The OHSU Neurotransmitter-Spring 2006 focuses on some presently available epilepsy services. The articles provided by the departments of Neurological Surgery and Neurology faculty describe some of the clinical interests and services offered as part of the Comprehensive Epilepsy Service available at Oregon Health & Science University.
OHSU Comprehensive Epilepsy Center

The OHSU departments of Neurological Surgery and Neurology are proud to be involved in the OHSU Comprehensive Epilepsy Center. The center was formed 18 years ago and comprises a multidisciplinary group of physicians, nurses, psychologists, therapists and neuroscientists dedicated to the evaluation and treatment of epilepsy. The only university-based epilepsy program in Oregon, the center has become a state and national resource, providing comprehensive clinical care, innovative research and consultation to referring physicians throughout the region. The center offers a full spectrum of comprehensive epilepsy care, from surgical treatment of complex epilepsy disorders to inpatient video-EEG monitoring. The goal of the center is to set the standard for state-of-the-art care for patients with epilepsy disorders.

In fall 2006, the center will move to the OHSU Center for Health and Healing, under construction in Portland’s new South Waterfront District. Epilepsy center staff will focus on the continuity of care and will help coordinate each patient’s treatment plan, including both outpatient services and hospital stays.

Patient referrals to the OHSU Comprehensive Epilepsy Center should be made by the referring primary care physician or neurologist.

For further information or appointments, please contact the OHSU Comprehensive Epilepsy Center at the numbers below.

Kim J. Burchiel, M.D.
OHSU Comprehensive Epilepsy Center Achieves Fourth Level Epilepsy Center Status and Expands Clinical Programs

by David Spencer, M.D.

In February 2006, the OHSU Comprehensive Epilepsy Center was awarded Fourth Level Epilepsy Center status by the National Association of Epilepsy Centers. This prestigious award is the highest status accorded to an epilepsy program. It designates the OHSU Comprehensive Epilepsy Center as a center with the most advanced technology and expertise able to manage the most challenging epilepsy cases, including high level epilepsy surgery evaluations. Selection as a fourth level program is a rigorous process that includes evaluation of all aspects of the program, from the qualifications of neurology and neurological surgery physicians to the institutional infrastructure and allied health services including pharmacy, radiology, psychiatry, and many other disciplines.

The OHSU Comprehensive Epilepsy Center is the only program in Oregon designated as a fourth level center.

The center also is expanding outpatient and inpatient evaluation services. In fall 2006, outpatient epilepsy clinics will move to the OHSU Center for Health and Healing, under construction in Portland’s new South Waterfront District. The new facility will provide easier patient access to clinics, and will include on-site laboratory facilities, imaging, and electroencephalogram (EEG) capabilities, not to mention spectacular views of the river. Neurology and neurological surgery clinics will run simultaneously in the same clinic space, providing a truly integrated and comprehensive service.

In July 2006, in the newly constructed Peter O. Kohler Pavilion located on Marquam Hill, inpatient video-EEG monitoring capacity will expand substantially from three monitoring beds to seven. The expanded inpatient monitoring unit will continue to provide evaluations for a variety of neurologic disease, including epilepsy presurgical evaluations with capability for both scalp EEG monitoring and intracranial EEG evaluations, differential diagnosis of seizure-like spells, and seizure characteristics and classification. This expanded monitoring unit will take full advantage of state-of-the-art technology being employed in the new facility, including high-speed networking and wireless communications with nursing staff, in addition to the expanded video-EEG patient monitoring.

State-of-the-art technology and first-rate facilities are essential. However, experienced staff and personnel are really what makes a successful program. A multidisciplinary approach like that in place for the OHSU Comprehensive Epilepsy Center involving a team of neurologists, neurosurgeons, neuropsychologists, psychiatrists, nurses and others is necessary to optimally guide the management of patients with epilepsy. Combined, OHSU epilepsy-trained neurologists (epileptologists) collectively have more than 100 years of clinical experience. As the only university-based epilepsy program in Oregon, the epilepsy team has expertise and active research programs in: neuroimaging, cognitive issues in epilepsy, complementary and alternative medicine approaches to the treatment of epilepsy, new antiepileptic medications, and several other areas.

(For a full listing of our staff please see page 2 of this issue.)

The Fourth Level Epilepsy Center status and expansion of outpatient and inpatient evaluation services are important steps in fulfilling our commitment to our patients with epilepsy problems. The center’s goal is to better serve the epilepsy diagnosis and treatment needs of the region. The expertise of highly specialized neurology, neurological surgery and neuroradiology physicians, combined with state-of-the-art imaging and neurophysiology technology, provides a capability unequalled in Oregon. The center’s aim is to provide prompt evaluations and feedback while maintaining its long-standing tradition of high-quality evaluation.

