysiologic testing.

Referral for further diagnostic evaluation is required for obtaining a comprehensive developmental profile. Ideally, this evaluation is performed by a multidisciplinary team, which may include a physician, psychologist, speech and language pathologist and occupational therapist. If a team is not available, refer to medical professionals with experience in diagnosing autism such as a pediatric neurologist, developmental pediatrician or child psychiatrist.

For diagnosing autism, the following instruments are often used: Gilliam Autism Rating Scale (GARS), a parent-completed questionnaire; Childhood Autism Rating Scale (CARS), completed by conducting a structured interview and direct observations; Autism Diagnostic Interview-Revised (ADI-R), a semi-structured interview which requires specific training on the part of the examiner; Autism Diagnostic Observation Schedule-Generic (ADOS-G) a semi-structured assessment involving interview and directed activities also requiring training and validation procedures. The ADI-R and ADOS-G are considered the gold standard diagnostic instruments and used often in research. These two tests usually are administered by psychologists and other nonphysician specialists.

Although the diagnosis is based on behavioral criteria, it is important to determine underlying medical conditions and comorbidities. It should be noted if history is remarkable for neurologic insults via trauma or infection, or if there is a history of any seizure activity, subclinical or overt, and if there is observed regression at any time. There is a higher prevalence of seizure disorders (25%-30% over the lifetime) so there should be a lower threshold for obtaining an EEG. Attention must be paid to sleep patterns, feeding difficulties, self-injurious behaviors and motor tics. Family history of neurologic and genetic disorders must be noted, as Fragile X syndrome, tuberous sclerosis, autism, schizophrenia and depression are known to be risk factors. Consider testing for the MECP2 mutation identified in Rett syndrome in girls diagnosed with autism. Gastrointestinal problems such as frequent diarrhea, constipation and difficulty with toilet training may require a referral to pediatric gastroenterology.

Physical examination of the autistic child should focus on certain aspects. Dysmorphic features or skin lesions may point to a syndrome or neurocutaneous disorders. Craniofacial anomalies/ENT abnormalities such as tonsillar and adenoidal hypertrophy contribute to feeding problems or poor sleep. Undetected dental caries causing pain and discomfort may exacerbate difficult behaviors, especially in noncommunicative children. Similarly, dermatologic conditions causing discomfort, rashes due to allergies, eczema, fungal infections, etc may have a similar affect on behaviors. Strabismus, poor visual acuity or poor depth perception contribute to poor coordination and motor planning. A simple ear examination in an autistic child is, all too often, not so simple, so recurrent otitis media may go undetected. Referring the child to an ENT specialist can prevent this occurrence.

Psychological testing using standardized tests determines cognitive abilities and measures adaptive functioning. Psychological evaluation plays an important role in the developing an intensive behavioral intervention using applied behavioral

Continued

CME QUESTIONS

4. Which of the following is not a diagnostic instrument used in the diagnosis of autism?
a. CARS
b. GARS
c. PDDST-Stage 1
d. PDDST-Stage 2

5. The following behaviors are pathognomonic of autistic disorder:
a. head-banging
b. rocking back and forth
c. lining up toys and objects
d. all of the above
e. none of the above

6. A 2-year old boy presents to your office for well-child care. Physical and neurological examinations are normal. He has a known history of frequent otitis media and had PE tubes, although his prior hearing tests have been normal. Mom is concerned that he still has not called her "mama" and does not turn when he is called by his name. You observe that it is hard to get his attention as he is playing with a new toy that he brought with him to the office.

The following are appropriate steps you could take, except:
a. Refer the child for an audiological evaluation by a pediatric audiologist
b. Have mother complete an M-CHAT
c. Refer for a speech and language evaluation
d. Watchful waiting and follow-up in six months

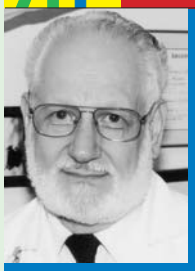
analysis. Speech and language pathology evaluations help measure various areas: receptive language, expressive language, pragmatic communication skills, and oromotor function. An autistic child with verbal apraxia will need an assessment for augmentative and alternative communication devices. Occupational therapy assessment is useful when there are deficiencies in functional skills, as the therapist can assist in setting goals and treatment plans for daily routines. Some occupational therapists have training in sensory integration therapy; however, this therapy's routine use for and effect on autistic individuals requires further controlled research.

No specific medical treatment exists for autism. Medications should be used with specific targeted symptoms and outcome measures must be made clear to the family. Stimulants and alpha-adrenergics may help to decrease hyperactivity, impulsivity and inattention. Atypical antipsychotics, particularly risperidone, may help to decrease self-injurious behaviors and aggression. Selective serotonin reuptake inhibitors (SSRIs) may help to decrease anxiety and/or obsessive tendencies and compulsions, widen an autistic child's range of interests and improve interpersonal contact. More importantly, medications should be used in conjunction with other therapies for addressing features interfering with therapy progress and day-to-day functions.

