A NEW WAY
OUT OF
DEPRESSION

Poverty’s Vexing Cycle • Kid-Size Dosing • When Disaster Strikes
FEATURES

12 Illuminating Depression’s Circuitry
Scientists seek a permanent cure by untangling flawed brain networks.

18 Poor Health
Confronting the vexing cycle of poverty and disease.

26 The Right Dose
Pharmacists customize drug dosages to maximize their effect and minimize toxicity.

30 When Disaster Strikes
UCSF steps up to mobilize critical and lasting emergency care the world over.

DEPARTMENTS

2 What Matters
3 Inside UCSF
11 Faculty Accolades
24 Big Picture
36 Philanthropy
37 Alumni Hub
48 Double Take
Roof with a View
Summer fog encroaches on the San Francisco skyline as seen from the roof of the Ray and Dagmar Dolby Regeneration Medicine Building on Parnassus.
It’s been a remarkable first year for me as chancellor of UC San Francisco, and I have had the privilege of meeting many of you who are passionately pursuing our missions of education, research, patient care, and community service. You are making UCSF stronger than ever.

One priority has emerged that is directly tied to UCSF’s service mission – addressing the inequity of health disparities. This issue is gaining new urgency, given the Bay Area’s growing affordability crisis. Every day, at our partner institution, San Francisco General Hospital, and in UCSF’s own hospitals and clinics, our practitioners, researchers, and patients confront poverty’s pernicious impact on health. Numerous faculty members have an unwavering focus on eliminating health disparities. Professors Nancy Adler, Tom Boyce, and Paula Braveman, for example, have dedicated their careers to uncovering links between socioeconomics and poor health, a theme that has recently begun to resonate more strongly with the broader medical community. Learn more about their valuable work on page 18.

Our dedication to public service extends well beyond the Bay Area. UCSF’s response to humanitarian disasters, including the Ebola outbreak in West Africa and the earthquake in Nepal, exemplifies our commitment to serving vulnerable populations around the globe. You can read on page 30 about a few of our many faculty and students who have volunteered for international medical crises.

By harnessing our spirit of service, innovation, and collaboration, UCSF has an enormous impact on the health of our community, region, state, and world – redefining what’s possible for the well-being of all.

Sam Hawgood, MBBS
Chancellor
Arthur and Toni Rembe Rock Distinguished Professor
PHOTO: ELISABETH FALL

UCSF TRIFECTA

“We are blessed,” said Harjinder Gogia, MD, smiling, as he and his wife, Surinder, watched their two older sons, Ravi and Paul, hood their youngest son, Shawn, at the UCSF School of Medicine’s graduation ceremony in May. His brothers, also UCSF graduates, placed Shawn’s hood and then hoisted him onto their shoulders.

Shawn didn’t always know he wanted to be a doctor. His brothers, his father, two uncles, and at least 10 other family members had all chosen to practice medicine. With so many doctors turning up at Gogia family reunions, everyone just assumed Shawn would study medicine, too. But he had other plans and entered UC Berkeley as a European history major.

He was a sophomore there when a volunteer position as a caseworker serving the indigent at the Suitcase Clinic changed his thinking. The student-run organization offers free health care and social services to underserved populations in the Bay Area. Liaising with clients sparked Shawn’s interest in homelessness and its effects on health. “Medicine can transform both on an individual level and on a community or societal level,” says Shawn. “I really like connecting with my patients, figuring out a diagnosis, and then determining what structural issues are keeping that person from getting healthy. Connection to patients, family, and community is what is most important to me.”

Shawn chose UCSF in part because both of his brothers are alumni, but his family’s ties to the school run even deeper. When Shawn was 6 years old, Ravi, then 11, was diagnosed with metastatic liver cancer and given just months to survive. With such a dire prognosis, Harjinder brought his son to UCSF for treatment. Ten years later, when Ravi began his studies at UCSF, he understood what it was like for a child to go through intensive treatment in a hospital setting and was inspired to start the Pediatric Stars program in his first year. The program pairs young patients with first-year medical students as mentors who connect with the children throughout their treatment and try to engage with them in ways aimed at making the process feel as normal as possible.

Both Ravi Gogia, MD ’08, and Paul Gogia, MD ’05, were exceptional students who graduated from UCSF with Alpha Omega Alpha honors (the Phi Beta Kappa of medicine). With two sons already in AOA, Shawn says his parents barely acknowledged the honor when he received it. “My dad said he thought it was something everyone got,” Shawn laughs. When he was nominated for the prestigious Gold-Headed Cane Award – an honor bestowed by classmates and faculty for best exemplifying the qualities of a true physician – only then did his father react. Matched for a residency at Massachusetts General Hospital in Boston, Shawn is ready for the next phase in his career. “There may even be another Gogia at UCSF,” Shawn says, flashing his contagious smile. “I have a cousin who just completed premed.”

– Carol Pott

“Connection to patients, family, and community is what is most important to me.”

– Shawn Gogia

BROTHERLY LOVE: School of Medicine alumni Paul and Ravi Gogia celebrate their younger brother Shawn’s graduation from the school.
App Fosters Long-Term Study of LGBTQ Health

Small-scale health studies of the lesbian, gay, bisexual, transgender, and queer (LGBTQ) community have yielded alarming results: Its members are more susceptible than the general population to depression and anxiety; they have a higher risk of suicide; and they are more likely to engage in smoking and other unhealthy habits.

Unfortunately, little is known about the specific factors that influence this community’s health because a long-term study has never been conducted. Until now.

UC San Francisco’s Population Research in Identity and Disparities for Equality (PRIDE) Study will be a national, online investigation aimed at better understanding the health of LGBTQ adults in the United States. The study currently uses an iPhone app to connect with and track sexual- and gender-minority adults over time to understand factors related to their patterns of health and disease. The app version of the study will soon be augmented with a web-based portal.

More than 13,000 participants have enrolled since the study launched in June 2015. They have posted thousands of health topics that are of interest to them and are actively helping design the study through these comments.

“There’s a real lack of evidence-based information on [LGBTQ] community health,” says research fellow Juno Obedin-Maliver, MD, MPH, who launched the study with Mitchell Lunn, MD, also a research fellow. “The current landscape for LGBTQ health is less of a map and more of a signpost in the desert. We aim to create that map.”

“Sleep is foundational.”

Cheri Mah, MS, sleep medicine researcher, answering the question “Is it better to sleep in or work out?” in Time magazine
ODD in Preschoolers Linked to Aging Biomarkers

Preschoolers with oppositional defiant disorder (ODD) behavior are likely to have shorter telomeres than their peers, according to a recent UC San Francisco study. A hallmark of cellular aging, shortened telomeres in adults are associated with an increased risk for chronic diseases and conditions like diabetes, obesity, and cancer.

Likened to the plastic tips of shoelaces, telomeres (light blue at left) cap the ends of chromosomes and act as buffers against the loss of protein-coding DNA during cell division. Telomere shortening happens naturally with aging, but mounting research indicates that psychological or biological stress – including early-childhood trauma, exposure to violence, maltreatment, or deprivation – can accelerate the process. The researchers also identified maternal clinical depression as a predictor of shortened telomeres in young children.

“These are the first steps in a new field aiming to understand early determinants of children’s telomeres,” says lead author Janet Wojcicki, PhD, MPH, an assistant professor of pediatrics. “There are no studies examining telomere length changes from birth to adulthood, so the long-term implications are unknown, but our results suggest that maternal mental health issues and child behavioral problems can impact children at the cellular level.”

Study Casts DOUBT on Vaping Value

The tobacco industry paints the use of e-cigarettes, known as “vaping,” as a less-dangerous nicotine-delivery system for smokers who can’t, or don’t want to, quit. That scenario assumes that as the number of smokers continues to decline, only those who cannot quit will remain.

However, a recent UC San Francisco study – spanning 18 years in the U.S. and six years in Europe – found the opposite: As the number of smokers declined, the remaining smokers smoked less and were more likely to quit.

The findings challenge the need to promote new forms of nicotine delivery, such as e-cigarettes, since smokers continue to quit as a result of proven policies and interventions, says Margarete Kulik, PhD, a postdoctoral fellow at the UCSF Center for Tobacco Control Research and Education and first author of the study.

The conclusions are significant because e-cigarettes are not harmless, Kulik says. A recent review of the science on e-cigarettes by UCSF researchers showed that besides nicotine, their emissions contain formaldehyde and other toxins. The review also showed that vaping is associated with significantly lower odds of quitting and with higher levels of dual use – smoking both e-cigarettes and regular cigarettes – among adults and youth.

The takeaway, Kulik says, is that current policies – including strong antitobacco media, smoke-free laws, and increased tobacco taxes – are effective at getting smokers to quit. So, she emphasizes, there’s no need to promote new forms of nicotine delivery, “especially ones like e-cigarettes that are very appealing to children.”

“We were somewhat surprised to see that this gap was so persistent over the years, given the female-dominated profession.”

Ulrike Muench, RN, PhD, an assistant professor in the School of Nursing, on her finding, published in the Journal of the American Medical Association, that even though about 90 percent of nurses are women, their annual salaries average $5,000 less than those of male nurses, in USA Today.
ASK THE EXPERT: Women’s Heart Health

Many people are unaware that cardiovascular disease is the leading cause of death in women over 40 and that it kills more women than men. “Heart disease is generally perceived as a condition that affects mostly men,” says cardiologist Anne Thorson, MD, an expert in women’s heart health. Yet one in three adult women has some form of heart disease, and once a woman reaches menopause her risk increases. Below, Thorson, associate director of the UCSF Center for Prevention of Heart and Vascular Disease, answers some frequently asked questions.

Do only older women need to worry about heart disease?
No. Women under age 65, especially those with a family history of heart disease, need to be aware of heart disease risk factors. Also, new research indicates that young women with pregnancy-related conditions such as preeclampsia (characterized by hypertension, or high blood pressure) or gestational diabetes may be at increased risk. Women of all ages should be aware of their risk for heart disease and learn what they can do to reduce their odds of it.

What are the risk factors for cardiovascular disease in women?
They are similar for women and men: high blood pressure, diabetes, high cholesterol, smoking, and a family history of heart disease. However, some of these factors play a larger role in the development of heart disease in women. For example, having diabetes or being a smoker increases the risk of heart disease for women more than it does for men. And mental stress or depression appear to adversely affect women’s hearts more than men’s. Also, women are more likely to be physically inactive than men – and inactivity is another risk factor for heart disease.

How do I know if I am having a heart attack?
The most common heart attack symptom for both women and men is a sensation of pain, pressure, or discomfort in the chest, possibly radiating to the left arm. However, women are more likely than men to have heart attack symptoms unrelated to chest pain, including shortness of breath; right arm pain; neck, jaw, shoulder, upper back, or abdominal discomfort; sweating; lightheadedness or dizziness; and unusual fatigue. Also, women’s symptoms may occur when they are resting. Since their symptoms can be subtler than chest pain, women frequently ignore or downplay them and go to the emergency room too late – after heart damage has occurred.

What can I do to prevent heart disease?
There are certain lifestyle changes anyone can make that will significantly reduce risk. For instance, adopt a diet low in saturated fat, cholesterol, and salt. Engage in moderate physical activity, 30 to 60 minutes at least five days per week. Don’t smoke and avoid secondhand smoke. Maintain a healthy weight. Work with your doctor to manage conditions that increase the likelihood of heart disease, including diabetes, hypertension, and high cholesterol. And if you are highly stressed, learn techniques for stress reduction.

