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

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Our Physician Liaison Service provides you with improved access to our physicians and medical services. Liaisons can expedite the referral process and assist in obtaining follow-up information and are available to help resolve difficulties.

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The Transfer Center is staffed 24/7 to coordinate the transfer of patients to UCSF Medical Center. The center provides quick access to our doctors and other members of our team. We evaluate the needs of each patient to ensure that appropriate care is provided. The center can also facilitate your patient’s return transfer.

CME Courses

<table>
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<tr>
<th>Course Title</th>
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<tr>
<td>Pituitary Disorders: Advances in Diagnosis and Management</td>
<td>October 24, 2015</td>
<td>Marriott Union Square San Francisco, Calif.</td>
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<tr>
<td>49th Annual Recent Advances in Neurology</td>
<td>February 10-12, 2016</td>
<td>Hotel Nikko San Francisco, Calif.</td>
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UCSF’s neurosurgery and neurology programs have been ranked the best in the western United States by U.S. News & World Report’s 2015-2016 Best Hospitals survey and have advanced from fifth to fourth best in the nation.

For the 14th consecutive year, the survey also ranked UCSF Medical Center among the nation’s premier hospitals, calling it the eighth-best hospital in the country.
New tools and techniques for minimally invasive spine surgery have the potential to speed patient recovery and reduce risks for an extremely common medical complaint. Today, surgeons can even complete a number of these procedures in the outpatient setting.

The challenge for referring physicians and patients is finding surgeons trained and experienced in techniques that truly meet the standards of being minimally invasive.

(continued on page 6)
Optimizing our patients’ recovery from illnesses and injuries of the brain, spine and central nervous system demands that we incorporate evidence-based understanding of everything from basic biology to the way hospital-based, family and social systems can support our efforts.

I believe our diligent efforts in this regard are why our departments of neurology and neurological surgery continue to be ranked among the best in the nation, this year advancing from fifth in the nation to fourth according to the Best Hospitals survey from U.S. News & World Report, making us number one on the West Coast. (This year also marks the 14th consecutive year UCSF Medical Center is among the nation’s premier hospitals, ranking as the eighth-best hospital in the country in the magazine’s survey.)

The articles in this issue of Neuroscience at UCSF Medical Center demonstrate how integrating broad, evidence-based findings benefits our patients.

- We are easing some spine patients’ recovery from surgery by extending the use of minimally invasive techniques to more conditions and, for appropriately selected patients, to the outpatient setting.
- Expert neurologists at UCSF have collaborated with nursing staff to more effectively screen patients for delirium and to implement protocols that prevent or treat this condition, which far too often complicates patients’ recoveries.
- For patients experiencing a first attack of radiologically isolated neuroinflammation, we are offering fast, comprehensive diagnostic testing and collaborative follow-up care with community physicians.
- A first-of-its-kind immunotherapy trial for glioblastoma – using CAR T cells, which have shown impressive results in other cancers – offers patients new hope.
- Our expertise in treating both adult and pediatric dystonia patients with everything from medicine and botulinum toxin injections to deep brain stimulation is easing the lives of individuals struggling with this rare disorder. Long-term follow-up – in collaboration with community physicians – is part of all of these programs. Such efforts demonstrate our passionate commitment to helping the patients that we share with you lead full and healthy lives.

Addressing All of Our Patients’ Complex Needs

Multiple studies have indicated that as many as one in five patients over the age of 65 experience delirium while in the hospital, making it one of the most common neurologic problems – and one that is often preventable and treatable.

“This is distressing to both patients and families, and it puts patients at risk for a number of long-term health challenges, such as difficulty with activities of daily living and cognitive decline; it’s even associated with higher mortality rates,” says neurohospitalist Vanja Douglas, MD.

He adds that the condition – especially when it involves hypoactivity as opposed to hyperactivity – is often underdiagnosed and that neurological and ICU patients are at heightened risk.

That’s why in November 2013 – at the urging of a multidisciplinary team on the neurology unit – UCSF began piloting an innovative comprehensive approach to preventing and treating delirium.

An Interdisciplinary Intervention

To develop and validate the program, Douglas brought in a team that included neurologists, neurosurgeons, anesthesiologists, nurses, pharmacists, physical therapists and occupational therapists.