Various treatments are reported in literature, yet many are unsupported by research. A good treatment program starts early and includes functional behavioral approaches. It is developmentally appropriate (builds on attention, imitation, comprehension, use of language play and social skills), highly supportive and structured, and involves the family in every step of the process. Among the various treatment modalities tried so far, behavioral approaches have proven to be the most effective in treating autistic children. Professor O. Ivar Lovaas of UCLA, via his 1987 study, popularized Applied Behavioral Analysis (ABA). Also known as intensive behavioral intervention (IBI), early intensive behavioral intervention (EIBI) or discrete trial teaching (DTT), ABA is used to teach autistic children how to learn by focusing on the building blocks of language development, imitation and matching through reinforced practice. Most importantly, therapies with goals incorporating speech-language, occupational, early intervention or preschool programming can be initiated even before a diagnosis.

References:

1. American Academy of Pediatrics Committee on Children with Disabilities. Technical Report: The Pediatrician's Role in the Diagnosis and Management of Autistic Spectrum Disorder in Children. *Pediatrics*. 2001; 107(5): 1-18
2. Butter E, Wynn J, Mulick. J. Early Intervention Critical to Autism Treatment. *Pediatric Annals*. 2003; 32(10):677-684
3. Lindsay R, Aman M. Pharmacologic Therapies Aid Treatment for Autism. *Pediatric Annals*. 2003;32 (10): 671-676
4. Manning-Courtney P, Brown J, Molloy C, Reinhold J, et al. Diagnosis and Treatment of Autism Spectrum Disorders. *Current Problems in Pediatric Adolescent Health Care* 2003; October: 283-304
5. Coury D, Nash P. Screening Tools Assist with the Diagnosis of Autistic Spectrum Disorder. *Pediatric Annals* 2003;32 (10):664-670



By L. David Mirkin, MD

Dr. Mirkin is director of pathology at Dayton Children's and is the chairman of Dayton Children's professional staff. He is the head of the division of pathology at Dayton Children's and a professor of pathology and pediatrics at Wright State University Boonshoft School of Medicine.

OBJECTIVES

After completing the article, the reader will be able to:

1. *Recognize the diagnostic features of carcinoid of appendix.*
2. *Discuss the origin of carcinoid of appendix.*
3. *Discuss the therapeutic approaches for carcinoid of appendix.*

CASE REPORT:
CARCINOID OF APPENDIX

A 12-year-old white female complained of very uncomfortable sharp pain in the right lower quadrant. She was able to urinate, had normal bowel movements, no emesis and her last menstrual period occurred two weeks before this examination. Patient had had recent sinusitis treated with amoxicillin. Physical examination revealed positive Rovsing sign and rebound at McBurney point. She was afebrile and the remainder of the physical examination was unremarkable. The laboratory data were significant for leukocytosis: 19.7 x 10^9/µL (normal range 4.5 - 13.5 10^9/µL) with 76% segmented neutrophils (normal mean 52%), 10% lymphocytes (normal mean 38%), 6% monocytes (normal mean 4.4%), and 0% basophils (normal mean 4.4%). With clinical diagnosis of appendicitis, an appendectomy was performed. The appendix showed transmural purulent exudate including the serosa and a yellow, solid, uniform lesion infiltrating the wall, with a rim of grossly uninvolved tissue extending up to 1.0 cm from the tip. Microscopic examination demonstrated acute inflammation and solid nests of small monotonous cells with round nuclei without prominent nucleoli infiltrating the muscularis and serosa focally forming acini or rosettes. The diagnosis was carcinoid of the appendix and acute appendicitis. No more treatment and follow-up were recommended.

FIGURE 1

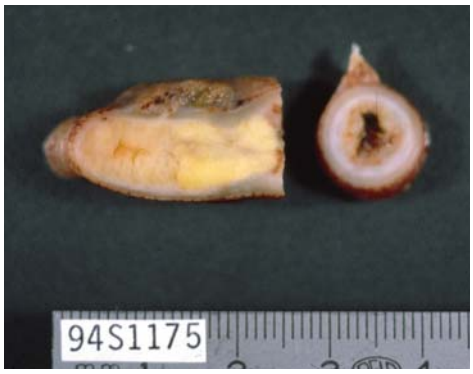
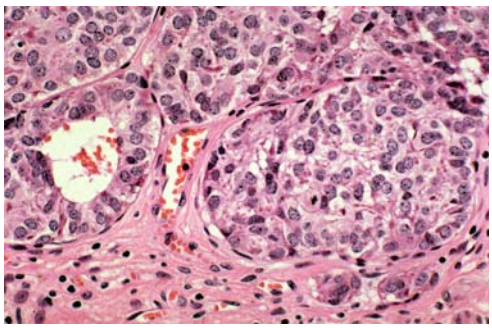


FIGURE 2



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CME QUESTIONS

7. The carcinoid tumor originates in:
a. Columnar cells
b. Goblet cells
c. Epithelial argentaffin cells
d. Ganglion cells
e. Schwann cells

8. Carcinoid of appendix tumors present:
a. Carcinoid syndrome most of the time
b. As an incidental finding with acute appendicitis
c. Often with an abdominal mass
d. Weight loss
e. Often with abdominal pain

9. The therapeutic consideration(s) include:
a. Age of the patient and size of the tumor
b. Diploid DNA pattern on flow cytometry of the tumor
c. Immunohistochemical reactivity of the tumor
d. Secretation of serotonin
e. Positive chromogranin