If I am diagnosed with heart disease, what are my treatment options?
It depends on your personal circumstances and family history, but treatment could be lifestyle-related, such as an exercise program to lower your weight (if that’s a factor) and reduce stress, or pharmaceutical in nature, such as taking a blood thinner or a baby aspirin. Interestingly, in a recent study published in the journal HeartRhythm, researchers found that women diagnosed with atrial fibrillation – a common arrhythmia, or irregular heartbeat – were less likely than men to be prescribed blood-thinning medications by their doctors, even though women with this condition are known to be at a higher risk of
Kidney Donor Launches Transplant Chain Reaction

Reid Moran Haywood’s kidney wasn’t a match for his friend who needed a new one, but he still wanted to donate it in gratitude for his lifetime of good health. Little did the Napa, Calif., resident know that his altruism would affect so many lives.

Moran Haywood’s donation set in motion a groundbreaking kidney transplant chain involving 18 patients – nine donors and nine recipients – at UCSF Medical Center and Sutter Health’s California Pacific Medical Center (CPMC) over the course of just 36 hours. It is believed to be the largest kidney transplant chain occurring in one city in such a short period.

Most of the patients were local, but a few traveled as far as Hawaii and Massachusetts. Six of the donated kidneys traveled, too – across town from one hospital to the other.

The donors – each a friend or family member of someone who needed a new kidney but who was incompatible with the related donor – were paired with someone else in the group with whom they were compatible. The pairs were matched using software developed by a former CPMC kidney transplant patient. Valerie McBride, RN, BSN, kidney transplant coordinator for UCSF Medical Center at Parnassus, coordinated the logistics, including organizing surgery dates, preoperative testing, patient education, and transportation of organs between the hospitals.

UCSF is one of the largest transplant centers for living kidney transplants nationally and has performed more kidney transplants overall than anywhere else in the country. CPMC is the nation’s largest nonacademic transplant program and a pioneer in paired kidney donations.

“This collaboration with CPMC enables us to broaden our pool of kidney transplant donors and recipients and treat them at two medical centers separated by only a few miles,” says John Roberts, MD, who holds an endowed chair in abdominal transplantation and is chief of UCSF’s Division of Transplant Surgery.

“The single biggest, unrecognized cause of headache is probably medication or pain-killer overuse.”

Neurologist and headache specialist Peter Goadsby, MD, PhD, on one of the 10 “sneaky things” that can cause headaches, in *Good Housekeeping*
UCSF Still Among America’s Best

U.S. News & World Report once again ranked UCSF’s School of Medicine and School of Nursing, as well as UCSF Medical Center, among the top 10 in the United States in its annual surveys of graduate schools and hospitals. UCSF Benioff Children’s Hospitals were also ranked nationally in nine pediatric specialties.

The School of Nursing tied for second overall, while the School of Medicine ranked third in the primary care category and tied for third in the research category. UCSF is the only medical school in the nation to rank in the top five in both research and primary care. In addition, the magazine’s most recent ranking of schools of pharmacy, dating from 2012, placed UCSF first for its doctor of pharmacy (PharmD) program. U.S. News does not rank graduate schools of dentistry.

And in its annual assessment of hospitals, the publication named UCSF Medical Center the eighth best in the country in 2015 – its 14th consecutive year in the top 10. Additionally, UCSF was ranked number one in the San Francisco-Oakland metropolitan area.

“Rather than determining which drug is best for the patient, we find ourselves making treatment decisions based on whether patients can afford drugs.”

Rheumatologist Jinoos Yazdany, MD, MPH, an associate professor and resident alumna, on the growing financial burden Medicare patients face in accessing arthritis medications that can cost up to $20,000 annually, in HealthDay
Dean Revealed: Questions for Talmadge King

International lung disorder expert, visionary leader, Harvard graduate, member of prestigious scientific societies—and now dean of UCSF’s top-ranked School of Medicine. Talmadge King Jr. assumed the helm of the school in July, after almost 20 years in leadership positions at UCSF, including chair of the Department of Medicine. We wanted to know what makes this impressive physician-scientist tick, and he was happy to oblige.

What makes a great leader?
You have to be passionate about what you do. You have to find the right people and put them in the right positions. You also have to understand people and how they work, because your job is to help them succeed. I’m hoping I have some of those features and can share them and help make life better for everybody.

What’s your vision for the School of Medicine?
For education, my vision is to guide our students to the greatness we know they can achieve. For research, it’s to have the resources and structure in place so our scientists can innovate and move forward. For clinical care, we should constantly be asking, “Is there a better way of doing this? How can we help our patients and help other physicians do a better job with their patients?”

What’s the best part about being a grandfather?
I have two granddaughters, ages 5 and 9, and it’s being able to spend time with them without worrying about all the things you do as a parent. You just allow the pure joy of the relationship to exist. And when I’m tired, I can take them back to their parents!

What book are you reading at the moment?
The Digital Doctor, by my friend and colleague [UCSF Professor] Bob Wachter. The other one on my bedside is Missing Microbes, which is about how antibiotics are destroying the microbiomes in our bodies.

What motto do you live by?
My mother used to always tell us “Just be nice.” One of Maya Angelou’s quotes that resonated with me is, “You shouldn’t go through life with a catcher’s mitt on both hands; you need to be able to throw something back.” Another is, “People will forget what you said, people will forget what you did, but people will never forget how you made them feel.”

What excites you about showing up to work every day?
Meeting the amazing individuals who work here. There are so many people who are dedicated to making the world a better place. That makes it fun to come to work.

If you could change one thing about medicine, what would it be?
It takes a long time before people benefit from advances in medicine. If we could figure out a way to do really good research, figure out things that change people’s lives, and then get them to the people faster, that would be really helpful. I also think health care in the U.S. should be universally available to everybody. It’s the right thing to do and also the most cost effective.

Who’s had the biggest influence on you?
I’ve been married to my wife, Mozelle, for 47 years. I have to say that she keeps trying to make me a better man. It’s been a hard job. Professionally, it’s hard to name one person. At every step, there was someone who really was helpful to me.

Any brief words of wisdom for those just starting their careers in health care?
If you really believe that you want to work in an environment where you can help people, this is one of the few where you can do that on a daily basis. You can make a difference and actually see that difference in the lives of the people you touch. It’s a tremendous career.
Yamamoto Joins Genome-Editing Advisory Group

Imagine possessing the technology to alter the genetic makeup of a dangerous organism – such as *Plasmodium*, the mosquito-borne parasite that causes malaria – and eliminate its threat. Researchers have dreamt of finding such a magic wand for years. The recent development of a sophisticated genome-editing technology, CRISPR-Cas9, brings that dream a big step closer to reality.

But genome-editing has a potentially nefarious side, too: It could be used to edit genomes in reproductive cells, conceivably changing the genetic information that is passed from one generation to the next.

That possibility prompted the National Academy of Sciences and the National Academy of Medicine to appoint a nationwide advisory group to guide research and clinical decisions about the use of genome-editing technologies to treat human disease. Among the experts named to the group was Keith Yamamoto, PhD, UC San Francisco’s vice chancellor for research and a postdoctoral alumnus.

“The simplicity of the CRISPR-Cas9 system allows any researcher with knowledge of molecular biology to modify genomes, making feasible experiments that were previously difficult or impossible to conduct,” Yamamoto and several co-authors said in an editorial published in *Science* last spring. This is “a source of excitement and unease … especially in light of concerns about initiating a ‘slippery slope’ from disease-curing applications toward uses with less compelling or even troubling implications.”

---

EASY TEST FOR PROSTATE CANCER RISK?

A simple blood or urine test soon may be all that’s needed to identify men with an elevated, genetically inherited risk for prostate cancer, thanks to a team of scientists from UC San Francisco and Kaiser Permanente.

The team’s recent study analyzed genetic samples and health records from more than 100,000 volunteers, making it one of the largest research projects in the United States to examine the genetic, health, and environmental factors that influence common diseases such as prostate cancer.

The researchers modeled prostate cancer risk using bits of DNA that commonly vary among individuals and that are associated with a higher risk of prostate cancer. Each of the genetic variants modestly alters risk, but men with multiple variants, placing them in the highest 10 percent for prostate cancer risk, were more than six times as likely to be diagnosed with the disease than men who ranked among the lowest 10 percent for prostate cancer risk.

The results suggest that large data sets like this may lead to more precise diagnostics. That would be a welcome addition to the fight against prostate cancer, because previous studies concluded that genes determine roughly half of the risk for prostate cancer. The disease kills more than 27,000 men each year in the U.S., more than any other cancer except lung cancer.
FACULTY ACCOLADES

Two groups of UCSF researchers received Allen Distinguished Investigator grants totaling $2.7 million from the Paul G. Allen Family Foundation to help uncover the biological roots of Alzheimer's disease. Diane Barber, PhD, professor and chair of the Department of Cell and Tissue Biology; Matt Jacobson, PhD, professor of pharmaceutical chemistry; Aimee Kao, MD, PhD, assistant professor of neurology; and Torsten Wittmann, PhD, associate professor of cell and tissue biology, are sharing a three-year, $1.3-million grant. Martin Kampmann, PhD, assistant professor of bioengineering and biophysics; Michael Keiser, PhD '09, assistant professor of pharmaceutical chemistry; and David Koke, PhD, assistant professor of physiology, were awarded a three-year, $1.4-million grant.

Stella Bialous, RN, DrPH, associate professor of social and behavioral sciences, received a 2015 World No Tobacco Day award from the Pan American Health Organization/World Health Organization in recognition of her contributions to advancing tobacco control in the Americas.

Harvey Brody, DDS '63, clinical professor emeritus of dentistry, was appointed alumni regent-designate to the UC Board of Regents. The two-year term rotates among the 10 campuses in the UC system.

Esteban Burchard, MD, MPH, postdoctoral alumnus, professor of bioengineering, and Harry W. and Diana V. Hind Distinguished Professor in Pharmaceutical Sciences II, was appointed to a panel advising the National Institutes of Health on how to develop the $215-million Precision Medicine Initiative.

Edward Chang, MD '04, associate professor of neurological surgery, was named the 2015 Blavatnik Laureate in the Life Sciences. The $250,000 award “honors the nation's most exceptional young scientists and engineers, celebrating their extraordinary achievements and recognizing their outstanding promise.” Chang's research has provided deep insights into how language is processed in the human brain.

Yifan Cheng, PhD, associate professor of biochemistry and biophysics, and Loren Frank, PhD, professor of physiology, were named Howard Hughes Medical Institute (HHMI) investigators this spring. The prestigious HHMI investigator program provides investigators with “long-term, flexible funding that gives them the freedom to explore and, if necessary, change direction.”

Joe DeRisi, PhD, professor of biochemistry and biophysics; Frank McCormick, PhD, professor emeritus at the Helen Diller Family Comprehensive Cancer Center; Robert Nussbaum, MD, former chief of genomic medicine at UCSF Medical Center; and James Wells, PhD, professor of pharmaceutical chemistry and Harry W. and Diana V. Hind Distinguished Professor in Pharmaceutical Sciences, were elected to the American Academy of Arts and Sciences, one of the nation's oldest learned societies and independent policy research centers.

John Featherstone, PhD, dean of the School of Dentistry, was elected to honorary membership in the American Dental Association. The accolade recognizes his outstanding contributions to the art and science of dentistry.

