



Early Intervention and Lifelong Monitoring Dramatically Improve Prognosis for Children with TSC

First identified by a 19th century French physician, tuberous sclerosis complex (TSC) is a congenital condition that affects one in every 6,000 births worldwide. TSC results from an inherited or spontaneous mutation in one of two genes, TSC1 and TSC2. These encode for two proteins (hamartin and tuberin, respectively) that, together, help regulate cell growth, proliferation, and differentiation.

TSC is characterized by the growth of benign tumors lesions in all the major organ systems, including the skin, kidneys, heart, lungs, eyes, and brain. Individuals with TSC can develop mild or severe complications in any or all affected organs, from minor skin lesions to severe epileptic seizures.

The most common manifestation of TSC — tumors (abnormalities in tubers are not tumors, but hamartomas) in the brain — are the most likely to cause serious problems. These tumors, which include cortical tubers, subependymal nodules (SENs), and subependymal giant cell tumors (SGCTs), which can cause seizures, cognitive disabilities, and behavioral disorders.

Early intervention improves prognosis

The symptoms of TSC not only vary widely among individuals; they can also vary dramatically over time in one patient—for example, a formerly quiescent SGCT may suddenly double in size, threatening organ function.

Because symptoms are so highly variable and also extremely subtle during infancy and early childhood, TSC can be very difficult to diagnose. Yet early diagnosis and intervention, coupled with lifelong monitoring, can dramatically improve the long-term prognosis for individuals with TSC.

With this goal in mind, in 2005 MGHfC established the Carol and James Herscot Center for Children and Adults with Tuberous Sclerosis Complex. Under the leadership of MGH pediatric neurologist and epileptologist Elizabeth Thiele, MD, PhD, one of the nation's foremost experts on TSC, the Herscot Center is one of only 25 TSC clinics nationwide.

Dedicated exclusively to TSC patients

The Herscot Center provides coordinated, comprehensive care for TSC patients of all ages. In fact, it is one of only a few in the United States that provides care for both children and adults; this is a very important factor when choosing where to refer patients for care, as individuals with this condition require management throughout their lives. The Herscot Center is also one of the most experienced in the nation, seeing an average

of two to three new patients each week, and providing ongoing care for some 300 patients.

Another major strength of the Herscot Center is that it is staffed by a multidisciplinary team of clinicians who are dedicated exclusively to the care of patients with TSC. This diverse team—which includes neurologists, psychiatrists, dermatologists, cardiologists, radiologists, neurosurgeons, pulmonary specialists, and renal specialists, as well as social workers, dietitians, and genetic counselors—works collaboratively with one another and the patient's primary physician to ensure that care is well-coordinated.

An active clinical research program

In addition to being one of the busiest TSC programs in the nation, the Herscot Center is one of the most active in terms of clinical research.

Currently, the center is participating one of the first clinical trials for TSC is underway, a study in a multicenter clinical trial that is evaluating an agent aimed at a molecular target involved in modulating signaling pathways that contribute to (we think all organ involvement in tsc—but study end point is kidney, planned studies we may participate in include lung and brain involvement) lung, kidney, and brain involvement in TSC. This is the first multicenter trial to assess a treatment targeting an underlying cause of TSC. Future trials studies will look specifically at this agent's impact on lung and brain involvement.

Another upcoming, prospective, study, will involve patients diagnosed prenatally with cardiac rhabdomyoma to determine if early intervention will improve their outcomes. The center is also conducting studies aimed at better understanding and characterizing neurologic and other aspects of TSC.

"While research is beginning to shed light on the cause of TSC, there is currently no cure for this disorder," says Dr. Thiele. "Fortunately, however, there are many effective treatments for the symptoms of TSC. If patients are diagnosed and treated early, and monitored throughout their lives by physicians with extensive experience in this disorder, most can enjoy a good quality of life and a normal lifespan."

For more information about or to refer a patient to the Carol and James Herscot Center for Children and Adults with Tuberous Sclerosis Complex, please call: 617-726-0241.