Discussion

Carcinoid tumors of the appendix are the most common neuroendocrine tumors of the gastrointestinal tract in children. They are found as an incidental finding in about one of every 300 routine appendectomies.[1] Rarely they present with an abdominal mass or pain. The carcinoid syndrome with attacks of severe cyanotic flushing, watery diarrhea, bronchospasm, sudden drop in blood pressure, edema, ascitis and right-sided heart failure due to stenosis of the bicuspid and pulmonary valves[2] is due to the secretion of serotonin, prostaglandins and other biologically active substances. It is extremely rare and almost always related to liver metastases. The tumor originates in the epithelial argentaffin cells and it is usually represented by a less than 1 cm in greatest dimension; fairly well circumscribed but not encapsulated yellow nodule that infiltrates the appendiceal wall and projects into the lumen of the distal one-third of the appendix (Figure 1). Microscopically carcinoid tumors are composed of solid nests, ribbons, trabeculae or glandular structures of uniform polygonal cells with round nuclei, inconspicuous nucleoli, amphophilic cytoplasm and scarce mitotic figures (Figure 2). The tumor cells are immunohistochemically reactive for chromogranin, an acidic protein expressed in neural tissues and endocrine cells (the most reliable marker) and a variety of peptide hormones. Electron microscopy shows neurosecretory type granules and mucin droplets. Most of these tumors have a diploid DNA pattern on flow cytometry. Differential diagnoses include adenocarcinomas, gangliocytic paraganglioma and granular cell tumor.

The majority of patients with neuroendocrine tumors of appendix have good prognosis. Appendectomy alone is considered adequate therapy for tumors smaller than 1 cm. Numerous cases of serosal extension and local lymph node involvement have been described, but only rare cases of metastasis after initial appendectomy have been reported. A right hemicolectomy has been recommended for tumors larger than 2 cm because of a significantly higher metastatic potential.[3] More aggressive therapy is advocated for younger patients or for those with tumors that show a high mitotic rate, deep mesoappendiceal invasion, or margin involvement.[4]

References

1. *Rosai J, Rosai and Ackerman's Surgical Pathology. 9th ed*. Edinburgh, UK: Mosby; 2004:765-768.
2. Wilander E, Carcinoid syndrome. In: Whitehead R, ed. *Gastrointestinal and Oesophageal Pathology*. 2nd ed. Edinburgh, UK: Churchill Livingstone; 1995:749.
3. Cooper HS, Carcinoid tumor. In: Mills ST, et al. eds. *Sternberg's Diagnostic Surgical Pathology. 4th ed*. Philadelphia, MA: Lippincott Williams & Wilkins; 2004:1577-1578.
4. Graeme-Cook F, Appendiceal neuroendocrine tumors. In: Odze RD, Golblum JR, Crawford JM, eds. *Surgical Pathology of the GI Tract, Liver, Biliary Tract, and Pancreas*. Philadelphia, MA: Saunders; 2004:499-502.

RESIDENCY REQUIREMENTS UPDATE:
FROM WORK HOURS TO COMPETENCIES

by Ann Burke, MD

Dr. Burke is the director of the residency program at Dayton Children's and assistant professor of pediatrics at Wright State University Boonshoft School of Medicine

Over the past two years, several new policies and requirements have been mandated by various accrediting organizations. Implementing some of these requirements in graduate medical education (GME) has caused heated discussion among program directors, faculty, residents and hospital administrators across the country. This article discusses the new major requirement in GME, work-hour regulations and Dayton Children's steps to compliance.

After completing medical school, graduate medical education (GME) begins and residents study a specific specialty such as pediatrics, internal medicine, surgery, etc. GME educators recognize the interplay between education and service. Each resident needs multiple experiences during their training, which compete for the resident's time. These competing priorities include varying amounts of clinical experience, patient care, educational conference participation, self-directed study, etc. The Accreditation Council for Graduate Medical Education (ACGME) recently decided to implement new limits on residents' work hours.[1,2] When these limits were implemented in June 2003, it was the first time the ACGME mandated a core set of limits on work hours across all specialties.

The "Common Duty Hours" are a product of the public's concern and scrutiny about fatigued physicians-in-training. The ACGME "Common Duty Hours" are very similar to legislation passed in the state of New York more than a decade ago. In 1984, Libby Zion presented to a New York City teaching hospital. She was misdiagnosed by a medical resident and died of bilateral pneumonia and sepsis. This woman's father Sidney Zion was a high-profile, former federal prosecutor and news columnist. As a result, the New York health commissioner convened an advisory committee to scrutinize some of the issues surrounding resident supervision and work hours. This group was known as the Bell Commission. Bertrand Bell, MD, a professor of medicine at Albert Einstein College of Medicine, led the commission. On July 1, 1989, the recommendations of the Bell Commission, which are the model for the ACGME recommendations, were passed into law by the New York State legislature.[3]

Many studies show that sleep deprivation, both chronic and acute, negatively influences performance in residents.[4, 5, 6] One study revealed that in the early morning hours, after nearly 24 hours without sleep, psychomotor performance can be impaired to such a great extent as to be equivalent to a blood alcohol level of 0.08% (the legal limit).[7]

To be proactive and provide leadership, the ACGME mandated the work hours. By doing so, the ACGME had hoped to avoid oversight of GME work hours by OSHA (Occupational Safety and Health Administration) and federal law makers. The ACGME has enforced and policed the new requirements; however, in spite of these actions, bills have been recently introduced into congress that could eventually mandate federal oversight of resident work-hours.

