Approximately one-third of patients with epilepsy get little or no relief from existing medical therapies. “These patients are suffering, and often their suffering may be unnecessary,” says epileptologist Robert Knowlton, MD, medical director of the rapidly growing UCSF Seizure Disorders Surgery Program. “Advanced technologies that more precisely pinpoint seizure activity and innovative surgical approaches can make surgery an option for increasing numbers of these patients.”

Studies have shown that for properly selected patients, surgery can allow many of these patients to become seizure-free or substantially reduce the frequency of their spells.

(continued on page 6)
Advances in the treatment of complex, refractory neurological disorders demand team efforts of clinicians, scientists, patients and their families. At UCSF, we have the good fortune to lead some of these important efforts and work in close collaboration with referring physicians throughout the region. This issue highlights some exciting recent work that provides hope for long-suffering patients and families.

For refractory epilepsy, our growing clinical team is using the latest diagnostic approaches to isolate the source of seizures and expand the number of patients who can benefit from interventions. Similarly, to address a broad range of historically undertreated neuropathic pain conditions, interdisciplinary teams now apply advanced techniques and technologies to dramatically reduce or even eliminate pain, so these patients can regain function.

In response to new insights regarding cryptogenic ischemic stroke, transient ischemic attacks and pulsatile tinnitus, we have newly created expert, interdisciplinary services to address these conditions in timelier, more effective ways. At one of the nation’s busiest programs for all types of spine tumors, we are pioneering and validating minimally invasive approaches for intradural and metastatic tumors to reduce complications and speed recovery time.

Finally, with its move to our new, state-of-the-art Mission Bay complex, our renowned Pediatric Brain Center at UCSF Benioff Children’s Hospital San Francisco is consolidating a variety of centers, clinics, research efforts and specialists in one physical space. The move expands access and enables more coordinated care for children and families with neurologic disorders throughout Northern California.

Bringing these advances to our patients in partnership with our physician colleagues in surrounding communities is enormously heartening – a constant reminder of why we do what we do. Together we have the opportunity to help those who need us most.

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text from Advances in Spine Tumor Surgeries Can Improve Patient Outcomes

When experienced interdisciplinary teams pioneer or leverage innovative surgical advances for the full range of spinal tumors, patients get new hope for successful treatment, says UCSF neurosurgeon Christopher Ames, MD, of the UCSF Spine Center. He and neurosurgeon colleagues Dean Chou, MD, and Praveen Mummaneni, MD, lead one of the busiest spine tumor programs in the country.

Multidisciplinary Evaluation to Determine Optimal Treatment

At regular Spine Tumor Board meetings, the UCSF Spine Center draws on neuroradiologists, neurosurgeons, orthopaedic surgeons, radiation oncologists, oncologists and pathologists to discuss treatment options for complex cases. In addition to radiation, chemotherapy and traditional open surgeries for primary and metastatic tumors, these boards can now consider:

• Minimally invasive surgeries for intradural and metastatic tumors
• Advances in stereotactic radiosurgery
• Combined intraoperative P32 therapy for tumors near sensitive organs (UCSF is among the first centers in the West to use this procedure)
Pioneering Minimally Invasive Spine Tumor Resection

Chou and Mummaneni are among the few surgeons in the country pioneering minimally invasive techniques for both intradural and metastatic tumors. “For intradural tumors, we published the results of a study in Spine in which the minimally invasive approach achieved comparable outcomes to open approaches, only with less blood loss and shorter lengths of stay,” says Mummaneni.

Given such results, he advises that any patient with an intradural spinal tumor that spans less than two lumbar segments should be referred for evaluation as a candidate for the minimally invasive approach. He and Chou have documented similar results for minimally invasive procedures on patients with metastatic tumors of the spine. During these procedures, says Chou, surgeons complete precisely the same tumor resection and rebuild of the spine as they do in open procedures. However, the decreased morbidity associated with the minimally invasive approach can improve the early surgical recovery for these patients.