They arrived at a program that begins with nurses assessing anyone over 50 with a two-minute assessment tool that Douglas and UCSF colleagues developed and which enables clinicians to
stratify patients into high- and low-risk groups for the development of delirium.

If the tool determines the patient is a high risk – or if the patient develops signs of delirium based on another screen nurses administer on every shift – that finding triggers an individualized care plan that leverages the fact that 30 percent of delirium episodes are preventable with simple, nonpharmacological interventions that are not widely used in hospitals nationally. Care plans typically include some or all of the following:

- Minimize nighttime disruptions to ensure proper sleep.
- Keep patients up and moving during the day by:
  - Keeping lights on and/or letting in natural light.
  - Scheduling physical and occupational therapy sessions where appropriate, which also implies less sedation. A body of ICU literature has shown that early physical therapy decreases delirium.
- Minimize the use of narcotics.
- Provide frequent reorientation for cognitively impaired patients.
- Check for hearing aid or eyeglass use for those who are hearing or visually impaired.

The medical center has now extended a version of this pilot to some of its ICUs and surgical units in cooperation with the departments of anesthesia and perioperative care, surgery and psychiatry. In addition, Douglas and his team are carefully measuring the results of the intervention.

“Anecdotally, we’ve seen a greater degree of engagement in the nonpharmacologic approaches to delirium prevention and treatment among our nurses and residents – and less dependence on pharmacological sedation of our delirious patients after the program’s institution,” says Douglas.

Depending on the findings, Douglas hopes the program may eventually extend throughout all UCSF hospitals. III

For more information, contact Dr. Douglas at 415-514-1575.

Risk Factors for Delirium

- Older age
- Pre-existing cognitive dysfunction
- Dehydration
- Severe illness
- Vision and hearing impairment
- Electrolyte abnormalities
- Overmedication

AWOL stands for Age ≥80 years, failure to spell “World” backward, disOrientation to place, and higher nurse-rates iLlness severity. CAM stands for Confusion Assessment Method.

In an effort to enhance understanding of what triggers multiple sclerosis (MS), neurologists at UCSF Medical Center are implementing an ambitious new program – ORIGINS – that will also speed diagnostic testing and enhance collaboration with referring physicians.

“Essentially, we’ve created a hotline for physicians to call when they have a patient who they suspect is in the throes of a first attack that could be MS,” says neurologist Carolyn Bevan, MD, who is co-leading the clinical aspects of the study. “In most cases, we will be able to see these patients within 24 hours for a comprehensive clinical assessment.”

Research, Clinical Care and Sensitive Support Combined
If researchers can identify the triggers for MS, physicians might be better able to:

- Prevent disease onset or progression.
- Enable a more personalized approach to treatment decisions by helping physicians understand which patients immediately need disease-modifying therapy versus those who need monitoring only.
- Identify targets that will help them better manage the course of the disease.

“But we want to make sure the research doesn’t delay clinical care,” says Bevan, who notes that patients can have all testing done within 24 hours or in the same day as the initial call.

The study will also enhance patient care through:

- Collaboration with referring physicians to help patients through the initial stages of disease.
- Timely access to comprehensive, state-of-the-art tests, including:
  - Brain, cervical and thoracic spinal cord imaging on a high-resolution 3T magnetic resonance imaging (MRI) scanner.
  - Lumbar puncture.
  - Blood testing for disorders that can mimic MS, as well as research tests for genomics, proteomics and understanding the microbiome component.
  - Visual evaluation, including optical coherence tomography.
- Faster time to appropriate therapy.
- Follow-up testing over time.

“We’re very sensitive to what these patients are experiencing emotionally, and at each step we make sure we’re not asking people to do more than they can handle,” says Bevan. Patients can expect to spend significant time with a UCSF clinician who is expert in the care of people with MS and related problems. Research coordinators – trained in patient care – will also work with patients and families throughout the day of testing.

Long-Term Follow-Up
“Another goal of this study is to understand how people do on their therapies over the long-term,” says Bevan. Thus, UCSF will ask these patients to return once or twice a year to undergo repeat testing.

