Because caring for brain tumor patients is especially stressful on caregivers – and that, in turn, can affect patient outcomes and quality of life – UCSF Director of Neuro-Oncology Susan Chang, MD, mobilized the resources necessary to create the UCSF Neuro-Oncology Gordon Murray Caregiver Program, one of the first of its kind in the country for neuro-oncology patients.

“The program is important because so much of caregiving has shifted to family members, who often have little or no training in how to care for loved ones with brain tumors,” says clinical nurse specialist (CNS) Margareta Page, who is the caregiver team’s nurse coordinator.

(continued on page 6)
Neurological disorders are rarely simple or short-lived. That’s why partnering across disciplines and settings is essential if we are to optimize patients’ treatments and quality of life. We know, for example, it’s not enough to offer the most up-to-date treatments for brain tumor patients, so we have instituted the UCSF Neuro-Oncology Gordon Murray Caregiver Program, which engages patients and families early on to make sure they have the resources they need when they leave the hospital. On the front end of the care continuum, this issue highlights a clinical trial in which an interdisciplinary team from seven institutions nationwide applies precision medicine in an effort to improve survival rates for patients with glioblastoma.

Along the same lines, our renowned UCSF Amyotrophic Lateral Sclerosis (ALS) Center has doubled its weekly clinic hours, provides telemedicine consults for homebound patients, works closely with local providers to troubleshoot potential problems and collaborates with the UCSF Memory and Aging Center in treating the approximately 50 percent of ALS patients who also suffer from cognitive impairment. For neuromuscular disorders, effective treatments also typically depend on close collaboration among multiple specialties, as well as strong communication and co-management with community physicians – precisely the approach of our UCSF Neuromuscular Service.

Finally, neurohospitalist Maulik Shah, MD, medical director of the UCSF Transfer Center, leads an effort to optimize care for acute neurological and other complex cases by drawing on relationships he has built with a wide range of community physicians.

Such collaborations are among our highest priorities.

Stephen L. Hauser, MD  
Robert A. Fishman Distinguished Professor and Chair  
UCSF Department of Neurology

S. Andrew Josephson, MD  
Carmen Castro Franceschi and Gladyne K. Mitchell Distinguished Neurohospitalist Professor and Senior Executive Vice Chair  
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Helping Patients Along the Full Continuum of Care

New Findings Enhance Comprehensive Care for ALS Patients

In 2001, a 52-year-old woman began experiencing slurred, confused speech accompanied by progressive behavioral changes – all potential signs of frontotemporal dementia (FTD). By 2002, the woman also began having difficulty swallowing and arm weakness, even as her behavior and communication skills deteriorated as she adjusted to new routines.

Physicians at the UCSF Amyotrophic Lateral Sclerosis (ALS) Center found the woman did indeed have ALS, but “The delayed diagnosis made her treatment more challenging,” says neurologist Catherine Lomen-Hoerth, MD, PhD, director of the UCSF ALS Center. The center is one of a select group nationwide that both the ALS Association and Muscular Dystrophy Association certify and help fund.

A Shared Mutation

Lomen-Hoerth says that despite the historic belief that ALS does not affect the brain, recent studies have shown that FTD and ALS share a genetic mutation. Moreover, approximately one in two patients have a dual diagnosis of ALS and cognitive/behavioral impairment, and many of these patients actually have FTD. The findings are changing the diagnostic and treatment process for both conditions.
"At UCSF, we co-manage these patients with the Memory and Aging Center because, for example, people with frontotemporal dementia may be unlikely to accept standard recommendations like PEG (percutaneous endoscopic gastrostomy) or BiPAP (bilevel positive airway pressure). They may refuse caregivers other than family or avoid exercise," says Lomen-Hoerth. "This understanding changes how we treat our patients, as well as how we counsel caregivers."

Extending Best Practices to More Clinics, Plus Satellites
All ALS patients, regardless of comorbidities, do better at places with the expertise, experience and resources necessary to follow the American Academy of Neurology’s revised best practice guidelines, issued in 2009. With that in mind, the UCSF ALS Center has doubled its weekly clinic hours and offers additional clinics twice a year in both Monterey and Santa Rosa. It also provides telemedicine consults for homebound patients and works closely with local providers to help troubleshoot potential problems; the center’s physicians are available 24/7 by either phone or pager.

“Timely, multidisciplinary care is essential,” says Lomen-Hoerth. “Our patients are often here four times a year, for half a day or more, meeting with our full team.” The team includes:

- A neurologist
- A nurse
- A psychologist
- A physical therapist
- An occupational therapist
- A respiratory therapist
- A social worker
- A dietitian
- A speech pathologist

“We look at the whole person and every aspect of the body affected by the disease – and we are very proactive in how we manage ALS,” says Lomen-Hoerth. “Research has shown that maintaining weight, getting exercise and using noninvasive breathing devices can improve the quantity and quality of our patients’ lives."