A summary of the 10-page document concerning residents:
- Duty hours must be limited to 80 hours per week, averaged over a four week period.
- Residents must be provided with one day free in seven from all clinical and educational activities.
- Inhouse call must occur no more frequently then every third night.
- Continuous on-call duty must not exceed 24 consecutive hours. Residents may remain on duty for an additional six hours to participate in educational/

OBJECTIVES

After completing the article, the reader should be able to:

1. Describe the reasons why the ACGME enacted the Work Hour Guidelines.
2. Name at least two specific aspects of the work hour rules.
3. Describe the system change at Dayton Children's that was made to facilitate compliance with the work hours.

Continued

CME QUESTIONS

10. The work-hour rules include all of the following except:
- a. Continuous on-call duty cannot exceed 24 hours, residents can stay to provide continuity for an additional eight hours.
- b. Residents cannot work longer than 80 hours per week averaged over a four-week period.
- c. Call (inhouse) cannot be more frequent than every third night.
- d. Residents must have one day free out of seven.

11. All of the following are true about the Bell Commission except:
- a. It was named after the young woman who died at a teaching hospital in New York City.
- b. It recommended changes in resident work hours that were similar to the current ACGME work-hour standards.
- c. It was called into existence due to all of the negative publicity about a young woman's death.
- d. The New York Legislature passed it's recommendations into law in 1989.

12. Sleep deprivation can cause psychomotor impairment equal to a blood alcohol level of 0.08%
- a. True
- b. False

didactic activites, maintain continuity of care, transfer care of patients or conduct continuity clinic, but may not accept new patients.

Pediatric residents at Dayton Children's abide by all of the above rules. Faculty have been educated on the rules, continuity clinics have been modified, and scheduling has been honed. The whole process of changing a culture is long and continuous. The faculty and Dayton Children's professional staff have accepted the conceptual change related to the work-hours, but have expressed concerns about patient continuity, professionalism and work ethic. During Dayton Children's ACGME site visit in August 2004, residents were interviewed about work hours. Likewise, the ACGME conducted an anonymous survey of the Wright State/Dayton Children's residents to assess compliance with regulations. A 76% response from residents was required; however, 100% responded and reported no violations of the rules. Currently, residents complete quarterly time sheets for the program director's and chair's review. The Designated Institutional Official, Margaret Dunn, MD, at Wright State, receives the quarterly reports.

Many facets of patient care and resident education changed to comply with the work-hour standards. Wright State Integrated Residency Program took an active and sensible approach to finding solutions. With continuity of care at risk since residents on-call the night before now left at the same time, a night float system was instituted for the senior residents on the wards. Interns continued to take every fourth night call. With this change, the housestaff overlapped and provided the necessary continuity.

Resident skills in "checking out" are more effective, information-filled and time-efficient resulting in streamlined "check out rounds." With the hiring of two general inpatient attendings for the 2004-2005 academic year, attending level continuity increased during the afternoon hours and had time for teaching residents and medical students, do walk rounds and re-check-patients. This program has been well received by the residents, medical students and professional staff members.

Community pediatricians admitting their patients to Dayton Children's encountered another issue created by the work-hour regulations. Before work-hour restriction, identifying resident coverage for patients was clear and simple. With the night float system and residents leaving post-call, identification became more challenging. By establishing aggressive initiatives, community doctors were ensured identification of the resident responsible for their patient's care. With input from community doctors on the professional staff executive committee, this system was developed and is working.

The ACGME work-hour rules have been the biggest cultural shift in GME in the past 25 years. The Wright State University Integrated Pediatrics Residency has made major modifications to business. The department of pediatrics multi-facted approach including general inpatient attendings, night float system, faculty education and increased communication with community pediatricians, have helped the transition be successful. In May, the Wright State residency program again received five full years of accreditation from the ACGME with no citations! Dayton Children's acceptance and compliance with the new work-hours regulations played a role in this achievement.

References

1. Statement of Justification/Impact for the Final Approval of Common Standards Related to Resident Duty Hours. www.acgme.org
2. The ACGME's Approach to Limit Resident Duty Hours: The Common Standards and Activities to Promote Adherence. www.acgme.org
3. Cherr, G. *The Origins of Regulated Resident Work Hours: New York and Beyond*. The American College of Surgeons, November 2002: Bulletin 23-27.
4. Samkoff, JS. A Review of Studies Concerning Effects of Sleep-Deprivation and Fatigue on Residents' Performance. *Academic Medicine*. 1991; 66:687-693.
5. Pilcher, JJ and Huffcutt, AI. Effects of Sleep Deprivation on Performance: A Meta-analysis. *Sleep*. 1996; 19:318-326.
6. Weinger, MB and Ancoli-Isreal, S. Sleep Deprivation and Clinical Performance. *Journal of American Medical Association*. 2002; 287:955-957.
7. Dawson, D and Reid, K. Fatigue, Alcohol and Performance Impairment. *Nature*. 1997;388:235.