Marcus Ferrone, PharmD, JD, associate professor of clinical pharmacy, was named 2015 Innovative Pharmacist of the Year by the California Pharmacists Association. The honor recognizes Ferrone’s work developing and compounding hyperpolarized carbon-13 pyruvate, a unique, specially labeled substance given intravenously to enhance magnetic resonance imaging signal strength.

Christine Miaskowski, RN, PhD, postdoctoral alumna, professor, and holder of the Sharon Lamb Endowed Chair in Physiological Nursing, was inducted into the International Nurse Researcher Hall of Fame by Sigma Theta Tau International, the honor society of nursing. The appointment honors nurse researchers who have achieved significant and sustained national or international recognition and whose research has improved the profession and the people it serves.

Ernest Newbrun, PhD '65, DMD, professor emeritus of dentistry, received a Lifetime Achievement Award from the Campaign for Dental Health for his decades-long support of community water fluoridation.

Howard Pollick, BDS, MPH, clinical professor of dentistry and director of the Dental Public Health Residency Program, received the 2015 Chancellor Award for Public Service in the faculty category. His selection recognizes his many contributions to UCSF’s public service mission.

Sally Rankin, RN, PhD '88, professor emerita of family health care nursing, was appointed to the MacArthur Foundation Endowed Chair. This UC-wide endowment rotates among campuses every 10 years and recognizes the new Center for Global Health Nursing in the School of Nursing.

Robert Wachter, MD, resident alumnus and professor of medicine, was named the most influential physician executive in the United States by Modern Healthcare magazine. It’s Wachter’s eighth consecutive appearance on the list and the first time he’s topped it.
NEW PATH TO HEALING:
If successful, scientists will – for the first time – map the disrupted circuits in the brain that cause mood disorders, then restore them to health.
In a hospital room at UC San Francisco’s Parnassus campus, a patient anticipates having an epileptic seizure. A dozen wires trail from her gauze-wrapped head to a bedside monitoring device. Hidden beneath gauze and bone lies an intricate network of electrodes – each roughly the size of a flattened grain of rice. They’ve been surgically implanted on the surface of her brain, with the goal of revealing the origin of her complex, near-weekly seizures. At the same time, she is volunteering as a participant in groundbreaking research on mood disorders like depression, as well as related disorders like anxiety.
Chang are uniting their Neurosurgeon Eddie Chang (left) operates on a patient with epilepsy. Chang’s team is mapping the regions of the brain that trigger seizures while also studying the circuits that mediate mood.

“We really want to go after this idea of using neural plasticity: remodeling the brain toward thinking about curative options.”

– Eddie Chang

This patient is one of about 60 who receive similar specialized surgical treatment annually from UCSF neurosurgeon Edward Chang, MD ’04, because a cure for their epilepsy is unusually elusive. The electrodes stay in place for up to three weeks as Chang and his colleagues at the UCSF Epilepsy Center map which region of their brain triggers the seizures in the hope that they can be alleviated through surgery.

These implanted electrodes also present a rare opportunity to study an even more elusive target: the source of human moods and emotions.

Simply being alive can be excruciating for those who suffer from severe depression or anxiety. Many derive little enjoyment from family, work, or play; some have a hard time functioning; and for a few, mood disorders are so irremediable that they take their own lives. Yet just as lasting happiness eludes those with intractable mood and anxiety disorders, definitive treatments have evaded those hoping to help such patients. For some, drugs and other therapies fail to fully resolve their suffering. For a few, treatment fails entirely.

But what if such troubles stem from flawed brain circuitry, which could be coaxed to support healthy neural processing instead? A research project headed by Chang aims to answer this question – and change the way we understand and treat mood disorders.

If successful, the project will for the first time map the networks in the brain that have gone awry, then remodel them to restore healthy functioning using a new type of device that could be permanently implanted in the brain. When the pathways corresponding with depression are activated, the pattern of activity would be picked up by specialized electrodes. The electrodes, which are currently in development, would emit a minute impulse. The stimulation would encourage the brain to shift its activity into new, healthier patterns – possibly for good.

“This would be revolutionary,” says Vikram Rao, PhD ’06, MD ’08, an assistant professor of neurology who’s on Chang’s team. “The problem is not that the whole brain is malfunctioning; it’s certain key circuits that mediate mood. The device would be able to intervene on those circuits and restore them to a more healthy state.”

Collaborative Genesis

Chang is a lean, soft-spoken 39-year-old who first operated on a human brain in July 2004. From his early days as a medical student at UCSF, where he also completed his residency, he was attracted to the skill and compassion necessary for neurosurgery. By the time he started this project, he’d already made groundbreaking discoveries regarding how the brain processes language – using many of the same tools now being applied to understanding mood and anxiety disorders.

One October morning in 2013, he learned from the New York Times that the Defense Advanced Research Projects Agency (DARPA) planned to spend more than $70 million to advance research on brain implants and therapeutic brain stimulation – exactly his area of research.

Chang thought, “Okay, let’s get ready for this.”

“We had all heard about it, but Eddie is the one who said, ‘Do you want to do something about this?’” says Vikas Sohal, MD, PhD, an assistant professor of psychiatry. “It’s definitely a team effort, but it’s his core vision of the themes and the people.”

That vision bore fruit; in the spring of 2014, the project was one of
When the Stars Align

The relationship between brain and mood has never before been looked at from such a detailed, structural standpoint. Doing so requires precisely siting electrodes on the surface of a living brain, slipping them under the skull like sliding a letter into an envelope.

“We are pioneering in this area in a way that is both ethical and a win-win for everyone involved,” Chang says.

Patients who have come to UCSF for epilepsy treatment – as well as others whom UCSF neurosurgeon Philip Starr, MD, PhD, is treating for Parkinson’s – are key to the project. They’re having electrodes implanted out of medical necessity, but in parts of the brain that researchers want to examine because of their impact on mood. In addition, it happens that people with epilepsy and Parkinson’s also suffer from a much higher rate of intractable depression than the general population.

In other words, chance has given the team access to an ideal pool of research participants. All the scientists need is the patients’ consent to study their moods and emotions as they undergo treatment – consent that is often granted. “It’s remarkable and humbling to see the interest patients have in participating,” says Heather Dawes, PhD, project co-director. “They know it's unlikely to benefit them directly, but they take the time to work with us anyway.”

The electrodes generate raw data that resembles an elaborate seismogram: multicolored lines that squiggle densely across the page, each representing activity in a different region of the brain.

That data is then correlated with patients’ moods: something inherently personal and subjective. Their feelings are quantified using an app that is based on research into how mood affects the performance of various concrete tasks. A tablet kept by patients’ bedside pings four or five times a day, reminding them to run through a few electronic exercises designed for the project by the software firm Posit Science, of which brain networks are activated in patients with mood disorders. In other words, depression people exhibit slower reaction times. On another, they’re

The results are then correlated with the real-time brain activity recorded by the electrodes. The goal is to develop a high-resolution map of which brain networks are activated in patients with mood disorders.

“I feel we are on the brink of a transformative insight,” Sohal says. “We are measuring things that honestly have scant examples of having been looked at in the context of depression. It could lead to totally different ways of treating depression from the way that we are right now.”

A Better Mousetrap

While the bulk of the data collection is taking place at UCSF, engineers at UC Berkeley, Cortera, and Lawrence Livermore are heading
“I feel we are on the brink of a transformative insight. . . . It could lead to totally different ways of treating depression.”

– Vikaas Sohal

up efforts to develop specialized electrodes and deep-brain stimulation devices that can be safely implanted for long-term therapeutic use. To be successful, the device will have to be entirely self-contained within the brain – battery, electrodes, software and all – just as an artificial pacemaker is permanently situated within the chest.

“It needs to be biocompatible, lightweight, small, flexible, with good battery life and certain electrical characteristics,” Rao says. “That’s a real engineering feat.”

Furthermore, the array needs to be closed-loop, meaning it will record the brain’s activity, then selectively deliver an electrical stimulus based on abnormal rhythms it detects.

Even better would be if the device doesn’t need to be permanent. “Unlearning depression” is what Rao calls the possibility that targeted manipulation of key brain circuits could reset an individual’s mood to a more normal state. If the brain learns to use the new pathway without the electrical tweaks, the device could eventually be removed.

“We really want to go after this idea of using neural plasticity: remodeling the brain toward thinking about curative options,” Chang says.

It may be a long shot that all will go as planned. Yet after only one year, the team has already achieved some level of success – perhaps changing the landscape of mood research for good. “This treatment has a very promising therapeutic effect,” Chang says.

Chasing the Rainbow

When Chang speaks about mood disorders, he often opens his presentation with an image of the Golden Gate Bridge – and the observation that it is possibly the top suicide location in the U.S.

“It’s not getting better. In fact, 2013 was a record year for suicide attempts from the bridge,” Chang observes. “As far as we can tell, the burden of disease, and the suffering, have never been higher. . . . Some even go for electro-convulsive therapy, where their whole brain is shocked. It turns out it’s very effective, but it’s only temporary and sometimes has negative effects on memories.”

The lay public tends to think of depression or anxiety as either a psychological weakness or a chemical imbalance. The latter view is due to highly publicized research on variations in neurotransmitters, such as serotonin and dopamine. In this view, the brain is simply awash in a sea of negative emotion; whole-body treatments such as drugs, therapy, or exercise may, or may not, be able to turn that tide. But until recently, no one had been able to pinpoint the specific physical structures in the brain responsible for the problems; previous generations of neuroimaging tools simply weren’t up to the task. Arguably, the closest attempt was the pioneering work of Helen Mayberg, MD, a neurologist at Emory University who was able to achieve improvements in mood with deep-brain stimulation.

However, she looked mostly at a single region of the brain, while the larger, network-level basis of mood disorders remains unclear. Furthermore, her approach was successful in small studies but thus far has failed in clinical trials, for unknown reasons.

“There are lots of different ways of conceptualizing depression, and we don’t know which one is right,” Sohal says. Yet refining the way we approach this issue isn’t an academic question for the millions of people worldwide who suffer from treatment-resistant psychiatric diseases.

“This particular collaboration is going to have an impact for an enormous number of our patients, starting with those suffering from depression but extending in the long run to those with anxiety, psychosis, and other such disorders,” State says.

If it’s successful, the project is likely to radically change the way depression is diagnosed and treated. Rather than relying on verbal descriptions of symptoms, diagnoses would be based on identifying specific mal-adapted circuits as the cause of various crippling mood disorders. Treatment could then be targeted accordingly. Overall, mood could come to be seen as a physical, not a moral failing: more akin to a broken bone than a broken heart. If such a paradigm shift occurs, Chang and his team foresee a secondary benefit for all patients with mood disorders, large or small: reduced stigma.

“Having knowledge about the physical mechanism of depression will help everybody view it differently,” Sohal says, adding that many of his friends, family members, and even patients currently feel that depression is not something real.

“As we make progress in this area, the stigma and marginalization that are just part and parcel of having a psychiatric illness will start to fade, I guarantee you,” State says. “It is going to have an enormous impact.”
When poverty becomes disease.

By Claire Conway

Talmadge King Jr., MD, dean of the UCSF School of Medicine, tells the story of an ER physician who had lost a document and was searching frantically for it in the garbage bins behind San Francisco General Hospital. What he found instead in the mountain of rubbish were crumpled prescription slips that patients had tossed in hospital trash cans throughout the week.