Chou does emphasize, though, that there are very strict criteria for when to use the minimally invasive approach. “We do not typically consider it for areas we cannot access safely, such as the neck and cervical spine, but most metastatic tumors are in the thoracic spine, where we can typically proceed safely.”

Deep Experience with Primary Bone Tumors

For rare and difficult-to-treat primary bone tumors in the spine – such as chordoma, chondrosarcoma, osteosarcoma and aneurysmal bone cysts – efficacy and cure rates are directly dependent on removing the specimen in a single piece with clean margins, says Ames. “These are invasive, challenging procedures, and surgical results depend on the skill and experience of the surgeons and collaboration among multiple disciplines,” he says. At UCSF, neurosurgeons are often joined by head and neck or thoracic surgeons, plastic surgeons, vascular surgeons and, where necessary, colorectal surgeons.

For more information, contact the UCSF Spine Center at 866-81-SPINE or 866-817-7463.
New Technologies and Techniques Ease Neuropathic Pain

Advances in neurosurgical technologies and techniques can provide significant pain relief for people suffering from chronic peripheral neuropathic pain, says neurosurgeon Line Jacques, MD, director of the UCSF Center for Excellence in Peripheral Nerve Disorders and Pain Surgery.

“The key is a comprehensive, multidisciplinary assessment – neurosurgeons, neurologists, anesthesiologists and other allied health professionals – to determine if these patients are candidates for surgical interventions and formulate the optimal course of treatment, including both short- and long-term management,” says Jacques.

Timely referrals matter because significant delays could result in treatable conditions becoming progressively worse or untreatable.

Next-Generation Neuromodulation Technologies
Fortunately, Jacques says, improvements in neuromodulation technologies address a wide range of conditions, often achieving pain relief of 50 percent to 80 percent for most patients.

- **New surgical paddle leads with 32 contacts** provide more anatomical coverage combined with tight electrical contact spacing for better electrical field control; this translates into significantly improved pain relief for failed back surgery syndrome. “We do a small laminotomy and use fluoroscopy guidance to place a surgical paddle lead into the epidural space,” says Jacques.

- **Rechargeable pulse generators** use sophisticated programming to electrically saturate offending nerves in complex regional pain syndrome.

- **Intrathecal drug delivery systems** treat patients with refractory nociceptive pain, as well as movement disorders and spinal cord injuries. Once programmed, the pumps often provide a lifetime of analgesic relief with minimal side effects.

- **Neurolysis and rhizotomies** address a variety of nerve-related pain syndromes.

- **DREZ (dorsal root entry zone) treatments** address refractory pain after procedures to treat brachial plexus avulsion injuries. The treatment isolates and ablates the segment of the injured nerve causing pain.

The center also partners closely with community physicians to ensure that the procedures translate into improved and measurable functional outcomes.

When to Refer

Refer patients to the UCSF Center for Excellence in Peripheral Nerve Disorders and Pain Surgery with any of the following conditions:

- Cancer pain
- Chronic headache syndromes, including cluster headache and intractable chronic migraine
- Complex regional pain syndrome
- Epidural fibrosis
- Failed back surgery syndrome

For more information, contact Dr. Jacques at 415-353-7500.
Adapting Neurovascular Approaches to New Knowledge

As understanding of stroke and other neurovascular disorders continues to increase, health systems must find new ways to incorporate that understanding in their treatment approaches, says vascular neurologist Karl Meisel, MD, director of the outpatient stroke clinic at UCSF Medical Center.

The clinic, which provides preventive care and screening for patients at high risk for stroke and other neurovascular conditions, recently added new services and protocols to:

- Evaluate and prevent recurrence of cryptogenic stroke
- Better address transient ischemic attacks (TIAs)
- Evaluate patients with pulsatile tinnitus

Cryptogenic Stroke

“We're finding a fair number of cryptogenic ischemic strokes that are cardiac in nature,” says Meisel, who recently returned to UCSF after establishing a stroke network in Michigan. “We’ve developed a protocol for thorough evaluation that identifies underlying cause, determines who needs monitoring and optimizes treatment pathways.”