VOIDING CYSTOURETHROGRAM (VCUG)

by Eizabeth Ey, MD

Dr. Ey is director of medical imaging and the head, division of radiology and nuclear medicine at Dayton Children's.

OBJECTIVES

After completing the article, the reader should be able to:

1. Review the indications for VCUG in children and discuss the implication of the results of the VCUG.

The radiographic voiding cystourethrogram (VCUG) is a diagnostic imaging test designed to evaluate the anatomy and function of the bladder by retrograde instillation of iodinated contrast. Fluoroscopic images of the bladder and kidneys are obtained intermittently during bladder filling. The urethra is demonstrated during voiding. The presence or absence of vesicoureteral reflux is documented and graded during the VCUG. Finally, the degree of bladder emptying is assessed. The primary disadvantage of the radiographic cystogram is the relatively high ovarian radiation dose (1,000 to 1,500 mrem). This is about 10 times the ovarian radiation received from a radionuclide cystogram.[1]

The most frequent indication for performing a VCUG is in the evaluation of urinary tract infection (UTI) in children.[2] Other indications for the VCUG include the evaluation of bladder dysfunction such as neurogenic bladder or bladder outlet obstruction, evaluation for urethral obstruction such as posterior urethral valves, evaluation of ano-rectal malformation and evaluation of trauma to the bladder and urethra.

Most urologists and nephrologists recommend that cystography be performed routinely in all infants and children under the age of 5 years with a documented UTI to establish the presence or absence, as well as the grade, of vesicoureteral reflux (VUR).[3] In addition, renal ultrasound is recommended in all children with UTI to evaluate the kidneys for anomalies, obstruction and scarring. Older children and adolescents with infection usually are assessed with ultrasound alone as the likelihood of reflux is low. When sonography in the older child shows either hydronephrosis or parenchymal scarring, further evaluation with cystography is indicated.

The radiographic VCUG is the examination of choice to evaluate first UTI in boys because it can determine the presence and grade of reflux as well as reliably identify urethral abnormalities the can cause or increase the severity of reflux. Because anatomic abnormalities of the bladder and urethra are extremely rare in girls, radionuclide cystography is increasingly replacing radiographic cystography for evaluating the presence or absence of reflux.[4] Because of its reduced radiation dose, radionuclide cystography has also replaced radiographic cystography for follow-up of children with reflux.

Vesicoureteral reflux refers to the retrograde flow of urine from the bladder into the ureter and collecting system of the kidney. Urine flows both antegrade through the urethra and retrograde into the ureter during urination. At the end of micturation, the refluxed urine flows back into the bladder and remains stagnant until the next episode of bladder emptying, increasing the risk of bacterial colonization. The reflux of urine then enables the bacteria to have access to the renal parenchyma.[5]

The frequency of reflux in children with asymptomatic bacteriuria is approximately 15% to 35%, whereas that in children with symptomatic UTI is 20% to 50%. By comparison, the frequency of vesicoureteral reflux in otherwise healthy children is less than 2%. The natural history of reflux is characterized by diminishing prevalence and severity with increasing patient age. Therefore, younger children with UTI have a greater likelihood of having vesicoureteral reflux and of having reflux of a greater severity.

Continued

Vesicoureteral reflux has a higher prevalence in Caucasian children and is familial. The chance of a child having reflux is about 66% if a parent had reflux. The chance of a sibling having reflux is 25%-50% if a child who is the index case for UTI also has reflux. The risk of reflux in a sibling is even greater if the child who is the index case also has evidence of renal damage. Of additional importance is the fact that 75% of siblings with reflux are asymptomatic.

FIGURE 1. *A spot film from a VCUG demonstrates Grade II right vesicoureteral reflux and Grade III left vesicoureteral reflux in a 3-week-old male evaluated for a febrile UTI. The urethra is normal.*

The International Reflux Grading System is the most widely used system to describe the severity of vesicoureteral reflux.[6] In this system, Grade I reflux refers to reflux into the ureter only. Grade II reflux refers to reflux into the ureter, renal pelvis and calyces without dilation or tortuosity. Grade III reflux refers to mild ureteral and pelvic dilation with no or mild blunting of the calyceal fornices (Figure 1). Grade IV reflux refers to moderate ureteral and pelvic distention with blunting of the calyceal fornices and Grade V reflux refers to marked ureteral and pelvic dilation and tortuosity with marked blunting of the calyceal fornices with lack of papillary impressions. The grade of reflux directly correlates with the likelihood of renal scarring. The goal of treatment of UTI in children is the prevention of renal scarring and subsequent renal insufficiency.

CME QUESTIONS

13. Radiographic VCUG is indicated in all children with urinary tract infection.
a. True
b. False

References:

1. Willi U, Treves S. Radionuclide voiding cystography. *Urol Radiol* 1983; 5:161-173.
2. Dick PT, Feldman W. Routine diagnostic imaging for childhood urinary tract infections: a systematic overview. *J Pediatr* 1996; 128:15-22.
3. Rushton HG. Urinary tract infections in children: epidemiology, evaluation and management. *Pediatr Clin North Am* 1997; 44:1133-1169.
4. Bisset GS III, Strife JL, Dunbar JS. Urography and voiding cystourethrography: findings in girls with urinary tract infection. *AJR* 1987; 148:479-482.
5. Hellstrom M, Jacobson B, Marild S, Jodal U. Voiding cystourethrography as a predictor of reflux nephropathy in children with urinary-tract infection. *AJR* 1989; 801-804.
6. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Moebius TE. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. *Pediatr Radiol* 1985; 105-109.