“Going forward, the conversations that ER doctor had with his patients changed. They became, ‘Well, you need these drugs. Which can you afford? How can I help?’” relates King. “Often it’s not that the patients aren’t adhering to advice. It’s that they can’t pay for the drugs, didn’t understand why they should take them, or simply that they did not feel the doctor even listened to them.”

Poverty collides with health every day at UCSF, compelling clinicians and scientists to engineer ways to disentangle the two, one complexity at a time. It’s the nurse trying to help a mom living in a single-room-occupancy hotel find refrigeration for her son’s antibiotic before an infection ruptures his second eardrum. Or the scientist gathering data on the toxic effects of stress on unborn children. Or the dentist trying to salvage the graying teeth in a toddler’s mouth – poverty’s most obvious portal.

Each is a temporary fix, merely scratching at the surface of what epidemiologists have long referred to as the “cause of causes” – poverty itself. This year marks the 50th anniversary of President Lyndon B. Johnson’s War on Poverty – part of his Great Society vision, which brought us such programs as Medicare, Medicaid, and Head Start. Yet the income discrepancy between rich and poor has not been as wide as it is now since the late 1920s, an era Mark Twain termed the Gilded Age due to the abject poverty that existed beneath a thin veneer of great wealth. Today, from their front-row seats on the health effects of poverty, scientists and clinicians at UCSF are carefully documenting, and trying to blunt, poverty’s debilitating toll as it cycles through families, from one generation to another.

Mounting Evidence

“Socioeconomic status is the most powerful predictor of disease, disorder, injury, and mortality we have,” says Tom Boyce, MD, chief of UCSF’s Division of Developmental Medicine within the Department of Pediatrics. Socioeconomic status is a term that often includes measurements of income, education, and job prestige – individually or in combination. The predictive power of income alone is perhaps most obvious when considering life expectancy. Impoverished adults live seven to eight years less than those who have incomes four or more times the federal poverty level, which is $11,770 for a one-person household, whether you live in Silicon Valley, the Rust Belt, or the rural South.

Discrepancies in life span grow significantly when race enters the equation. Paula Braveman, MD ’79, MPH, director of UCSF’s Center on Social Disparities in Health, points to a recent life-expectancy study that used education to reflect socioeconomic status and that also considered race. “They found that white people with more than 16 years of education lived 14.2 years longer than black people with less than 12 years of education,” says Braveman, who has published extensively on social disparities for more than two decades. “It’s shocking. It reflects the combined effects of socioeconomic disadvantage and additional racial inequities.”

As dramatic, perhaps, is the association being born into a poor family has with brain development. Programs like Head Start, which intervene with 4- and 5-year-old children to provide increased cognitive stimulation, have shown in randomized trials to significantly improve the IQ of participating children. “Yet when the intervention stops, those gains go away,” says Boyce,
the Lisa and John Pritzker Distinguished Professor of Developmental and Behavioral Health. The research is proof positive of the critical need for, and effectiveness of, early and lasting enrichment, which he believes would be ideal by age 3.

In one of his own studies, Boyce and his colleagues put electroencephalogram (EEG) caps on 8- to 12-year-old kids from low-income and affluent families as they played a game. The EEG caps tracked the kids' brain activity while the game directed them to select a unique stimulus from a group of similar-looking stimuli. The researchers found fundamental differences in brain function. “The kids from poor families had lower IQs and less effective executive functioning, which takes place in the prefrontal part of the brain – things like working memory, semantic fluency, and cognitive flexibility, the capacity to readily switch tasks,” reports Boyce. All are essential for academic achievement and advancement.

Boyce points to a recent study in Nature Neuroscience showing that the further you go up the scale in parental education, the more folding – or cortical surface area – is evident in a child’s brain. Cortical surface area sets humans apart from other species; our brains fold inward to squeeze more surface area into our skulls. The kids with the better-educated moms had literally more brain in regions supporting language, reading, executive functions, and spatial skills. “These differences are the central nervous system underpinnings of growing up in poverty,” says Boyce. “It is especially important to understand that finding neurobiological differences among children from disadvantaged communities does not imply that the differences are genetic in origin. Rather, many or even most such socioeconomic disparities in brain structure and function are the direct consequences of early rearing in impoverished, chaotic, and stressful conditions.”

Chronic disease – which accounts for 70 percent of deaths in this country – is also deeply rooted in poverty. UCSF’s Center for Vulnerable Populations (CVP) is devoted to helping populations at risk for poor health and inadequate health care because of social vulnerabilities. Researchers at CVP report that chronic conditions are striking minority communities earlier and more often. Take diabetes: 10 years ago, one in 11 kids had prediabetes; now it's one in four. “If you look at minority populations, 50 percent of African American and a third of Latino children will develop diabetes in their lifetime. Those are staggering numbers, and if you look at the poor among them, they are even more so,” says Kirsten Bibbins-Domingo, PhD ’94, MD ’99, director of the CVP. “These diseases usually happen in middle age, but we are already seeing real chronic disease manifestations in people in their 20s, teens, and even younger.”

Poverty’s Path to Bad Health
Research forges a solid, convincing link between low socioeconomic status and bad health. Yet understanding how and why people in poverty are statistically at greater risk for disease is more complex. Diet and exercise play a big role in determining a person’s health status; however, research shows that health behaviors like these are largely driven by the context of where people live. Poor neighborhoods are more likely to have higher crime rates, lower-performing schools, and little access to healthy foods. “It’s difficult to exercise in an unsafe neighborhood, or to eat well in a neighborhood where healthy foods are either not sold or are more expensive than unhealthy options,” says Nancy Adler, PhD, director of UCSF’s Center for Health and Community. Transportation and time also factor into health behaviors. A person who has strung together three jobs to make ends meet for his or her family, and who must travel by bus to each job, likely does not have the luxury of time for exercise.

Then imagine layering on top of poverty a sick child. Take, for instance, a family with a child just diagnosed with severe asthma – a chronic condition commonly found in children living in areas exposed to high levels of automobile exhaust. “The mom may not have a job that lets her leave to take care of her child. She has to deal with health insurance, accessing specialists, and getting and affording medications,” says Anda Kuo, MD ’98, a resident alumna, and the founding director of UCSF’s Pediatric Leadership for the Underserved, a residency training program. “All of that is incredibly stressful, and we know that, ultimately, impoverished children with a chronic disease or cancer diagnosis face higher rates of morbidity and mortality than others.”
In fact, the sheer stress and adversity of poverty itself is perhaps its most toxic component, impacting multiple systems in the body. “We know that kids growing up in poverty are more exposed to toxins, noise, turmoil, and violence,” says Boyce. “These exposures damage the capacity of the brain to develop optimally.” They provoke the body to produce the hormone cortisol, which sets the body on high alert so that people can maximize their capacity to escape a threat. Put in evolutionary terms, this means that if you encounter a lion, your body releases cortisol so you can get away.

“Cortisol basically shuts down functions you don’t need in a moment of extreme stress, like reproduction or digestion. Your blood pressure goes up, it mobilizes glucose, so you have energy for the escape,” says Adler. That’s fine when you encounter a lion every once in a while. But when you encounter stress every day at home or work, it takes a toll.

People who have a continually heightened response to stress can acquire an allostatic load – wear and tear on the body caused by stress – that permanently throws off their endocrine system and causes it to overproduce cortisol. Their cortisol level goes up and doesn’t come down, putting them at lifelong risk of cardiovascular disease. Others exposed to constant stress have a “hypo-response,” a flattening effect, and they don’t produce cortisol even when it is needed, creating a heightened risk for autoimmune diseases like arthritis, explains Adler.

“Poverty gets under our skin and leads to biological changes that can last into adulthood, even when circumstances change, and, in some cases, affect the next generation through maternal health,” says Bibbins-Domingo. There is emerging evidence that the stresses of poverty could create a lasting effect through what are called epigenetic changes in how our genes are expressed, and that these effects may even happen in utero.

“So, cyclically, poverty leads to poor health and poor health leads to poverty,” says Bibbins-Domingo, who holds the Lee Goldman, MD, Endowed Chair in Medicine. “If that cycle happens across generations, then you are talking about major, seemingly intractable effects on communities living in poverty.”

**Dodging the Bullet**

How, then, does a clinician prevent or treat disease in poor patients if unstable housing, low-performing schools, and exposure to toxins and violence conspire to undermine their health? UCSF practitioners and researchers have long been developing programs and studies to circumvent the social determinants of health. “People ask, ‘What can a doctor do about homelessness?’” says King. “A lot, it turns out.” While King was chair of the Department of Medicine, physicians at San Francisco General Hospital (SFGH) took note that certain patients experience frequent hospitalizations. After a bit of investigation, they found that often these patients didn’t have stable housing in which to convalesce. This led SFGH to develop a respite-care program involving short-term housing for homeless persons who are either recovering from a hospitalization or receiving medical care for a condition that renders them too ill to live on the street or in a shelter.

Stuart Gansky, DrPH, director of UCSF’s Center to Address Disparities in Children’s Oral Health, has had great success in changing the standard of care for impoverished children at risk for dental disease. His group showed, in a randomized trial of poor children...
The Abecedarian Project was an early education program in North Carolina for children from infancy through age 5 who were at risk for developmental delays and school failure. The project’s long-term effects have revealed diminished signs of metabolic syndrome, in the form of lower blood pressure, lower blood sugar, decreased waist fat, and more normal cholesterol levels that together decrease the risks of heart disease, stroke, and diabetes. 

Source: Campbell, Heckman, et al.; Science, 2014

in San Francisco, that fluoride varnish, which is used routinely in Europe in older children, prevents cavities when applied twice a year to preschoolers’ teeth. It can be applied quickly, easily, and to great effect by pediatricians for families with no access to dental care. He points to cultural competence as the key to his study’s success. “In a related study, our medical anthropologists and social scientists held interviews to learn about the experience people had, what works and doesn’t work in the context of their lives,” recalls Gansky, who holds the John C. Greene Endowed Chair in Primary Care Dentistry. “We hired bicultural, bilingual people to whom patient families can relate.” Staff learned that many parents couldn’t bring their children to the clinic during the workweek because of work conflicts or distance. “We held follow-up visits on Saturdays or in evenings,” he reports. “We created playrooms for siblings. We paid for bus vouchers.”

Back to the Drawing Board

Gansky’s study came up with a viable, cheaper alternative than a trip to the dentist, but like all of these programs, it does not address the roots of poverty itself. Though the health care system alone can’t solve poverty, many practitioners and researchers, particularly in the arena of pediatrics, are trying to travel further upstream to intervene before deprivation-related illness sets in and wreaks havoc with families. In doing so, they are rethinking the scope of primary care, particularly in its earliest and most inclusive point of entry – pediatrics.

“First we need to throw out all our assumptions about what pediatricians do,” says Boyce, “particularly now that children can be immunized and have an ear infection treated at a Walmart.” Using community policing as a model, Boyce envisions child resource centers in every neighborhood where parents, who themselves may have been poorly parented, can get expert care and advice in how to break the cycle of adversity. “Could there be child resource centers where social work and primary education is done? Where pediatricians can collaborate with teachers, social workers, and parents?” asks Boyce. “It’s certainly a broader, better model than we have now.”

Adler is also considering ways to extend the reach of the pediatrician beyond the clinic doors. She is working with Laura Gottlieb, MD, MPH, and colleagues at UCSF Benioff Children’s Hospitals of San Francisco and Oakland and at SFGH to screen families for problems with housing, nutrition, violence, and schooling and to link them with needed services. As part of this effort, they are examining the impact on the child. Half the families are randomly assigned to receive a paper listing of resources that address their identified needs. The other half interact with a trained volunteer or community health worker, who helps link them to the services and follows up by phone. Preliminary findings are encouraging and suggest greater benefit for those who receive the active intervention.