Exciting Treatments on the Horizon
Another advantage of an academic medical center is its ability to connect patients with clinical trials, either at UCSF or at other institutions. In the next year, Lomen-Hoerth says promising stem cell and gene therapy trials are expected to begin enrollment, providing additional options for patients with this devastating disorder.

For more information, contact the ALS Center at 415-353-2122.
Ultrasound Adds to Powerful Arsenal for Combating Neuromuscular Disorders

Effective treatment for neuromuscular disorders often depends on a combination of clinical expertise and close collaboration among specialties that can include neurology, neurosurgery, orthopedics, rheumatology and hematology/oncology, says neurologist Ann Poncelet, MD, of the UCSF Neuromuscular Service.

“Expertise and experience with electromyography and nerve conduction studies [EMG/NCS] is an especially important skill set for everything from routine radiculopathies and carpal tunnel syndrome through multifocal neuropathies, motor neuron disease and neuromuscular junction problems,” says Poncelet.

Ultrasound Emerges

“EMG and NCS are still the gold standard, but ultrasound is an active area of research and an evolving noninvasive technique that can support and enhance EMG and NCS for a variety of conditions,” says UCSF neurologist Laura Rosow, MD. Rosow is fellowship-trained in the use of ultrasound for neuromuscular concerns; her addition to the Neuromuscular Service expands access to this rare expertise.

She says ultrasound can be helpful in the assessment of conditions that include:

- Focal neuropathies (e.g., carpal tunnel syndrome, ulnar neuropathy)
- Brachial plexopathies
- Amyotrophic lateral sclerosis
- Diaphragmatic paralysis
- Myositis
- Protocols for stiff person syndrome and periodic paralyses
- Phrenic nerve studies of the diaphragm
- Skin biopsies to gauge epidermal nerve fiber density in small fiber neuropathies
- Single fiber EMGs for neuromuscular disjunction when a blood test is inconclusive

Rosow says the ability to visualize nerves and muscles in real time can help characterize certain types of nerve injuries and can allow the examiner to identify anatomic anomalies, such as a persistent median artery in carpal tunnel syndrome. Ultrasound can also be a noninvasive alternative to EMG in assessing the diaphragm for patients with respiratory involvement.

“It can provide anatomical information for surgical planning and, in the future, might even be a diagnostic alternative if a patient doesn’t want an invasive measure,” says Rosow.

Interdisciplinary Expertise for Common and Rare Conditions

The introduction of ultrasound is just one example of the value provided by a center with experts comfortable doing studies and providing treatment for everything from simple to complex cases.

At UCSF, for example, the neuromuscular service offers:

- Protocols for stiff person syndrome and periodic paralyses
- Phrenic nerve studies of the diaphragm
- Skin biopsies to gauge epidermal nerve fiber density in small fiber neuropathies
- Single fiber EMGs for neuromuscular disjunction when a blood test is inconclusive
- Amyotrophic lateral sclerosis
- Diaphragmatic paralysis

The group also collaborates closely with other services and community physicians for disorders that can be particularly challenging to treat, such as neuropathies associated with hematologic malignancies and monoclonal gammapathy, vasculitic neuropathy, laryngeal conditions like vocal fold immobility, or autoimmune neuromuscular disorders like myasthenia gravis.

“When trying to figure out whether vocal fold immobility is from laryngeal neuropathy or is more of a mechanical problem, we’ll work with otolaryngology to perform a laryngeal EMG,” says UCSF neurologist Jeffrey Ralph, MD.

“For autoimmune neuromuscular disorders, our close collaboration and monthly case conferences with colleagues in rheumatology can make all the difference when we face challenging decisions about medications and co-managing neuromuscular and systemic involvement,” says Poncelet. “We also emphasize strong communication and co-management with physicians from all over California.”

For more information, contact the Neuromuscular Clinic at 415-353-7500.
When a patient with a brain hemorrhage arrives at a hospital without an available neurosurgeon, typically the hospital reaches out to a tertiary care center to get the patient an urgent evaluation and appropriate care. If that tertiary care center is UCSF Medical Center, the first contact is with the Transfer Center. “Our job is find the proper balance between getting patients here quickly, getting them here safely and making sure when they get here we are fully prepared for their arrival,” says Neurohospitalist Maulik Shah, MD, medical director of UCSF’s Transfer Center. “The challenge is that there are a lot of moving parts in the process.”

A Complex, High-Speed Process
Shah says the Transfer Center’s urgent tasks include:

- Obtaining clinical information, such as labs and imaging
- Connecting the appropriate on-call physician with the referring physician
- Anticipating how long the transfer will take and then suggesting immediate treatments and what the emergency transport vehicle will need to keep the patient stable
- Ensuring a bed is available
- Coordinating and preparing a team of clinicians at UCSF for the patient’s arrival

Shah’s focus since assuming his role in September 2015 is to constantly seek ways to strike that proper balance between speed and safety for all transfer patients. As a neurohospitalist who has been fielding Transfer Center calls for years, he has a particular interest in optimizing care for acute neurological emergencies and maintaining close connections with referring neurologists in the community.