ANSWER SHEET

PEDIATRIC FORUM,
VOLUME 16,
NUMBER 2

Instructions

To obtain CME credit you must:

- Answer the questions from each article and complete this answer sheet.
- Complete the program evaluation located on reverse side.
- Return your completed answer sheet and program evaluation by mail or fax to:

Katie Hill, coordinator
Department of Continuing Medical Education
The Children's Medical Center of Dayton
One Children's Plaza
Dayton, OH 45404-1815

Fax 937-641-5931

The answer sheet and program evaluation must be received by **December 5, 2006** for the credit to be awarded.

Upon completion of all requirements, Wright State University will issue a memorandum of credit to you for your permanent records.

Answers (Please circle the BEST answer.)

1.	a	b	c	d	
2.	a	b	c	d	
3.	a	b	c	d	
4.	a	b	c	d	
5.	a	b	c	d	e
6.	a	b	c	d	
7.	a	b	c	d	e
8.	a	b	c	d	e
9.	a	b	c	d	e
10.	a	b	c	d	
11.	a	b	c	d	
12.	a	b			
13.	a	b			

Please type or print clearly

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Practice name _____

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THANK YOU!

Physician accreditation statement and credit designation

Accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education (CME) for physicians. Wright State University (WSU) takes responsibility for the content, quality and scientific integrity of this CME activity. This educational activity is designated for a maximum of two hours in category 1 credit toward the American Medical Association Physician's Recognition Award. Each physician should claim only those hours of credit he or she spent on the activity.

PROGRAM EVALUATION

PEDIATRIC FORUM,
VOLUME 16,
NUMBER 2

1. Did the material presented in this publication meet the mission to enhance health care delivery in our region through education based on the essentials and policies of the Accreditation Council for Continuing Medical Education? (Circle one response.)

   Strongly agree Agree Neutral Disagree Strongly disagree

2. Did the material presented in this publication meet the educational objectives stated?
   _____ Met the stated objectives
   _____ Did not meet the stated objectives

3. Please rate the contents of this issue using the following scale:
   1 = Poor, 2 = Fair, 3 = Good, 4 = Very good, 5 = Excellent
   (Circle one response for each.)

	Poor				Excellent
Timely, up-to-date?	1	2	3	4	5
Practical?	1	2	3	4	5
Relevant to your practice?	1	2	3	4	5

4. Please describe any changes you plan to make in your clinical practice based on the information presented in this program.
   _____
   _____
   _____
   _____

5. Are there any other topics you would like to have addressed in this publication?
   _____Yes
   _____No
   If yes, please describe: _____
   _____
   _____
   _____

6. Any other comments/suggestions for future educational programs for health care providers?_____
   _____
   _____
   _____
   _____
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   _____

Physician accreditation statement and credit designation

Accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education (CME) for physicians. Wright State University (WSU) takes responsibility for the content, quality and scientific integrity of this CME activity. This educational activity is designated for a maximum of two hours in category 1 credit toward the American Medical Association Physician's Recognition Award. Each physician should claim only those hours of credit he or she spent on the activity.

NEWS AND UPDATES

THE CHILDREN'S MEDICAL CENTER OF DAYTON

GRAND ROUNDS TO GO!

Dayton Children's will soon be offering select Grand Rounds topics on CD or DVD for you to view on your desktop, on your television or in your portable DVD player for CME credits.

Indicate your interest below. Call 937-641-3620, fax the form to 937-641-3454 or mail to:
The Children's Medical Center of Dayton
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City

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State

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Please send
☐ DVD ☐ CD
If available, would you view Grand Rounds on our website?
☐ Yes ☐ No

Dayton Children's first with high-definition MRI

The upgraded MRI in medical imaging makes Dayton Children's the first in the area offering high-definition MRI (HDMR). This new technology decreases scan times, lessening the need for sedation in pediatric patients. "Offering HDMR will allow our patients to benefit from clearer, more accurate and faster scans," says Elizabeth Ey, MD, medical director of medical imaging. This system also provides Dayton Children's pediatric radiologists the benefits of unprecedented imaging speed and clarity in cases where patients are difficult to image because of movement. For more information on HDMR, visit the media center on our website (www.childrensdayton.org) or call 937-641-3491.

Ambulatory care building groundbreaking; parking changes

Groundbreaking for the ambulatory care building at Dayton Children's took place November 3. The new building at the east end of the medical center will house key outpatient pediatric specialty services. This has resulted in some parking changes for parents and families. Parking maps and written directions are available to physician offices. If you have not received these materials, please call 937-641-3666. A shuttle service with a wheelchair lift is provided for the convenience of patients, parents and families parking on the levee. See page 18 for more information and maps.