“We insert someone in the system who flags issues for a pediatrician: ‘This is somebody who needs legal help, enrollment in food stamps,
“We know that, ultimately, impoverished children with a chronic disease or cancer diagnosis face higher rates of morbidity and mortality than others.” – Anda Kuo

housing,” says Adler. “The pediatricians can’t be responsible for all those things, but they can be a part of a system that connects families with resources.” Though her intervention is pediatric in focus, it is a multigenerational approach that addresses the family’s situation holistically.

The Center for Vulnerable Populations (CVP) is also engaging the passion and fury of adolescents and young adults to drive change in their own communities. The CVP has partnered with Youth Speaks and Youth Radio, powerful mouthpieces among San Francisco’s teens and young adults, to use video, radio, and the spoken word to relay messages about such perils as tobacco, e-cigarettes, and sugary, processed foods. These are messages delivered by youth, for youth, in ways that are more effective and less costly than the $245 billion spent on treating people with diabetes each year. CVP also led the development of San Francisco’s EatSF program, in partnership with the Department of Public Health, to distribute vouchers for fruits and vegetables in the city’s poorest communities. EatSF increases the purchasing power of people in these neighborhoods, allowing them to buy healthier food, which in turn stimulates vendors to stock such items.

Kuo is leading a charge to unite all of UCSF’s efforts to ensure that child wellness and equity are a reality – for all Bay Area children and their families – by developing a Child Health Equity Collective. Boyce, Adler, and Braveman – all three considered leading experts in their field – will be essential parts of the collective. “It will pull people out of silos – whether pediatrician, oncologist, internist, epidemiologist, or neurologist – to talk about how better to reach struggling families,” says Kuo. “I want to see the children of the Bay Area leading lives determined by their own efforts and talents, not the incomes of their parents. That is the essence of the American dream.”

**Why Now?**

Poverty and its effects on mental and physical health are the subtext of many of the year’s headlines, be they on stories about the Black Lives Matter movement, about rising levels of violent crime, or about efforts to establish a living wage. An expansion of Medicaid and an increase in the minimum wage were among the top recommendations of the Ferguson Commission report, compiled by a panel of experts to help heal the Missouri town torn by the fatal shooting of an unarmed black teen. The panel supported its recommendations with a chilling statistic: The average life expectancy in the mostly black Missouri suburb of Kinloch is more than three decades less than in the mostly white suburb of Wildwood.

Being able to quantify the biological wake of poverty across generations is a powerful tool. “When physicians are at the table framing these issues with health,” says Bibbins-Domingo, “that elevates the discussion from politics.” It also helps that physicians have come to the table with stronger evidence. “When people were talking about poverty and health or disease 25 years ago, I think they couldn’t say a lot about the mechanisms apart from obvious ones, like malnutrition and toxic exposures in the home or the neighborhood,” says Braveman. “Now we can talk about countless studies on the biologic mechanisms of the stress of always being on the edge of a cliff and barely holding on.”

But generating change will require more than convincing evidence, according to Adler. She believes we must shift the focus of health care away from how we treat disease to acknowledging why the disease happened in the first place. “The analogy I like to use is this: If you are hit by a truck, you are going to want to be treated at SFGH; it’s San Francisco’s only Level I trauma center,” she says. “But, in the end, your health is going to be more affected by the fact that you were hit by the truck than by how the health care system managed your care. Poverty is that truck.”
Remembering Nilani
May 18, 2008 – Aug. 3, 2015

She was a miracle worker, a sweetheart, a healer, a friend. She coaxed small, seriously ill patients out of their beds. She eased their anxieties before surgery. She let them dress her in a tutu or spray her with blue paint, just to put smiles on sad faces. She was Nilani, or Lani, the beloved service dog at UCSF Benioff Children’s Hospital San Francisco; Lani died this summer after five years of bringing love, laughs, cuddles, and comfort to young patients and their families.

The instant she walked into a patient’s room, Lani knew precisely what was needed – whether it was playing a game of fetch, climbing right up into the bed, or consoling a parent with a gentle nuzzle. As news of Lani’s passing spread, condolences and social media posts poured in, many from parents whose children had befriended Lani in their final days.

To learn more about Lani and the hospital’s Animal Assisted Therapy Program, visit bit.ly/ucsf-lani.

“May you find strength knowing how deeply she touched the lives of so many children and adults alike. We will miss you so dearly, Lani girl.”
“My son was among the first patient room visits Nilani made as a service dog for UCSF. Even if times were tough, seeing Nilani made him smile and forget some of the pain.”

“Lani gave big smiles to my child for almost four years. She will be missed, but I know she is playing ball with him in heaven.”
THE RIGHT DOSE

How pharmacy researchers are making medicine more precise.

by Koren Wetmore

In the pediatric bone marrow transplant clinic, pharmacist Janel Boyle's past and present collide.

She drifts past young patients — many of them infants and toddlers — and notes their beaming smiles and balding heads. Her gaze shifts to the parents, their expressions tense but hopeful.

The scene reminds her of her childhood, of time she spent in the hospital visiting her sister, Jenny, who at age 2 was diagnosed with acute promyelocytic leukemia. Boyle fights back tears as she recalls Jenny's suffering both during and long after years of chemotherapy and radiation treatments. Although her sister survived the cancer, she continues to this day to endure side effects caused by the very drugs used to treat her disease.

"Jenny developed metabolic syndrome, thyroid cancer, and cognitive issues. Even simple things, such as learning to balance her checkbook, were difficult," says Boyle, who holds a PharmD and a
Pharmacist Janel Boyle (far left), who is developing dosing models tailored for children, comforts a young patient with her mother in the infusion clinic at UCSF Benioff Children’s Hospital San Francisco. The clinic features a play area for siblings (right) so families can stay connected during treatment sessions.

Boyle considers this point as she examines the chart of a patient she met with recently. She first saw him several years ago, when he was 6 months old, underweight at just 14 pounds, and contending with kidney damage. He was scheduled to receive fludarabine, a drug used to enhance stem cell uptake, in preparation for a bone marrow transplant. He, too, had leukemia.

Just like Boyle’s sister, this baby had faced the risk of potential long-term side effects due to his treatment. However, his age, low weight, and impaired kidney function suggested a more immediate threat: If dosed according to the standard guidelines, which are based on adult data, he could be cured of his cancer only to die a few months later as a result of irreversible brain toxicity.

Based on a computer model that Boyle developed, the baby received half the recommended dose, to account for his age, weight, and kidney status. The result? A successful transplant with no toxic aftermath.

“This child was given an individualized dose, and three years later he came into the clinic a thriving toddler, with normal physical and social development and a full head of brown hair. Seeing and talking with him was by far the best part of my day,” Boyle says.

Her computer models, which calculate the dosage for individual patients, harness the power of pediatric cancer drugs while limiting their toxic effects. She’s one of several researchers at the UCSF School of Pharmacy who’s advancing precision medicine — a field UC San Francisco is helping to shape — by transforming the way drug dosing is determined.
"At the end of the day, there is a dose that is subtherapeutic, one that is therapeutic but not toxic, one that is therapeutic and toxic, and one that is flat-out toxic. So dosing is an integral component in being precise with one's medicine," says School of Pharmacy Dean Joseph Guglielmo, PharmD and a resident alumnus. "It's estimated that somewhere between 30 and 40 percent of the drugs people take do nothing for them. Yet people rarely consider whether their dose could be wrong."

If you receive the wrong dose or the wrong medication, your results could range from not getting better to feeling worse to even dying. According to the Food and Drug Administration (FDA), more than 700,000 people each year experience serious drug reactions, and more than 117,000 die from them.

By contrast, a more precise, individualized dose could boost a drug's effectiveness against your disease while reducing or eliminating any potential side effects.

DEMystifying dosing Each time you pop a pill or apply a medicine patch, you’re trusting a less-than-perfect dosing formula that’s based mainly on your age or weight. Meanwhile, other factors – such as your genetics, gender, lifestyle, diet, and even the supplements you take – can affect which drug you need, along with how much and how often you may need it. That's because those and other factors influence how much of a drug enters your bloodstream and how quickly it exits your body. This entry-exit balance, known as absorption and clearance, is what determines the amount of a drug in your blood at any given time. If the level goes too high, you risk side effects. Too low, and the drug fails to do its job.

At the heart of this balance are so-called membrane transporters – proteins and enzymes on the surface of cells in your intestines, liver, and kidneys – which grant or deny entrance to a drug. Genetic variations in these transporters can cause you to absorb more or less of a drug or to eliminate it so quickly that it never reaches a therapeutic level in your bloodstream.

For example, a common genetic variant in the liver transporter OATP1B1 slows its ability to clear the cholesterol-lowering statin drugs pravastatin (Pravachol), rosuvastatin (Crestor), and simvastatin (Zocor). This raises the amount of the statin circulating in the blood and can lead to muscle pain and even death. So if you need a statin drug, getting screened for this variant could help you avoid these risks by opting for a safer, more effective medication.

What you eat or drink can also interfere with these cellular gatekeepers. Simply downing a glass of grapefruit juice, for example, can wreak havoc with intestinal transporters and cause you to absorb too much of some statin drugs, increasing your risk of liver and kidney damage. That same glass of juice can cause the transporters to absorb less of other medications, such as the allergy medicine fexofenadine (Allegra), potentially reducing the drugs' effectiveness.

"Even dietary supplements can affect these transporters, as can lifestyle choices such as smoking," says Kathy Giacomini, PhD, a professor of bioengineering and therapeutic sciences and co-director of the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation. "Cigarette smoking is known to induce a drug-metabolizing enzyme. So for some drugs, smokers need a higher dose because they're inactivating it so quickly."

Different drugs when taken together can also battle it out at the cellular level. An elderly patient who has taken repaglinide (Prandin) for her type 2 diabetes for years without problems, for example, may suddenly develop headaches, nausea, and joint pain after another doctor prescribes cyclosporine, an immunosuppressant, to treat her rheumatoid arthritis.

Strangely, the side effects stem from the diabetes drug, not the new arthritis drug. "This happens because repaglinide enters the liver through a transporter that cyclosporine inhibits. So the diabetes medi-
Precise dosing will likely change the way you interact with your pharmacist. Rather than dashing out of the drugstore with a prescription and a list of potential side effects, you may chat about how to tailor your medication dosing to meet your specific needs.

“You might be told something like, ‘You’re about to go on this new medication, so we’re going to start you on 200 milligrams rather than 400 milligrams because, based on your genetics, we predict that you may absorb more,’” says Kathy Giacomini, PhD, co-director of the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation. “And then,” she continues, “they’ll monitor you. There will be more discussion and maybe even a follow-up visit.”

With your genetic information on file, your pharmacist might also be prompted to switch your medication because of potential, genetically linked side effects. Or the pharmacist may ask you about habits such as smoking and adjust your dosage based on your answer.

In short, your visit and your medicine will become much more personal.

cation has trouble clearing, which raises the drug’s level in her blood and causes side effects,” Giacomini explains.

Gender can also play a role in the dose you may need. Last year, for instance, the FDA cut the recommended dose of a popular sleep drug, zolpidem (Ambien), in half for women after studies showed that they clear zolpidem more slowly than men. This left women with more of the drug in their bodies the next morning, which could impair driving.