For questions about the program, call 503 494-5682 (adults) or 503 494-5856 (pediatrics).

Welcome to epilepsy care in the 21st century!

OHSU Comprehensive Epilepsy Center Services Offered

The OHSU Comprehensive Epilepsy Center provides a full spectrum of medical services for patients with epilepsy. For some patients with medically intractable seizures, surgery to remove epileptogenic areas of the brain may be feasible.

- Extraoperative corticography and stimulation mapping (brain mapping)
- Selective microsurgical amygdalohippocampectomy
- Neocortical resection
- Subpial transection
- Modified hemispherectomy
- Corpus callosotomy

- Stereotactic computer-assisted navigational planning and guidance
- Innovative research programs include: the use of vagal nerve stimulation for patients in whom drugs are ineffective but who are not otherwise candidates for other epilepsy surgery
- Team approach
- A full spectrum of above services for children
Surgery for Epilepsy
by Martin C. Salinsky, M.D.

Epilepsy is one of the most common neurological disorders, affecting one in 200 people. Despite improvements in antiepileptic drug (AED) therapy, nearly one-third of epilepsy patients fail to achieve seizure control. These patients are often unable to work or drive, and suffer the physical, social and emotional consequences of uncontrolled, unpredictable seizures. Surgical treatment is now widely accepted as the most effective option for many of these patients.

Now in its 18th year, OHSU’s Comprehensive Epilepsy Center program combines clinical experience with advanced imaging capabilities to improve surgical outcomes and minimize seizure related disability.

The rationale for epilepsy surgery is straightforward. For most patients, seizures emanate from a specific area of the cerebral cortex, commonly referred to as the epileptic focus. Although not always evident on magnetic resonance (MR) images, the focus is usually associated with a structural brain lesion. Resection of the epileptic focus and the associated lesion should eliminate the seizures. The key to successful epilepsy surgery is careful localization of the epileptic focus and any associated structural brain abnormalities. This is accomplished through a combination of ictal electroencephalogram (EEG), ictal EEG is an EEG recording taken during a typical seizure, and MR imaging. The importance of MR imaging cannot be overstated. Studies have shown significantly better outcomes for patients with MR image-visible lesions compared with those without. The yield of MR images is improved with higher field magnets and with sequences designed to highlight potentially epileptogenic lesions. At OHSU, we routinely use high-field (3 Tesla magnet) strength MR and optimized epilepsy protocols to demonstrate a small or subtle lesion that may not otherwise be visible.

Who is an appropriate candidate for epilepsy surgery?
Patients are candidates for epilepsy surgery if seizures are medically refractory, and to some extent disabling. The disability may be physical, emotional or economic, often all three. The precise definition of "medically refractory" has been the cause of much debate. However, recent studies have provided a working definition. The majority of patients who respond to antiepileptic drug therapy do so on the first performed AED therapy trial, (assuming the AED is tolerated and that an appropriate AED has been selected). Nearly all those who ultimately respond to AEDs will become seizure free within two or three AED trials. Patients who fail therapy at this point may be defined as medically refractory, as only a small percentage will become seizure free with further AED trials. The importance of being seizure free must be emphasized. Psychosocial studies show that even one or two seizures a year can have a disabling impact on an individual. Rates of unemployment and even mortality are significantly increased in patients with any residual seizures, compared with those who are seizure free.

What surgeries are performed?
The guiding philosophy of OHSU’s Comprehensive Epilepsy Center program has been to remove the least amount of tissue consistent with an excellent outcome, and to perform the least invasive evaluation toward that end. The best example of this approach has been surgery for temporal lobe epilepsy (TLE), the most common form of medically refractory epilepsy, and the most common type of epilepsy surgery performed worldwide. The single most common pathology in TLE is mesial temporal sclerosis (MTS), a scarring of the hippocampus and amygdala. Standard surgery for this condition involves resection of the anterior 4–5 cm of the temporal lobe neocortex, followed by resection of the medial temporal structures, an anterior temporal lobectomy. But why remove any of the temporal lobe neocortex when the problem is in the medial temporal lobe? Beginning more than a decade ago, OHSU changed from the standard anterior temporal lobectomy to a much more selective operation, the selective microsurgical amgdalohippocapcomectomy (SMAH). This surgery involves removal of the diseased mesial temporal structures and avoids resection of the temporal lobe neocortex. Our results, and those from other centers, show this selective procedure works as well as the older procedure, while decreasing the amount of resected brain by greater than 90 percent (see figure above). More than 80 percent of surgically treated OHSU patients are seizure free at one-year follow-up. Many return to work, to driving, and have the opportunity to fully realize their potential.