Or visit the Herscot Center website at www.massgeneral.org/tsc.

Restoring Nutritional Status and Improving Bowel Function: The MGHfC Pediatric Intestinal Rehabilitation Program

A significant number of patient visits to pediatricians and pediatric gastroenterologists are for symptoms related to chronic intestinal problems. Motility disorders, such as gastroesophageal reflux and constipation are commonly seen in clinical practice.

Young patients with severe, chronic intestinal disorders invariably benefit from the combined expertise of a multidisciplinary team of specialists who are focused primarily or exclusively on these often- complex conditions.

The Mass General Hospital for Children's Pediatric Intestinal Rehabilitation Program offers just such an approach—providing multidisciplinary, comprehensive evaluation, medical and surgical treatment, nutrition support, and follow-up care for infants, children, adolescents, and young adults with a broad range of chronic intestinal disorders, including:

- Hirschsprung's disease
- chronic intestinal pseudo-obstruction
- short bowel syndrome
- motility disorders
- necrotizing enterocolitis
- intestinal neuronal dysplasia
- intestinal failure
- radiation enteritis
- gastroschisis
- intestinal atresia
- malabsorption

The goal of the program is to restore nutritional status and improve bowel function for children with these disorders by marshaling all the varied resources within MGHfC. According to pediatric gastroenterologist and program medical director Leonel Rodriguez, MD, MS, patients come from

around the nation and the world to have access to the program's services and specialists.

In addition to pediatric gastroenterologists, the Pediatric Intestinal Rehabilitation Program team includes MGHfC pediatric surgeons who specialize in these disorders, nurse practitioners, a dietitian, a child-life specialist, and access to a child psychiatrist. The team's physicians coordinate treatment plans with the child's



referring primary and specialty physicians, and communicate directly and regularly with them and the child's parents to ensure that care is well-coordinated.

The Pediatric Intestinal Rehabilitation Program has full access to the state-of-the-art diagnostic technologies and specialized expertise of the MGHfC Pediatric Motility Center, which focuses on the medical treatment of motility disorders and is also directed by Dr. Rodriguez. Through this center, patients with dysmotility (which includes many patients with chronic intestinal disorders) have access to diagnostic tests such as antroduodenal or colonic manometry and the

expertise of pathologists and radiologists who specialize in intestinal disorders.

In addition to providing comprehensive diagnosis and treatment, the members of the Intestinal Rehabilitation Program are actively engaged in a wide range of basic and clinical research initiatives aimed at advancing the understanding and treatment of intestinal disorders.

Basic research is largely directed toward understanding the development of the enteric nervous system, and how abnormalities of nerve cell development in the intestine lead to various types of dysmotility, including Hirschsprung's disease, chronic intestinal pseudo-obstruction, and severe constipation. The role of neurotransmitter deficiencies in children with disorders of intestinal function is another area of current research.

The range of clinical research currently underway is broad, and includes both retrospective and prospective studies aimed at evaluating the use of new diagnostic tools and the efficacy of novel therapies. These include outcomes studies of various surgical interventions, trials evaluating new agents to treat dysmotility, and studies of new diagnostic tools with which to measure gastrointestinal motility and transit.

For more information about the Pediatric Intestinal Rehabilitation Program or to refer a patient, please call 617-724-0954.

MGHfC Cleft Lip/Palate and Craniofacial Clinic: Expert, Well-Coordinated, Multidisciplinary Care

Approximately seven percent of births in the United States involve craniofacial anomalies. Whether common or rare, all craniofacial anomalies are complex, varied, and affect each child uniquely.

To ensure the best possible outcomes, these deformities require early intervention, long-term management, and the combined expertise of a well-coordinated, multidisciplinary team of highly experienced pediatric specialists.