If your liver or kidneys are failing due to age- or disease-related changes, this, too, can affect which drug and dose you need.

With so many variables, choosing the best medication and dose can be a matter of trial and error – unless your doctor and pharmacist have tools to help factor all the variables into your prescription.

Fortunately, such tools are being developed today.

GETTING IT RIGHT

Researchers in the UCSF School of Pharmacy are working on the development of more precise dosing methods by building computer models based on real-world patient evidence. Although labor- and time-intensive, their work could one day result in personalized prescriptions calculated by software programs that account for each patient’s individual characteristics.

“It could be really personalized – how much you take, how frequently, and for how long,” says Rada Savic, PhD, an assistant professor at the School of Pharmacy. A specialist in pharmacometrics, she’s developed dosing models for drugs used to treat diabetes, tuberculosis, malaria, HIV, and cancer. “For some people, this could mean that taking half a typical dose four times a day works much better than the full dose twice a day.”

But building effective models requires data from across many patient populations to discover which factors matter for each medical condition and drug used to treat it. It can take years to gather enough data to identify how they impact dosing, drug levels, and patient outcomes. The models’ complex calculations must also be refined and then validated through clinical trials.

Savic’s team, in collaboration with Boyle, created a dosing model for busulfan, a drug used to enhance stem cell uptake during bone marrow transplants. It’s currently being validated in infants as young as 6 weeks old.

“Our model has worked unbelievably well in these little babies, where they are not dying of toxicity. When a new patient comes through, my heart races because I’m hoping the model does what we predicted. Every time it works, I do a little dance,” Boyle says.

While most UCSF dosing models are still being validated, some – such as Savic’s model for rifapentine, a drug used to treat latent TB – have been added to the FDA’s Guidance for Industry advisories.

InsightRX, a spin-off from Savic’s UCSF lab, is now helping put models into an easy, user-friendly format that busy pharmacists and clinicians will be more likely to use. The San Francisco start-up creates software solutions that allow users to enter a patient’s variables and receive drug and dose recommendations, while keeping the complex calculations in the background.

Currently being developed for a handful of drugs, the software will eventually be applied to a broad range of medications, says Boyle, who serves as a consultant to the company.

Although the initiative is still in its early stages, she predicts that more precise dosing will improve not only care for current patients, but also their lifelong outcomes. “We’re maximizing how well a drug can work in their bodies while limiting the terrible effects it might have on all their systems. So for children with cancer, it means they may not suffer negative effects in adulthood,” Boyle says. “They might be able to forget that they ever had leukemia.”

PHOTO: SUBJUG

Your Future Prescription

Precise dosing will likely change the way you interact with your pharmacist. Rather than dashing out of the drugstore with a prescription and a list of potential side effects, you may chat about how to tailor your medication dosing to meet your specific needs.

“You might be told something like, ‘You’re about to go on this new medication, so we’re going to start you on 200 milligrams rather than 400 milligrams because, based on your genetics, we predict that you may absorb more,’” says Kathy Giacomini, PhD, co-director of the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation. “And then,” she continues, “they’ll monitor you. There will be more discussion and maybe even a follow-up visit.”

With your genetic information on file, your pharmacist might also be prompted to switch your medication because of potential, genetically linked side effects. Or the pharmacist may ask you about habits such as smoking and adjust your dosage based on your answer.

In short, your visit and your medicine will become much more personal.
Behind makeshift orange fencing, the Ebola isolation unit in Bo, Sierra Leone, lies shrouded in a haze of smoke from the constant fires burning contaminated bedding and clothing. UC San Francisco physician Andrea Tenner, MD, MPH, looking like an astronaut in a head-to-toe protective suit, peers through foggy goggles as she reviews duty lists with local colleagues before entering the hot zone – the testing ward for patients with possible Ebola virus infection. She weaves her way through the labyrinth of protective barriers, ending up in the suspect ward, where patients who’ve exhibited Ebola symptoms anxiously await their test results.
FROM EARTHQUAKES TO EBOLA

UCSF’s history of disaster response dates back to the 1906 San Francisco earthquake. While the city was still wracked with aftershocks, the university set up improvised outdoor hospitals in Golden Gate Park to aid the sick and wounded, plus temporary kitchens to feed the public. With that pioneering spirit, UCSF also started the first dedicated AIDS treatment clinic in 1983, a time when much of the world remained silent in the face of the epidemic.

In the past 20 years, globalization and variations in international responses have brought about dramatic changes in the approach to humanitarian crises and to the actions volunteers can take, especially in foreign countries. Formerly, experts rushed in to deliver hands-on care, often without considering the impact their presence and eventual departure would have on ongoing projects in the field. While the motivation behind the aid was admirable, its benefits often fell short of the goal; once volunteers headed home, local staff often found it impractical to sustain the level of care the visitors provided.

Today, the goal for both researchers and clinicians is not to throw U.S. expertise at indigenous crises and other global health challenges, but to respond by reducing the burden of disease while also empowering local leaders, strengthening local health systems, and leaving behind a sustainable model.

Currently, more than 470 UCSF faculty members are conducting ongoing research and training projects in 135 countries around the world. Hundreds more, like Tenner, step in when their specific skills are needed, volunteering to work with in-country partners and collaborate with international nongovernmental organizations like Médecins Sans Frontières, the International Rescue Committee, and many others. These efforts not only provide expertise, training, and capital to resource-limited populations, but also give UCSF faculty and students a chance to gain experience working in challenging settings.

THE ESSENTIAL INGREDIENTS

No matter where or when a disaster or epidemic strikes, several factors are key to an effective response. Speed is one. UCSF Chancellor Sam Hawgood, MBBS, responded quickly in October 2014 to President Obama’s call for U.S. experts to help stem the Ebola epidemic in West Africa. He issued safety guidelines, coordinated training with federal agencies, and set up a vacation donation bank so qualified clinicians like Tenner could volunteer to go.

Flexibility is another key factor. “You can’t be a cowboy,” Tenner says of her experience in Sierra Leone, where she was unexpectedly asked to oversee three isolation units and coordinate patient triage. “Of course, this work is risky. But it’s a calculated risk. You have to do everything in your power to protect yourself and others. In a resource-limited environment, everyone has to do their part.”

In the Bay Area, Tenner is an assistant clinical professor of emergency medicine, director of the Department of Emergency Medicine’s Global Health Fellowship program, and an emergency physician at San Francisco General Hospital. Her training in infectious diseases and disaster preparedness primed her for the last-minute duty change and the tension of the hot zone. But, she adds, “You think you are ready, but every day brings something new. You do what you can with available resources, but in this environment, relieving pain and suffering is not always possible.”

Stamina, both physical and emotional, is also necessary. For example, those responding to the Ebola epidemic were directed to provide all care, from triage to treatment, without any direct patient contact. This “no-touch” policy was set after an unprecedented number of health care workers died from the disease. As well, wearing full protective gear is not tenable for long shifts and, as a result, explains Farrah Kashfipour, RN, MS ’14, “many patients die in pain, isolated from their families. It is the sad nature of the epidemic.” An alumna of the UCSF Global Health Sciences program, Kashfipour spent six weeks in Liberia providing patient care and training health care workers.

“No one wants this: not patients, not nurses, not doctors,” says Phuoc Le, MD, MPH, of the no-touch policy. Le, an assistant clinical professor of medicine and pediatrics, worked in Liberia at the height of the epidemic, unable to place a stethoscope on his patients’ chests, feel their
“You think you are ready, but every day brings something new. You do what you can with available resources, but in this environment, relieving pain and suffering is not always possible.”

– Andrea Tenner

abdomens for masses, or even shake their hands.

Additionally, demonstrating cultural sensitivity is critical. There is often tension between local customs – such as those obliging families to wash and prepare bodies for burial – and World Health Organization (WHO) infection-control guidelines. Balancing cultural sensitivity with disease containment isn’t always clear-cut – it’s individual to each situation. “How can you take the lessons learned from epidemics and disease response ... and apply that sustainably?” muses George Rutherford, director of UCSF’s Prevention and Public Health Group and the Salvatore Pablo Lucia Professor of Preventive Medicine.

And ensuring that staff and volunteers are adequately trained is perhaps most important of all. UCSF’s HEAL Initiative (Health, Equity, Action, and Leadership) arose from recognition of that need. Le and the other co-founders of HEAL, who met while responding to the 2010 earthquake in Haiti, quickly realized the need to educate those who wanted to help but were unprepared to work in resource-limited settings.

“Health professionals have no business going into disasters or health crises without experience or training in disaster response and knowledge of how to work in resource-constrained settings,” says Le. “A doctor who can only perform with all the latest equipment is useless in an emergency response. Before you set foot in a disaster, you need to have training so you don’t cause harm and can be impactful and effective.”

This type of training prepares one to expect the unexpected. Le, for example, was asked in Haiti to coordinate patient care among 10 hospitals; it wasn’t what he’d anticipated doing, but it was what needed to be done. “Contributing to a direct need ... was extremely rewarding,” Le says. He also made house calls, an activity now embodied in HEAL’s philosophy of actively bringing care to the patient rather than waiting passively at the hospital.

The World Over

UCSF’s global disaster and medical response efforts focus on sustainability and cultural awareness, training local staff, strengthening existing health systems, and doing it all with sensitivity for local customs. Here is a sample of programs that further those goals:

- **Global Health Sciences**, established in 2003, was the first international research and service institute of its kind in the U.S.; it offers graduate and fellowship programs like the two-year HEAL Initiative, continuing education programs like Global Health Bootcamp, and an annual Global Health Summit.

- **Global Health-Hospital Medicine Fellowship**, a two-year program, offers training in teaching skills, quality improvement, patient safety, and systems improvement in resource-limited settings.

- **School of Nursing Center for Global Health** offers graduate coursework and a fellowship program, and supports research and medical response projects.

- **Institute for Global Emergency Care**, a collaboration between UCSF, the University of Cape Town, and Stellenbosch University in South Africa, advances emergency care in sub-Saharan Africa and strengthens health systems to increase their ability to respond to disasters.

- **Global Health and Disaster Medicine Fellowships**, Department of Emergency Medicine, offers one- and two-year programs in emergency response and response-system development.

Many domestic programs keep an eye on world events, too. A case in point is the California Poison Control System (CPCS), a service of the UCSF School of Pharmacy. Primarily a free statewide hotline for Californians exposed to poisons or toxins, the program shifts gears during public events involving exposure to nuclear, chemical, biological, or other noxious agents. For example, after the 2011 tsunami in Japan, the CPCS fielded over 150 calls from people concerned about radiation emissions from the Fukushima Daiichi nuclear plant.
ONE SIZE DOESN’T FIT ALL

Unlike Haiti and West Africa, some places have an established medical infrastructure and prefer not to have an influx of foreigners descending upon the chaos. The April 2015 earthquake in Nepal, for example, called for a different response.

It was 3 a.m. on April 25 when Nepal native, Bibhav Acharya, MD, a UCSF assistant professor of psychiatry, learned that a 7.8-magnitude earthquake had hit Nepal’s capital, Kathmandu. Acharya was visiting his brother in Boston and was up with jet lag, checking email, when he saw news of the quake. His first concern was for family members still in Nepal. For several hours, he and his brother tried desperately to reach their parents, but phone lines were dead or jammed and online access was down. Five hours later, they finally talked to their family and learned they were safe.