“Patients and their community physicians will have access to yearly, detailed imaging and visual diagnostics, which should be helpful for monitoring the course of the disease,” says Bevan. “We hope this will strengthen our community of treating neurologists and ophthalmologists because we’ll be working as a team to get patients through the diagnostic process as quickly as possible.”

For more information or to enroll a patient in the study, call Dr. Bevan at 844-REFER-MS.

To be eligible for the study, patients must be:

- Experiencing a first attack of radiologically isolated neuroinflammation.
- Within 90 days of symptom onset.
- Untreated, or 30 days removed from any steroid treatment.
In late 2014, UCSF opened a first-of-its-kind clinical trial for glioblastoma. A joint project with the University of Pennsylvania, the trial adapts a cancer immunotherapy known as chimeric antigen receptor (CAR) T-cell therapy, which has achieved better than 90 percent response rate and indications of durable response in some blood cancers.

UCSF neurosurgeon Hideho Okada, MD, PhD, is leading the UCSF phase of the trial in partnership with longtime collaborator Carl June, MD, the Penn oncologist credited with developing the therapy.

**How It Works**

In CAR T-cell therapy, clinicians collect patients’ T cells, modify them to detect an antigen associated with a particular cancer and then reintroduce the targeted T cells to improve patients’ immune systems’ anticancer response. The hope is that the procedure leads to the body permanently recognizing and fighting a particular type of cancer, should there be recurrence or activity in tumor tissue that surgery could not remove.

“For this trial we are targeting EGFRvIII [epidermal growth factor receptor variant III], which occurs in about 20 percent of glioblastomas,” says Okada. To date, scientists have confirmed the antigen only in glioblastomas, not in normal tissue, so the team believes targeting EGFRvIII in this trial poses little risk of the treated T cells attacking other organs.

To enroll in the initial phase of the trial:

- Patients must have a newly diagnosed glioblastoma.
- Their tumor must express EGFRvIII.
- There must be about one square centimeter of tumor remaining after surgery.

Physicians will harvest T cells of potential candidates after surgery but before radiation and chemotherapy begin. If the patient’s tumor does express EGFRvIII, clinicians send the T cells to Penn, where scientists modify them to target EGFRvIII and then return them to UCSF. Patients receive one infusion of the treated cells during their recovery period from radiation and chemotherapy.

**Possible Expansion**

While the current trial is only for newly diagnosed glioblastoma, Okada hopes eventually to add a cohort of recurrent patients as well, who will receive the CAR T-cell infusion two weeks before surgery, allowing researchers to examine the resected tumor for evidence of efficacy.

Having worked on immunotherapy for 20 years, he is excited by the targeted approach of the CAR T-cell therapies, in contrast with the more global immune system activation prompted by other immunotherapies. He says, “I don’t want to cause irresponsible hype, but I have never seen this kind of robust power.”

For more information, contact Dr. Okada at 415-353-7500.

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**Clinical Trials for Brain Tumors**

The UCSF Brain Tumor Research Center has a broad portfolio of clinical trials for any type of primary brain tumor, from the newly diagnosed through multiple recurrences. Trials might involve:

- Targeted agents
- Molecular blockers
- Immunotherapy
- New surgical techniques
- Intratumoral drug delivery

“Because of the complex nature of how patients fit protocols, the earlier we see them, the better,” says Nicholas Butowski, MD, director of Clinical Services in the Division of Neuro-Oncology. “We have good access through email or phone, and we will call back the same day for new-patient evaluations.”

For more information, contact New-Patient Coordinator Doris Rivas at 415-353-2193.
**Spreading, Not Cutting, Muscles**

“Our group of minimally invasive spine procedures is based around making a very small incision – around 16 millimeters – and using a tubular device that spreads the muscle fibers of the lower back, rather than cutting them,” says UCSF neurosurgeon Aaron Clark, MD, PhD. Clark recently completed a fellowship at the University of Tennessee with the neurosurgeon who developed the device and pioneered the accompanying techniques.

“Once you place the tube on the spine, you use a microscope to look down the barrel and then complete a normal spine operation using all the same techniques [as open procedures], but minimizing the destruction of tissue in getting down to the spine,” says Clark.