“We have robust neurohospitalist, neurovascular and neurosurgical teams here, and we are updating our protocols for hyperacute neurological emergencies like stroke and status epilepticus,” says Shah, who is coordinating the process. “The goal is to prioritize important clinical factors, improve communication and anticipate potential delays before they occur.”

Continuous Quality Improvement
As part of the process, Shah examines previous cases to identify potential barriers to optimal care and create a core set of metrics to measure the success of any changes. Once the protocols are reviewed, approved and updated, Shah will implement training for clinical and administrative teams at the Transfer Center.

He says the past years have provided invaluable experience, as well as a collegial relationship with many community physicians, who are invaluable in helping him to troubleshoot some of the challenges. “We’ve been focused on improving transfers for decades, but there is always room for improvement,” he says. “We need to continuously make sure that patients who need our help get here as quickly and safely as possible, so we can continue to be a first-choice resource for hospitals throughout the western United States.”

For more information, contact Dr. Shah at 415-502-2510. For all transfer requests – 24 hours a day – call the UCSF Transfer Center at 415-353-9166.
Organizing and administering medications
• Communicating with the health care team
• Managing and observing the surgical incision
• Monitoring for medication side effects
• Potential postoperative complications and how to manage them

Self-care

Building Relationships and Personalizing Support

“How these are important services, but people aren’t always ready to hear about them at that first visit, so we also make a number of follow-up calls,” says Page. “The timing needs to be right to build relationships and trust.”

Once a family is engaged, the caregiver team assesses their needs and tailors the support across the trajectory of the illness. “We look at physical, practical, emotional and spiritual domains,” says Page. “Some caregivers are struggling with insurance and work issues, some with parenting, others with neurological symptoms, and still others with the diagnosis of a life-limiting illness.”

The Caregiver-to-Caregiver Peer Support Program and the monthly dedicated caregiver support group meeting are examples of newly available services. The peer support program offers new caregivers an opportunity to speak with experienced caregivers, who provide confidential emotional, practical and informational support. Research shows these interactions have benefits for both those giving and those receiving the support.

“All of the elements of this program are aimed at helping caregivers achieve mastery and a sense of self-sufficiency to optimize their quality of life and the quality of life of their loved one,” says Page.

For more information, call CNS Margaretta Page at 415-353-2966.
Years of research and multiple clinical trials have failed to increase the survival rate for progressive and recurrent glioblastoma. Of the approximately 12,000 patients diagnosed each year in the US, about half die within 15 months of diagnosis; most of the rest typically die within five years.

In an effort to finally see some improvements in survival rate, UCSF brain tumor experts recently led an innovative pilot trial with funding from the Ben and Catherine Ivy Foundation. An interdisciplinary team from seven institutions nationwide found that it was feasible for a specialized tumor board to deliver individualized treatment recommendations within 35 days of tumor tissue collection. The recommendations were rooted in genomewide analysis strategies and RNA sequencing that the Translational Genomics Research Institute (TGen) performed.

The pilot will inform a larger trial that will study the efficacy of the treatment recommendations. That trial will open in the spring of 2016.

**Approach Is Validated**

In the pilot, TGen completed the sequencing, and the tumor board suggested alternative or adjuvant therapies within 27 days on average. Recommendations were rooted in genomewide analysis strategies and RNA sequencing that the Translational Genomics Research Institute (TGen) performed.

The pilot will inform a larger trial that will study the efficacy of the treatment recommendations. That trial will open in the spring of 2016.

**Why It Matters**

He says both trials are important steps toward true precision medicine for glioblastoma.

“Because TGen’s panel is a more comprehensive sequencing, we get more extensive and nuanced information about alterations in factors such as epidermal growth factor receptor [EGFR],” says Butowski. “Then, based on the literature, empiric experience and available treatments, we can make more informed choices about what drugs make the most sense, how to dose and in what sequence.”

Some unusual options showed promise in the pilot trial, including:

- The antiparasitic drug mebendazole
- The tricyclic antidepressant clomipramine
- A combination therapy of a cyclin-dependent kinase 4 (CDK4) inhibitor and an EGFR inhibitor

Butowski expects that in the larger trial, some refinements will emerge from other elements of the pilot. For example, the team removed tissue from both the edges and the core of the tumor and found the locations can present distinct therapeutic targets. In addition, the team used patient-derived xenograft models to better understand response and resistance to the various therapies.

“We’re still trying to find the needle in this haystack of data, so there is still a lot of debate about the alternatives, but this is a much more comprehensive approach, which we expect to refine as we go forward,” says Butowski.

For more information about the upcoming trial, contact New-Patient Coordinator Felecia Kuo at 415-353-2193.
UCSF Medical Center, UCSF Box 0940, 505 Parnassus Avenue, San Francisco, CA 94143

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

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.