Thrombophilia program offered

The department of hematology/oncology and the West Central Ohio Hemophilia Center at Dayton Children's are pleased to announce a thrombophilia program. The program provides comprehensive care to children and adolescents with thrombophilic disorders. Services include diagnosis, laboratory evaluation, treatment and counseling. For more information, call 937-641-3111.

Central scheduling continues to grow

Central scheduling has expanded it services and now includes more than 30 pediatric specialty programs and clinics. The latest additions to central scheduling are audiology, cardiology testing, developmental pediatrics, gastroenterology clinic, genetics, hematology/oncology clinic, nephrology clinic, neurosurgery clinic, nuclear medicine and urology clinics. New patient appointments can be made by calling 937-641-4000 or faxing 937-641-4500. Referrals can also be made through our website www.childrensdayton.org. Go to: For Health Care Professionals — Making a Referral (in right-hand navigation).

Springboro Testing Center opened

Dayton Children's Springboro Testing Center is now open for the convenience of children and their families south of Dayton. The testing center offers basic medical imaging and laboratory testing for infants, children and teens with your referral. The Springboro Testing Center is located just off St Route 741 at 60 Remick Boulevard in the Ledgestone Professional Park in the Marketplace at Settler's Walk — in front of the Coffman YMCA. The center is open Monday-Friday, 8:30 am to 5:30 pm; Saturday, 8:30 am to 12:30 pm. Call 937-641-5700 for information.

PCTI-Dayton researching for kids

Pediatric Clinical Trials International, Inc. (PCTI) Dayton is conducting clinical trials with physicians in Children's Health Clinic, nephrology, pulmonology, dermatology, gastroenterology, oncology and infectious disease. Trials include, but are not limited to, RSV, ringworm (tinea capitis), high-risk RSV, cystic fibrosis, hypertension and infant flu vaccine. Upcoming studies include childhood immunization, tonsillitis/pharyngitis and oral iron chelator for thalassemia and sickle cell disorders. For more information, call PCTI-Dayton at 937-641-3000 extension 8039 or visit our website at www.childrensdayton.org.

NEWS AND UPDATES

PARKING CHANGES

Construction of the new ambulatory care building at the east end has caused some parking changes. We expect these changes to be in effect for several months.

Please remind your patients to allow a few extra minutes to get to their appointments.

- Large parking area at the east end of the hospital (levee parking). The first four rows of this parking lot are for parents, families, volunteers and visitors.

- A shuttle service will pick up parents, families, volunteers and visitors in the large parking lot at the east end of the building (levee parking lot) and at the main hospital building. The shuttle will run 8:30 am to 5:30 pm, Monday through Friday.

- Parents, families and visitors should enter the hospital through the main entrance or the Taggart entrance. Both have canopies and drop-off areas.

- Shuttle access. Shuttle drivers will be able to help with strollers or wheelchairs. The shuttle is equipped with a wheelchair lift.

- Hospital security staff will help with parking during peak times.

SEE PARKING MAP ON THE FOLLOWING PAGE.

We thank you for your patience as we make improvements to benefit all children in our region. We encourage all visitors to use our shuttle service since access to the hospital will be blocked at different times during construction.

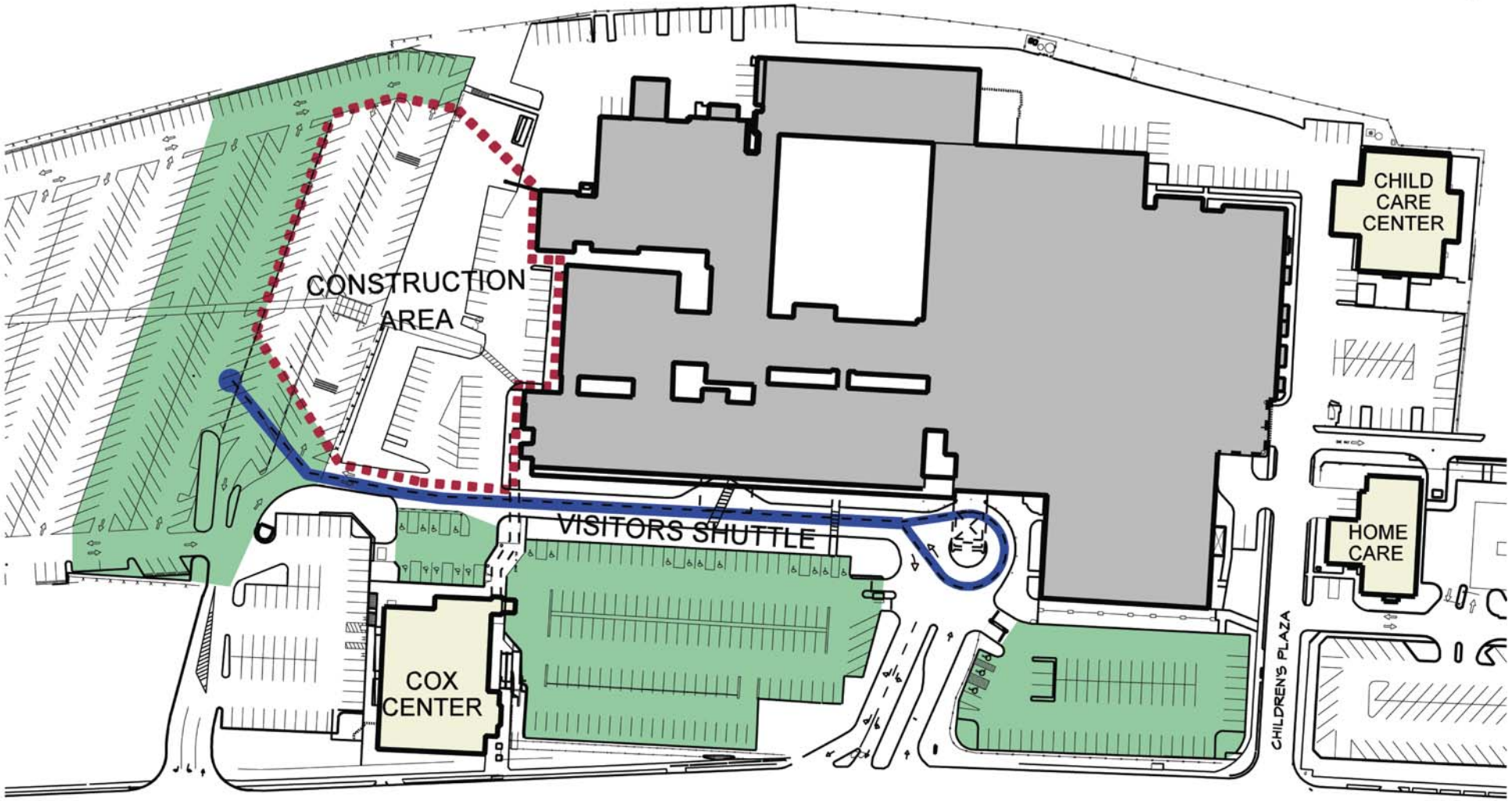
If you would like your office to have maps of this new, temporary, parking arrangement, please contact the marketing communications department at 937-641-3666.