Neuroimaging is critical
Epilepsy surgery is not limited to seizures beginning in the temporal lobe. However, localizing the seizure focus in other areas can be more difficult and neuroimaging is critical. Localizing the seizure focus can be difficult without the advantage of imaging abnormalities, and surgery may not be possible. Many patients were previously and often unsuccessfully studied with invasive intracranial electrode recordings in an attempt to localize the seizure focus.

Imaging advances have provided physicians with a tool to localize the epileptogenic focus, even in situations where the MR image is negative. That tool is ictal single photon emission computed tomography (SPECT) fusion imaging. This non-invasive procedure involves promptly injecting a radioisotope into the blood stream during an epileptic event. The radioisotope fixes in the area of brain activation and can be imaged on high-resolution gamma cameras. These images are then fused or co-registered to a high-resolution MR image to obtain improved anatomical resolution. Sensitivity is further improved by subtracting interictal images from ictal images, thereby removing background noise. This technol-
Selective Microsurgery for Epilepsy
by Kim J. Burchiel, M.D.

The state-of-the-art surgical treatment of epilepsy can be summarized as: less is more. Operations that a decade or two ago would have involved a large craniotomy in an awake patient have been largely replaced by procedures performed through small incisions on patients under general anesthesia. Advancements in image-guided surgery have constituted a large part of this trend, but technology has also helped make epilepsy surgery more limited and more specific. Using advanced imaging such as high-field (3 Tesla) magnetic resonance (MR) imaging, single photon emission computerized tomography (SPECT), positron emission tomography (PET), and magnetoencephalography (MEG), the surgeon has much more guidance for surgical procedures than was ever available in the past. Operations can be tailored for individual patients, rather than the “one size fits all” approach of the past.

Nowhere is this change more evident than in temporal lobe surgery. Temporal lobe epilepsy, so-called partial complex, is the most common medically intractable form of epilepsy in adults. Past operations removed large portions of the temporal lobe en bloc because the understanding of the disorder was limited. Now, it is clear that the vast majority of these seizures emanate from the mesial, or most medial, parts of the temporal lobe, which include the amygdala, hippocampus, and parahippocampal gyrus. With this knowledge, surgery can be directed specifically to those regions. With the accuracy of image-guided neurosurgery, the responsible regions of the mesial temporal lobe can now be removed with precision through cranial openings that would have been unthinkable a decade ago. The figure on the right compares two operations, anterior temporal lobectomy (ATL) and selective microsurgical amygdalohippocampectomy (SMAH). The former procedure is a scaled down version of the older temporal lobectomy approach, and the latter is the most minimally invasive temporal lobe surgery for epilepsy. Both are viable options today, and both are descendents of older, and larger, operations. Developed a decade ago and now routinely used, the SMAH procedure is one that OHSU specializes in. Approximately 8–10 of these procedures are performed annually at OHSU.

During the SMAH procedure, patients are under general anesthesia and image-guidance is used throughout the surgery. A small vertical incision is made just in front of the ear, and then a 1½ inch opening is made in the bone over the temporal lobe, see figure below. Using image-guided control, the brain is entered, and the surgeon then enters the spinal fluid space in the temporal lobe, the “temporal horn”. With the use of microscopy, the surgeon can identify the amygdala and hippocampus, and these are removed, along with the surrounding parahippocampal gyrus, using microsurgical technique. The surgeon then uses image-guidance to confirm that the hippocampus has been adequately removed. Once the wound is closed, the patient is awakened, and then spends one night in the intensive care unit (ICU). Patients typically spend 2–4 days in the hospital recovering from surgery prior to discharge.

For the most common cause of temporal lobe epilepsy, mesial temporal sclerosis (MTS), results for these surgeries are outstanding. Approximately 90 percent of patients will be seizure free, or have rare non-disabling seizures after either surgery (Engle Class I-II). Patients are often able to decrease or eliminate medications, and can eventually return to driving a car, employment, and other activities of daily living.

The surgical treatment of epilepsy is the last resort for patients with medically unresponsive seizures. That said, modern neurosurgical techniques can produce a high rate of good results, returning many patients to a more normal and productive life.
Doernbecher Children’s Hospital Childhood Epilepsy Program
by Colin Roberts, M.D. and Nathan R. Selden, M.D., Ph.D.

Seizures in children: the problem
Forty-five thousand children under the age of 18 are diagnosed with epilepsy each year in the United States. Many are infants and younger children. Although seizures in children are often caused by conditions different from those seen in epileptic adults, a similar proportion (30 percent or more) never fully respond to medical therapy.

Children with poorly controlled seizures often experience significant learning and memory deficits, which are frequently progressive and debilitating. Damage from intractable seizures can be seen early in a child’s life, often after the failure of two or three anti-seizure medication trials (i.e. “medically refractory epilepsy”). In such children, surgical treatment may offer dramatic benefit, in many cases curing their epilepsy and often realizing significant improvements in cognitive performance and quality of life. Historically, seizure surgery has been withheld until adulthood, due to clinicians’ fear of damaging the developing brain and in the hope that children might “outgrow” their seizures. Numerous scientific and clinical studies now strongly suggest that early surgery for children with medically refractory epilepsy can save them from years of uncontrolled seizures, medication side effects and cognitive decline.