Many procedures that are still commonly done as open surgeries – such as laminectomies and discectomies for spinal stenosis, disc herniation and foraminal stenosis, standard anterior discectomies and some lumbar fusions – can now be done using these minimally invasive techniques.

For appropriately selected patients, trained and experienced surgeons can often complete these procedures – which are associated with less blood loss and statistically significantly reduced levels of narcotic pain medication after surgery – in the outpatient setting.

“We can even do multilevel procedures this way,” says Clark.

**Inpatient Versus Outpatient**

Deciding on whether to do the procedure in the inpatient or outpatient setting depends on the nature of the problem and whether or not patients are medically healthy enough to undergo a same-day procedure. At UCSF, surgeons and anesthesiologists collaborate to make the decision. Yet regardless of whether the procedure is done on an outpatient or inpatient basis, patients are generally up and moving within hours after surgery. Many are back to normal activities within two weeks.

“We’re still doing a great operation, using techniques that have worked for decades,” says Clark. “It comes down to less tissue destruction and much better pain control than we’ve had in the past.”

For more information, contact Dr. Clark at 415-353-7500.
New Medical and Surgical Approaches for Dystonia

“Because dystonia is rare and uncontrolled symptoms cause so much distress, every dystonia patient should see a movement disorder neurologist at least once,” says Jill Ostrem, MD, medical director of the UCSF Movement Disorders and Neuromodulation Center (formerly the Surgical Movement Disorders Center).

One of four Bachmann-Strauss Dystonia & Parkinson Foundation Centers of Excellence nationwide, the UCSF center treats approximately 1,500 patients with dystonia and 4,000 with Parkinson’s disease annually.

Team-Based, Comprehensive Care
“Prognosis and treatment depend on understanding whether the dystonia is the result of a genetic cause, brain injury, exposure to a medication or the first sign of Parkinson’s disease – and on whether the dystonia symptoms are focal, segmental or generalized,” says Ostrem. As part of the diagnostic process, UCSF offers access to a neurogenetics clinic, which enables neurologists to sharpen the prognosis while advancing understanding of the disease.

Once physicians have determined the type of dystonia, treatment options include:

- Medication
  - Levodopa/carbidopa
  - Anticholinergic medications such as trihexyphenidyl
  - Baclofen
  - Muscle relaxants such as clonazepam
- Botulinum toxin injections
- Surgery
  - Ablation
  - Deep brain stimulation

While medication is often the first step, for some adults with focal dystonia, Ostrem may suggest treatment with botulinum toxin injections. At the center’s botulinum toxin injection clinic, neurologists have had good success using either electromyography (EMG) or ultrasound guidance to target muscles overactive in dystonia.

Deep Brain Stimulation Extended to Children
When medical therapy or botulinum toxin injections fail to provide an acceptable quality of life, surgery — including deep brain stimulation (DBS) — becomes an option. UCSF has vast experience treating adults with the procedure and now — with the addition of a dedicated pediatric neurologist and the new UCSF Benioff Children’s Hospital San Francisco at Mission Bay — can offer DBS to many more appropriately selected pediatric patients.

“Children with primary generalized dystonia have been excellent responders,” says neurosurgeon Philip Starr, MD, PhD.

For the pediatric procedures, surgeons implant deep brain stimulator leads using interventional magnetic resonance imaging (MRI), with children under general anesthesia. Adults can now choose the same “asleep” method, or they can remain awake under light sedation.

“We also consider DBS for patients with secondary forms of dystonia, like cerebral palsy,” says Ostrem. Any patients who undergo DBS should have biannual follow-ups with a movement disorder neurologist, who can program and optimize device settings.

Because lifelong follow-up is important for any dystonia patient, the UCSF center offers mental health support and works closely with referring neurologists to help continually coordinate these patients’ care.

For more information, contact Dr. Ostrem or Dr. Starr at 415-353-2311.

When to Refer for DBS

Patients should consider DBS for dystonia if:

- They receive a clear diagnosis from a qualified movement disorder neurologist that excludes other neurological problems.
- The dystonia interferes significantly with normal activities or is causing social isolation.
- They have failed treatment with a variety of medications and/or cannot be treated effectively with injections of botulinum toxin.