Thank you for your cooperation.

Parents, families and visitors – Important parking information

PARKING CHANGES

DAYTON CHILDREN'S
The Children's Medical Center of Dayton



- Visitor Parking
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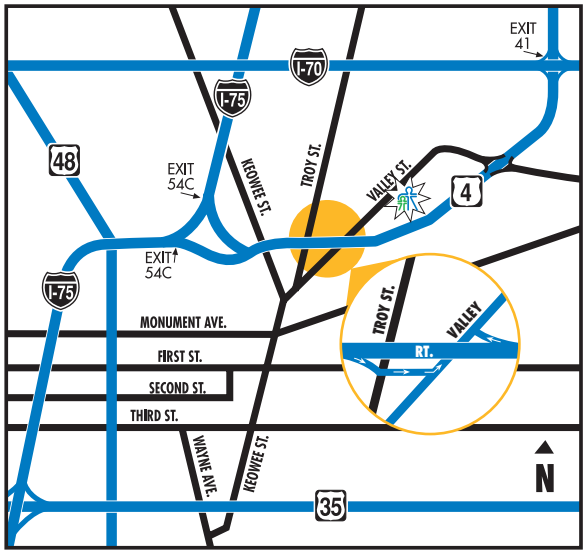

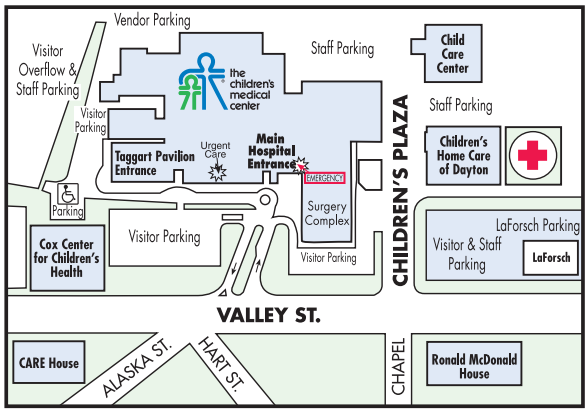

Street Directions

FROM THE NORTH:

I-75 south, Exit 54C to Rt. 4; stay left when exiting I-75; Rt. 4 north to Valley St./Troy St. exit. Go through first stop sign at bottom of exit ramp. Valley Street is the next stop sign. Turn left.

FROM THE SOUTH:

I-75 north, Exit 54C to Rt. 4; Rt. 4 north to the Valley St./Troy St. exit. Go through first stop sign at bottom of exit ramp. Valley Street is the next stop sign. Turn left.

Or I-675 north, Exit 13 to Rt. 35; west on Rt. 35 to the Keowee St. exit; right on Keowee to Valley St.; right on Valley St.

FROM THE EAST:

Rt. 35 west to the Keowee St. exit; Keowee St. north to Valley St.; right on Valley St. From I-70 exit 41, take Route 4 south to Stanley Ave./Findlay St. exit. Turn right at the bottom of exit, then left at the first light on Stanley Ave. This is Valley St.

FROM THE WEST:

Third St. east to Keowee St.; left on Keowee St. to Valley St.; right on Valley St.

For Your Information

Parking is available in front of The Children's Medical Center of Dayton. The hospital is also accessible by bus. Call RTA at 226-1144 for schedule and route information.

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