Then Acharya sprang into action – but not by hopping on a plane to Nepal. “The first impulse for most health professionals is an emotional one. You feel like you want to go there,” says Acharya. “Nepal didn’t need experts to fly in. Yes, hospitals were damaged – even providing care in tents. But they had trained staff and a supply chain. Instead of experts, they needed resources.” International organizations were mobilizing, but most were focused on Kathmandu, even though the rural areas were the hardest hit.

So Acharya and his brother launched a campaign on the crowdfunding website Indiegogo, setting a goal of $20,000. The response was quick and surprising; in just two weeks, they raised over $1 million. As a co-founder of two Nepali nonprofits, Acharya knew how to get the funds to the rural communities that larger charities might overlook. He also developed a mental health training curriculum and translated WHO protocols for responding to mass fatalities into Nepali and posted them online. The resources are now being used to train clinicians in Nepal. In addition, Acharya and his colleagues are working with WHO to develop management supervisory plans for doctors in the earthquake-affected areas. “If you send a doctor like me in for a few weeks, who takes over my case load when I leave? Focusing on training and capacity-building is significantly more important than a shortsighted, time-limited emergency response.”

HELPING FROM HOME

Back on campus, UCSF takes the findings from these projects and examines how to respond more safely and effectively. Robyn Gershon, MHS, DrPH, researches occupational and environmental health and safety in high-risk work situations and focuses on assessment and risk management in crisis situations. For example, she designed and conducted the largest human factors analysis of a high-rise evacuation, evaluating the 9/11 World Trade Center disaster. Not surprisingly, she found that organizations which actively promote workplace safety and preparedness produce a workforce that is able to react more quickly and calmly during evacuations due to disasters. Her conclusions contributed to critical revisions in New York’s high-rise fire-safety laws.

And as a capstone project for her degree in global health sciences, Liza Dernehl, MS ’15, studied health care workers returning from the Ebola outbreak in Sierra Leone.
“Focusing on training and capacity-building is significantly more important than a shortsighted, time-limited emergency response.”

– Bibhav Acharya

and Liberia. She found that the stigma of Ebola, the frustration of working in a resource-limited environment, and the inability to provide basic life-sustaining care, brought on periods of depression and anxiety for returnees. “Complex humanitarian crises and mass-casualty scenarios bring on stressors for health workers,” says Dernehl. The solution, she notes, is through predeployment preparation, strong psychosocial support, and improved public understanding about the nature of outbreaks. “We can provide psychosocial support and preparation for responders, but unfortunately,” she adds, “we are far from achieving public understanding of epidemics.”

A committee co-chaired by George Rutherford and Associate Chancellor Theresa O’Brien, PhD ’07, which was formed to develop guidelines for the Ebola response, is reviewing the lessons learned and determining the need for a standing committee to facilitate rapid, coordinated responses.

“What should our institutional posture be in relation to health crises? UCSF has a duty to protect the people of California,” explains Rutherford. “You can either solve an outbreak here or solve it there. We chose to solve Ebola there to protect the public and preserve safety. These crises will continue to happen, and hopefully our response will become part of our regular course of business, while we remain true to our mission of reducing the burden of disease and easing health disparities around the world.”
Fresh Vision for Mental Health Inspires Transformative Gift to UCSF

A new, state-of-the-art mental health building encompassing clinical care, research, and training will soon rise near UCSF’s Mission Bay campus, thanks to a generous $50-million gift from an anonymous donor. The facility’s centerpiece will be an innovative child, teen, and family center that will bring together a wide-ranging set of programs focused on better understanding disorder prevention and treatment of children, adolescents, and young adults.

Scheduled for a spring 2019 opening, the 140,000-square-foot structure will be within walking distance of UCSF Benioff Children’s Hospital San Francisco and UCSF’s neuroscience research community. It will represent the realization of a long-standing goal at UCSF: to respond to the pressing needs of families in the region for superlative mental health care by employing a 21st-century vision of psychiatry that embraces and translates the latest research advances in neuroscience, genomics, and the social sciences.

The building will house UCSF’s Department of Psychiatry as well as outpatient services and so-called dry lab research space. Most important, the facility will bring together clinicians and researchers from multiple disciplines to address the most important problems in psychiatry, psychology, and related fields – prevention and community outreach, the integration of pediatric and adult medicine with psychiatry care, and the development of novel and improved treatments.

Matthew State, MD, PhD, the Oberndorf Family Distinguished Professor and chair of psychiatry at UCSF, expressed gratitude for the donation and said unifying diverse disciplines under one roof embodies the growing recognition that a holistic approach to medical and psychiatric care is best for patients.

“There have been artificial separations between medicine, pediatrics, neurology, and psychiatry for far too long. In addition to leading to poorer outcomes and higher costs, these separations have helped foster the stigma surrounding mental illness,” says State, a renowned researcher on neurodevelopmental disorders, especially autism spectrum disorder. “With this landmark gift, we are going to break down these barriers, improve the care of our patients and their families, and help erase that stigma.”

“This visionary gift, in addition to enabling us to offer state-of-the-art mental health care, will leverage UCSF’s pre-eminent basic and clinical research programs in pediatrics and adolescent medicine to benefit the mental health of children and families,” says Sam Hawgood, MBBS, UCSF chancellor and the Arthur and Toni Rembe Rock Distinguished Professor. “Public service also is one of our core missions. This facility will help us bring the benefits of UCSF’s world-class research and clinical care to the most vulnerable populations in our region.”

UCSF’s Developmental Medicine and Adolescent and Young Adult Medicine divisions, both part of the Department of Pediatrics, also will be located in the building, allowing for the full integration of pediatric and mental health care.
Alumni Hub

UCSF Alumni Shine at 2015 Reunion

Everyone says UCSF Alumni Weekend gets better each year, and the numbers confirm it. With nearly 2,000 alumni and friends enjoying a multitude of professional and social events, alumni attendance was up 32 percent from 2012, when the all-school reunion premiered.

“Our alumni take a lot of pride in the quality of their UCSF education, and they come back with a very positive feeling,” says Don Kishi, PharmD ’68, a professor of clinical pharmacy and president of the Alumni Association of UCSF. “Having all the alumni meet together, rather than separately by school, fosters greater collegiality and supports the growing trend toward interprofessional education, research, and practice.”

In attendance were many of the 150 outstanding living alumni who were honored with the UCSF 150th Anniversary Alumni Excellence Awards. The honorees – several of whom are profiled in the following pages – were recognized for their achievements in education, patient care, research, service, and business and industry. Please visit ucsfalumni.org/award150 for a complete list of winners.

Book your room now for Alumni Weekend 2016, April 8-9, 2016, at San Francisco’s Fairmont Hotel.
Call 800/441-1414 or visit ucsfalumni.org/aw for more details.
Cynthia Brattesani was elected graduating speaker by her UCSF graduating class and won the Dean’s Citation Award from then-Dentistry Dean John Greene, DMD, MPH. She’s been nationally recognized as one of the Top 25 Women in Dentistry (Dental Products Report, 2014) and as an Outstanding New Dentist Leader (American Dental Association, 1996), to name just some of her honors.

But when she learned of her UCSF Alumni Excellence Award, she got downright teary. “I’m so proud to tell my patients that I’m a UCSF grad,” she says.

WHAT ABOUT ME?: Brattesani’s brother grew up wanting to be a dentist, and when they were kids, he told her she could be his assistant. That was what most dental practices looked like in the early ’70s, but before long, she decided she’d be a dentist, too.

“I had my eye on UCSF as far back as I can remember,” Brattesani says. “I wanted to be a part of that big, important place.”

LONGING TO BELONG: Being an active part of her family, her city, her school, and her profession is a big motivator for Brattesani. She was born and raised in San Francisco by Italian parents, both of whom were brought to California as children by parents looking for a better life. With fluency in Italian and dual citizenship, Brattesani travels to Tuscany every summer to visit family, friends, and the Italian culture she loves.

“My parents instilled in me a strong work ethic,” she says. A high-energy individual who maintains a bustling private practice on Union Street, she juggles patients, professional conferences, seminars, lectures, and leadership activities with family life, including her Italian-born husband and 17-year-old son.

CORE VALUES: Reminiscing about her UCSF education, Brattesani remembers the day one of her teachers said, “It’s your profession now,” and that really stuck. She got involved in association activities while still in school and at age 33 was elected president of the San Francisco Dental Society. She continues to be active with the California and American Dental Associations.

She believes that dentists treat patients, not teeth, and is an early adopter of new technologies – like CAD/CAM, digital X-rays, fluorescence, and 3-D imaging – anything that can reduce radiation exposure, optimize the patient experience, and increase quality of care.

“I’m passionate about never wanting my business or my profession to stagnate,” she says. “I want to make it the best it can be.”

UCSF ALUMNI IN ACTION

Of students in the School of Dentistry Class of 2018, 60 percent are under-represented minorities.

Nelson Artiga-Diaz, DDS ’75, MPH, UCSF health sciences clinical professor emeritus, played a key role in building the school’s externship program, which still provides low-cost treatment to thousands of underserved patients in community clinics throughout Northern California.
“What I discovered was that I loved dental hygiene. I found out that teeth are fascinating.”

“As soon as I got to San Francisco, I was hooked,” says William Metzler, who first visited the city in 1966 during a brief stop on his way to Army service in Vietnam. Not long after his discharge, he returned to San Francisco and stayed for nearly 50 years.

Metzler attended City College of San Francisco on the GI Bill and discovered he had a deep interest in biology. He saw dental hygiene as a way to get his foot in the door of UCSF’s research labs. “What I discovered was that I loved dental hygiene,” he says. “I found out that teeth are fascinating.”

**A CLOSE COHORT:** Metzler was the first man in UCSF’s dental hygiene program, but he felt right at home with his cohort of 22 women, many of whom, like him, were a bit older than typical college students.

“I enjoyed my time at UCSF very much,” he says. “I was in a wonderful class, and the teachers were terrific, especially Jean Poupard [BS ’59], who was head of the program for many years.”

He meets his classmates regularly at their self-organized reunions and saw about 10 of them at the Alumni Excellence Awards ceremony, where he was deeply moved to be honored. “I was flabbergasted,” he says.

**LIFELONG LOYALTY:** Metzler attended classes while working his way up at a Financial District restaurant, from dishwasher to co-owner of that establishment and two others. When he graduated, he devoted himself to his dental hygiene career, working in the same Noe Valley dental practice for 25 years with a staff and patients he adored.

He admires one colleague in particular: His wife of nearly 30 years, Barbara, worked as a dental hygienist in the same office. They retired together in 2002 and moved to the Sacramento Delta, where he stays busy playing golf and serving as a librarian in a community library.

He also is secretary-treasurer and webmaster of the 5th Battalion, 60th Infantry Association, a group of nearly 1,000 Vietnam veterans. The association gathers every other year for a chance to catch up and talk about their lives, then and now.

“It’s incredibly powerful to hear these guys who served together speak,” says Metzler. “We are bonded for life through our shared experiences.”
Lynn Goldman has been a trailblazer in a field that didn’t even exist when she was in college or medical school. When she returned to UCSF in May to receive her Alumni Excellence Award, she couldn’t help but notice that many of the faculty presentations focused on her chosen field of public health and prevention.

PASSION FOR PREVENTION:
Since 1993, the educator, epidemiologist, pediatrician, and former Environmental Protection Agency (EPA) regulator has worked in the heart of the nation’s capital. Her career vision, she says, was sparked by the Berkeley Free Clinic (still in operation after 46 years), where she worked her way up from volunteer to paid administrator during her UC Berkeley undergraduate years.