Localizing the cause
Depending on the seizure’s nature and focus of onset within the brain, surgery for childhood epilepsy can take many forms. The most effective procedures are used to treat partial or focal-onset epilepsies and involve surgical resection of a localized seizure focus in the brain.

Identification of a seizure focus is a highly technology-based, multi-step process. At Doernbecher Children’s Hospital, the first step is a brief hospital admission for highly specialized seizure monitoring; digital video electroencephalography (video-EEG). Children with refractory epilepsy are observed for one or more days with continuous seizure activity video recording along with simultaneous measurement of seizure electrical pattern, using electrodes placed on the scalp. Careful scrutiny of multiple seizures and their associated pattern of electrical activity provides the first, general clues to the brain location of a potential seizure focus. Networked computer systems and powerful 3-D representation software aid Doernbecher’s team of child neurologists in analyzing these complex data.

The second step is use of imaging technology to precisely pinpoint very subtle malformations in brain tissue that might generate the seizure activity seen on video-EEG. High-field (3 Tesla) MR imaging is now standard for seizure localization studies at Doernbecher. Together with clinicians and scientists at OHSU’s Advanced Imaging Research Center, there is research interest in further refining the ability to identify tiny “blemishes” on the surface of a child’s brain that may be the root cause of seizures.

In a third and final step, specially trained teams in the Doernbecher Epilepsy Center give intravenous injections of metabolic tracers within seconds of seizure onset, allowing radiologists to construct a map of brain activity at the moment of a seizure, known as ictal single photon emission computed tomography (SPECT) fusion imaging. These ictal SPECTs and positron emission tomography (PET) studies of brain metabolism between seizure episodes help to confirm that a particular area of brain malformation is the actual location of seizure onset. Doernbecher is one of only a few pediatric hospitals in the United States providing SPECT fusion imaging for children with epilepsy.

Prior to recommending any invasive procedure, a team of child neurologists, a pediatric neurosurgeon, radiologists, nuclear medicine specialists, and nurses meet to consider the potential risks and benefits of surgery, the impact on cognition and neuropsychology, and quality of life.

The role of surgery
A relatively high proportion of children with epilepsy harbor subtle malformations of the brain surface: cortical dysplasia. Seizure foci that result from cortical dysplasia often reside outside the temporal lobe (where surgical results are most successful in adult patients). For these reasons, precise localization of the seizure focus is the mainstay of successful surgery in children. Furthermore, children are more likely to require removal of a seizure focus in close proximity to “eloquent” cerebral cortex that is necessary for motor, sensory, speech or other cognitive function.

One method used to identify seizure foci while protecting nearby areas of cortex is surgical implantation of small platinum electrodes (embedded in a soft, silicone sheet) onto the surface of the brain. Seizure activity is recorded through these electrodes to map the precise boundaries of the seizure onset zone. The brain is also electrically stimulated to map important functions of adjacent brain areas, such as: language, movement and vision. This so-called “extraoperative” mapping is ideal for children, who cannot cooperate with the “awake surgery” technique that is sometimes used in adult seizure patients.

Absolute precision in localizing the seizure foci and eloquent brain areas, and in mapping of these areas onto the physical surface of the brain during surgery to remove a seizure focus, is required. At Doernbecher, the surgical team uses a computer surgical navigation system to combine anatomical information from high-field MR images with functional information from extraoperative mapping. At the time of surgery, computer-based maps and a precise surgical plan are correlated with the actual brain surface with an accuracy of approximately 1 millimeter, facilitating safe, minimally invasive surgical techniques. In most cases, complete...
More details about the outcomes of epilepsy surgery:

**Non-focal epilepsy**
For children with forms of epilepsy in which a discrete seizure focus cannot be identified, Doernbecher offers vagal nerve stimulator (VNS) implantation as a possible treatment. In severely affected patients this palliative device, resembling a pacemaker, may significantly reduce seizure occurrence, severity and medication dependence.

**Childhood epilepsy and Doernbecher**
At Doernbecher the Childhood Epilepsy Program brings together a team of highly-qualified surgeons, physicians, scientists and specialists to offer comprehensive care and treatment for children with epilepsy. The program includes cutting-edge surgical therapy for intractable epilepsies, vagus nerve stimulation, pediatric clinical trials of new anti-epileptic drugs, complex brain imaging, comprehensive neuropsychological assessments, and ketogenic diet therapy.
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For more information, contact Joanie Mastrandrea at mastrand@ohsu.edu or 503.494.6207