An experienced, collaborative team is critical. At UCSF the team includes neurovascular neurologists, neurosurgeons, neurointerventional radiologists and cardiologists. The cardiologists conduct systematic testing that might include transesophageal echocardiography (TEE) and long-term cardiac monitoring aimed at finding arrhythmias that can lead to stroke.

Depending on the etiology, treatments can vary from aspirin to novel anticoagulant medications. For patients who aren't candidates for anticoagulation, surgery may become an option. Those with atrial fibrillation can consider the minimally invasive percutaneous LARIAT epicardial suture procedure, which was pioneered by UCSF cardiologist and electrophysiologist Randall Lee, MD, PhD.

TIAs

New understanding of TIAs has enabled more flexible and more appropriate risk stratification and preventive actions, says Meisel.

Given the risk associated with TIAs – 25 percent of all strokes are preceded by a TIA – UCSF has created an outpatient TIA clinic rooted in an alliance among the neurology, family medicine and emergency departments.

If a TIA patient is not at high short-term risk for stroke based on radiological and neurological findings, the clinic ensures timely care by treating these patients in an expedited outpatient setting and providing a 1- to 2-day follow-up with a neurologist.

“For the neurologist delivers individualized risk reduction strategies to more effectively prevent secondary strokes,” says Meisel.

Finding Answers for Pulsatile Tinnitus

Finally, pulsatile tinnitus – which is sometimes associated with neurovascular disorders – has long been a frustration to both patients and physicians, but new imaging techniques under investigation could enable clinicians to locate and treat the problem.

In response, an interdisciplinary team of UCSF neurointerventional radiologists, vascular neurologists and otolaryngologists has established a clinic to systematically evaluate pulsatile tinnitus patients.

In cases where vascular malformation is the cause, the team can use neurointerventional techniques to redirect blood flow and ease or eliminate the condition.

For more information, contact Dr. Meisel at 415-353-8897.

When to Refer

Refer to UCSF Medical Center any patient who has experienced:

- Aneurysm, arteriovenous malformations and other brain vascular abnormalities
- Cryptogenic stroke
- Ischemic and hemorrhagic stroke
- Pulsatile tinnitus
- TIA with an ABCD2 score of 3 or less without significant carotid stenosis

MRI derived slip-streams of blood flow the jugular bulb of a patient with pulsatile tinnitus. Ongoing research is correlating images like these with patient symptoms to determine if there are endovascular methods to suppress tinnitus.
New Hope, Expanded Access
for Patients with Refractory Epilepsy
(continued from front cover)

More Precise Patient Selection
Patient selection, however, is critical. At UCSF, interdisciplinary teams conduct a multistage evaluation that goes beyond a patient history, physical examination and traditional electroencephalogram (EEG).

“Standard EEGs are two-dimensional, so can only locate certain types of seizure activity,” says Knowlton. “When we have good reason to suspect a patient may be a surgical candidate, we can now use three-dimensional neuroimaging and other advanced techniques to better determine if surgery is viable and, if so, how best to proceed.”

The techniques, which are often complementary, include:

• Magnetoencephalography (MEG).
• Stereo-EEG (SEEG), in which implanted electrodes yield a 3-D view of seizure activity. “What appears as widespread seizure activity on a standard EEG might actually be revealed as more focal and so more appropriate for surgery,” says Knowlton.
• Ictal single-photon emission computed tomography (SPECT), which injects a short-acting isotope in the patient’s brain to photograph vasculature at the moment of seizure. “If there is focal seizure activity, it lights up like a Christmas tree,” says Knowlton. “But the pictures are noisy and require experience with state-of-the-art algorithms to analyze properly.”

Expanded Surgical Options
If patients are surgical candidates, the UCSF team offers a full menu of surgical options:

• Anterior temporal lobectomy
• Neocortical epilepsy surgery
• Visualase thermal laser ablation, a minimally invasive procedure for very discrete seizure activity that uses a wire with a laser tip to heat and ablate problem tissue
• Vagus nerve stimulation (VNS) therapy
• NeuroPace reactive neural stimulation (RNS), which uses an implantable, battery-powered device to detect abnormal electrical activity and deliver electrical stimulation to normalize the activity and avert seizures

“The FDA approved NeuroPace RNS to treat medically refractory seizures in November 2014, and we are among the first centers on the West Coast to use the procedure,” says UCSF neurosurgeon Edward Chang, MD, surgical director of the UCSF Seizure Disorders Surgery Program and a renowned expert in epilepsy surgery.