The optimal management of cleft lip/palate is a strong case in point. Treatment typically involves a precisely timed sequence of seven or more surgical procedures that begin at three months of age and conclude when the patient is a teenager. In addition to multiple surgical repairs performed by plastic surgeons and, later in the child's development, oral and maxillofacial

surgeons, treatment usually also involves the participation of many other specialists, such as orthodontists and/or pediatric dentists, speech/language therapists, and otolaryngologists. Other craniofacial anomalies may involve even more surgical interventions and pediatric specialists.

Several years ago, the MassGeneral Hospital for Children (MGHfC) established a multidisciplinary clinic to provide well-coordinated treatment for infants and children with craniofacial anomalies. Since that time, this monthly clinic has grown in scope and size, and now provides comprehensive evaluation and treatment for some 100 new patients a year, with the capacity to manage more.

Patients referred to the MGHfC Cleft Lip/Palate and Craniofacial Clinic are evaluated, typically in a single visit, by all the core members of the clinic's multidisciplinary team, beginning with a geneticist, who evaluates the child's family history and complicating factors that might impact treatment.

Following a multidisciplinary conference the same day, an action plan—whether longitudinal observation or a comprehensive treatment plan involving multiple operations at Massachusetts General Hospital—is presented within several weeks to the child's referring physician and parents. Whenever possible, services such as orthodontia and speech/language therapy are coordinated with local providers so that patients can receive ongoing treatment close to home.

Reflecting the complex nature of craniofacial anomalies and their potential impact on multiple aspects of a child's body and life, the MGHfC Cleft Lip/Palate and Craniofacial Clinic team encompasses numerous specialties. For a listing of these specialties and the clinicians on the team, please visit

http://www.massgeneral.org/children/specialtiesandservices/cleft_lip_palette/default.aspx

A dedicated Clinic Coordinator (Elizabeth Shannon, PhD, PNP) ensures easy and prompt access to all services and specialists for referring physicians, as well as timely communication among the clinic's staff, referring

For more information or to refer a patient to the MGHfC Cleft Lip/Palate and Craniofacial Clinic, please call the Clinic Coordinator, Elizabeth Shannon, PhD, PNP, at 617-643-0815, visit the website at massgeneral.org/children or send an email to eshannon1@partners.org.



BEFORE



AFTER

physicians, community providers, and parents. The Clinic Coordinator also arranges for patients to receive the services of other healthcare specialists, such as social workers, as needed.

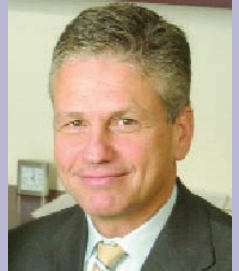
A unique strength of the MGHfC Cleft Lip/Palate and Craniofacial Clinic is that it is an integral part of Massachusetts General Hospital, with its vast resources. This is especially valuable to expectant parents whose child is diagnosed prenatally and are delivering at Mass General. Long before their child is born, these mothers/parents can receive a visit from a member of the clinic, who provides reassurance, information about feeding and other important issues, and appointments for evaluation and treatment once the child is born.



Cascades

NEWSLETTER TO PHYSICIANS WINTER 2007

MGHfC Chief of Pediatric Surgery Joseph P. Vacanti, MD, is Awarded John Scott Medal



Joseph P. Vacanti, MD, MassGeneral Hospital for Children chief of Pediatric Surgery, was recently named the recipient of the John Scott Medal, joining such luminaries as Marie Curie, Thomas Edison, the Wright brothers, and Jonas Salk for this prestigious honor.

A pioneer in the interdisciplinary field of tissue engineering, Dr. Vacanti was selected in recognition of his contributions in designing

implantable, biodegradable systems that make it possible to generate new tissue and potentially even organs for use in patients undergoing reconstructive surgery or transplantation.

Awarded by the City of Philadelphia, this medal has been presented annually since 1834 to individuals whose inventions have contributed to the "comfort, welfare, and happiness of mankind." The award is named for John Scott, a

Scottish druggist who, in the early 19th century, established a fund to recognize "ingenious men or women who make useful inventions."

One of two recipients of the 2007 John Scott medal, Dr. Vacanti formally received the award at a ceremony in November.

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