“With our expanded capacity, we can now evaluate and, if appropriate, complete surgeries within six months of initial contact,” says Knowlton. “We are excited to have both the capacity and expertise to offer long-suffering patients.”

For more information, call Nurse Specialist Lucinda Rinaldo of the Seizure Disorders Surgical Program at 415-353-2437.

When to Refer

Refer the following patients to the UCSF Seizure Disorders Surgical Program:

• Patients with suspected partial (focal) epilepsy who are not free of all disabling seizures after two or more antiseizure medication trials
• Cognitively disabled patients with atonic seizures (drop attacks) that result in severe falls, thus limiting their freedom to ambulate

Image from ictal single-photon emission computed tomography (SPECT) image highlights focal seizure activity.
Diagnosing and treating brain-related disorders in children typically involve coordination among multiple specialties.

“With our move to Mission Bay, the Pediatric Brain Center [PBC] at UCSF Benioff Children’s Hospital San Francisco is consolidating its expertise in one physical space to expand access and better coordinate care for patients and families throughout Northern California,” says pediatric neurologist Heather Fullerton, MD, medical director of the PBC.

The PBC ties together the work of multiple specialty centers, clinics, research efforts and specialists. It offers a single intake number and a concierge service, with nurses and physicians conducting triage and coordinating care for a comprehensive range of complex brain diseases (see accompanying box).

“Now referring physicians and families can conveniently coordinate visits with multiple specialists in one day, which is especially important for those traveling from far away,” says Karen Seth, practice manager for the PBC.

**Comprehensive Care for Children’s Brains**

The move coincides with the expansion and refinement of PBC services.

- An expanded pediatric stroke program includes three board-certified vascular neurologists and a focus on improving the cognitive and language outcomes for children who have had strokes, so schools can better educate them.
- Rehabilitative medicine is now tightly integrated with pain and palliative care specialists.
- A new pediatric movement disorders specialist expands access to deep brain stimulation for conditions such as cerebral palsy and Tourette’s syndrome.
- Having more neurointerventional radiologists allows expanded use of advanced imaging tools.
- Increases in the number of neuropsychologists and social workers can help referring physicians, families and schools ease reintegration after treatment.
- New multidisciplinary clinics will address neurofibromatosis, neuro-oncology and hereditary hemorrhagic telangiectasia.

**Accelerating Translational Research**

In addition, close proximity to leading neurological researchers tightens the translational research loop. “We can leverage the full range of expertise to advance the standard of care for many brain-related conditions and ensure our patients are the first beneficiaries,” says Fullerton.

Consider a condition like diffuse intrinsic pontine glioma (DIPG), a childhood brain tumor for which there is no existing standard of care; most children die within nine months of diagnosis. The UCSF PBC, under the leadership of Surgical Director Nalin Gupta, MD, PhD, is leveraging stereotactic biopsies for DIPG to test a precision medicine approach. In a feasibility trial led by Sabine Mueller, MD, PhD, the PBC is profiling molecular features of biopsied tissue to determine which of four FDA-approved drugs offers the best chance for successful treatment.

“Our tumor board includes experts in genomic analysis and several neuro-oncologists and neuropharmacologists,” says Mueller. “If we are successful, we will be able to individualize therapy not just for DIPG, but, possibly, for other brain tumors as well.”

“A one-stop shop helps patients take full advantage of these kinds of services,” says Fullerton.

For more information, contact the Pediatric Brain Center at 855-PBC-UCSF or 855-722-8273.
Neuroscience

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For more information, visit www.cme.ucsf.edu

Mark R. Laret, Chief Executive Officer, UCSF Medical Center

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