“It was frustrating that our patients kept coming back because we weren’t treating the upstream causes of their problems,” she says. “I could see the connection between their poor health and their environment, and that inspired me to explore prevention and the social determinants of health.”

ATYPICAL CANDIDATE: Goldman chased her multitude of interests in math, conservation, environmental health, and biochemistry through her bachelor’s degree in environmental health and her master’s in public health from Johns Hopkins. She was among the first to graduate from UCSF’s joint medical program with UC Berkeley, which confers both master’s and MD degrees in five years.

“UCSF is not a cookie-cutter school,” Goldman says. “I didn’t look like your typical premed student, so many schools wouldn’t even interview me. But UCSF has always been willing to look for special things that people can contribute.”

PROTECTING OUR RESOURCES:
Her own key contribution, she says, was championing the Food Quality Protection Act of 1996 during her five-year tenure at the EPA. It was the first national environmental statute to regulate pesticides used on foods and to establish special protections for babies and infants.

“The law profoundly changed the pesticide industry,” Goldman says. “At the time, I felt a huge responsibility to the American people to keep our food, water, and air safe and clean.” She was elected to the National Academy of Medicine (formerly Institute of Medicine) in 2007 and joined George Washington University as dean of public health in 2010.

“When I came back for Alumni Weekend, it was wonderful to see how Mission Bay has evolved,” she says. “From the perspective of someone who was here four decades ago, it’s unbelievable how all these fabulous partnerships have benefited education and health care at UCSF.”
Tino Bernadett grew up in Chico, Calif., where his Mexican-born father was the only Spanish-speaking family doctor in town. Tino describes Faustino Sr. as one of his heroes, a man completely dedicated to serving others. As a boy of 14, Bernadett witnessed his first surgery. While visiting the small Mexican village of Norogachi with his father, who provided volunteer medical services there for two weeks each year, he watched his dad remove a large nail from a man’s foot. “The patient was eternally grateful,” Bernadett says, “and I was hooked on medicine.”

IN CHARGE OF A LIFE: He completed his undergraduate degree at UC Davis before arriving at UCSF, where he became fascinated with the physiology of anesthesia. “You take a person, you put them to sleep, and then you bring them back to life,” he says. “You are in charge of their life.”

Bernadett practiced as an anesthesiologist and later as a pain management expert. “There are many different ways to be humanitarian,” he explains. “For me, it was important to give back to my community. The specialty I chose gave me the best opportunity to do that.”

A LIFE OF SERVICE: Modeling his values on another of his heroes, Cesar Chavez, Bernadett believes in giving back to his community, including his alma mater. At UCSF, he supports the Program in Medical Education for the Urban Underserved (PRIME-US); the endowed UCSF student scholarships he created with his wife, Martha Molina Bernadett, MD; and the endowed UCSF Faustino and Martha Molina Bernadett Presidential Chair for Medical Education, a gift matched by the UC Office of the President.

Bernadett was recognized with the UCSF Alumni Excellence Award this year, and he and Martha also received the 2015 California Conference for Equality and Justice Humanitarian Award for their lifelong commitment to humanity and social justice. “Most of our country does OK,” he says, “but 10 to 15 percent of the population lives in less fortunate conditions. Drive through East Los Angeles, and it’s hard to believe what you see.”
Gene O’Connell followed an unconventional career path, from being a single mom taking courses at City College of San Francisco to being the first woman and first nurse to serve as CEO of San Francisco General Hospital – always approaching her work through the lens of her decades-long practice of Buddhism.

“UCSF gave me the knowledge to do my work, and Buddhism gave me the strength,” she says.

After earning her associate’s degree, O’Connell worked at UCSF as a gynecologic oncology nurse, but while on a temporary assignment at San Francisco General Hospital (SFGH), she decided to stay there for good.

“I realized that San Francisco General was where I belonged,” she says. “I saw so much need, so many opportunities to apply what I’d learned.”

**RISING THROUGH THE RANKS:** O’Connell continued to work full time while she pursued her bachelor’s and master’s degrees. “Being able to go to UCSF was like going to the Emerald City,” she says. “I got the best education imaginable.”

She made strong connections around the hospital and soaked up knowledge at every turn. Her efforts were noticed, and she held a succession of roles before landing the CEO position.

**NURSE/BUDDHIST/CEO:** In Buddhism, O’Connell finds a supportive community whose principles she tries to apply in her daily life.

“Valuing the individual helped me a lot in dealing with the politics of being CEO,” she says. “Caring deeply for patients also guided my decisions. In that sense, my nursing background was the foundation for my success as CEO.”

When the city passed a $900-million bond in 2008 for badly needed refurbishments at SFGH, O’Connell felt she’d achieved her goals and so retired after a 35-year health care career.

**STAYING CONNECTED:** On winning the Alumni Excellence Award, O’Connell says she’s proud to be counted among a distinguished group of graduates, especially the 25 nurses with whom she shared the honor.

In retirement, she remains involved with UCSF, helping train the next generation of nurses. “I want to let them know that I struggled, but I graduated and thrived – and they can too.”

---

**GENE O’CONNELL,**
**RN, BS ’87, MS ’89**

**Hometown:** Boston, Mass.

**Now:** Corte Madera, Calif.

**Position:** Associate clinical professor, UCSF School of Nursing; member, Marin General Hospital Board of Directors

**Hobbies:** Yoga, Buddhist practice, community service, spending time with her five grandchildren

---

**UCSF ALUMNI IN ACTION**

Nursing is UCSF’s most popular major – chosen by 9,203 alumni over the years.

Gail Perin, RN, MS ’69, followed her mother’s footsteps into nursing and began her career as a pediatric oncology nurse in the UCSF Department of Pediatrics. She was a pioneer in the field, becoming the first nurse specialist on the UCSF pediatric oncology team and advocating, long before the advent of hospice care, for dying at home.
“I was interested in helping families learn prevention and wellness.”

From the age of 15, Michele Rigsby Pauley knew she wanted to find a career working with kids. If she imagined making a difference in young lives, that dream has certainly been realized. She has influenced some 600,000 children and their parents through Cedars-Sinai’s Community Outreach Assistance for Children’s Health (COACH) for Kids and Their Families, a mobile clinic for underserved Los Angeles communities.

PURSUING PREVENTION: She earned her RN degree at the University of San Francisco, then worked in UCSF Medical Center’s pediatric ward. “After about five years, I realized I was interested in helping families learn prevention and wellness,” she says. A nurse practitioner role was a good fit for what she wanted to accomplish. She earned her master’s degree from UCSF in 1990 and certification as a pediatric nurse practitioner (PNP) soon after.

“I had a great experience at UCSF and felt well prepared upon graduation,” she says. She has fond memories of Pat Jackson Allen, RN, MS ’69, former director of the PNP program and recipient of the 2015 Jane Norbeck Distinguished Alumni Award. So at Alumni Weekend, when Rigsby Pauley received her Alumni Excellence Award, she also had a chance to reconnect with Allen. “It was a surprise and an honor to receive the recognition,” she says. “And Alumni Weekend was fabulous, especially reminiscing with Pat.”

HEALTH ON THE GO: One of the first nurse practitioners at Cedars-Sinai just as the role was catching on in Southern California, Pauley worked in a pediatric clinic, seeing patients and training medical students and residents. Mobile clinics also were catching on, and she was asked to help launch COACH for Kids. She continued as a nurse practitioner when the program was founded in 1994 and has been director since 1996.

The program’s initial staff of five had a lot to learn. Many of their patients were homeless, lacked transportation, or had no money to pay for needed prescriptions.

COACH began stocking its own medications and added a social worker, dental health services, and nutrition counseling. Rigsby Pauley now oversees two mobile units and 22 staff members, often serving on community task forces and working at local health fairs.

“I need to be knowledgeable about all the issues that affect health in these neighborhoods,” she says. “These families get to know us and we get to know them, so trust is an important element of COACH’s success.”

MICHIE RIGSBY PAULEY, RN, MSN ’90
Hometown: Los Angeles, Calif.
Now: Los Angeles, Calif.
Position: Program director, COACH for Kids and Their Families, Cedars-Sinai Medical Center
Hobbies: Gardening, historical travel, community events

PHOTOS: ELENA GRAHAM
JOYCE YU-CHIA LEE, PHARM.D ’06
Hometown: Taipei, Taiwan
Now: Singapore
Position: Associate professor of pharmacy and clinical pharmacist, ambulatory care, National University of Singapore
Hobbies: Traveling in Asia, spending time with her husband and friends

Born in Taiwan and raised in Japan, Joyce Lee immigrated to the U.S. with her family when she was 13 years old. Just one year after earning her PharmD, she had the opportunity to return to Asia and is now bringing the innovative care she learned at UCSF to patients in Singapore.

UCSF NEIGHBORS: In high school, Lee thought she might become a journalist, but a chance encounter changed her mind.

“One day the neighbor’s dog jumped over our back fence,” Lee says. While looking for the dog’s owner, her mother met neighbors Kevin Mark, PharmD ’94, and Phyllis Mark, PharmD ’93, who were pharmacists and UCSF alumni. The Marks told Lee about their lives as pharmacists and their educational experiences at UCSF, setting her on a new path.

FROM SF TO SINGAPORE: While earning her undergraduate degree at UC Davis, Lee worked as a pharmacy technician at Rite Aid. She was set to continue retail pharmacy work but, through her experience at UCSF, discovered she wanted a different type of interaction with patients. “UCSF’s curriculum is very hands-on,” she says. “We learned how to have a personal touch. I realized that my real passion is helping people with chronic illnesses.” When she learned that the National University of Singapore was recruiting American-trained pharmacists, she decided to take the leap. Now Lee heads six clinics and trains pharmacists to assist patients with chronic disorders. She also helped establish the university’s new PharmD program and the first ambulatory care residency program in Asia.

A MATCH MADE AT UCSF: In August, Lee married Alexandre Chan, PharmD, resident alumnus, MPH, whom she first met at UCSF. He is her colleague at National University of Singapore, as well as an oncology pharmacy specialist at National Cancer Centre Singapore.

At age 35, Lee was one of the youngest UCSF Alumni Excellence awardees and among those who traveled the farthest to attend the event. She says the best part of the experience was accepting the award alongside Lisa Kroon, PharmD, resident alumna, and chair of UCSF’s Department of Clinical Pharmacy.

“She was a kind and encouraging teacher who always reminded us to put ourselves in our patients’ shoes,” Lee says. “She was one of the UCSF professors who made me who I am today.”
“It doesn’t seem like work to me. I do it because I get to help people.”

Ken Schell’s initial reaction upon learning he’d been chosen for a UCSF Alumni Excellence Award was that someone was pulling his leg. “I thought my classmates were pranking me. I can think of at least two dozen people who deserve the honor more than I do,” he says.

Being honored for his work is like icing on the cake: “When I reflect on my professional years, it doesn’t seem like work to me,” he says. “I do it because I get to help people.”

INSPIRED BY BIOLOGY: Schell’s lifelong interest in science led him to study biology at UC San Diego, after which he worked in an immunology research lab at the Salk Institute. When two separate colleagues inspired him to check out UCSF School of Pharmacy, he paid a visit; in a matter of hours he knew the program was right for him.

His classmates, for whom he has high praise, elected him class and student body president. He says their camaraderie was fostered by the outstanding faculty.

DOING IT RIGHT: Schell’s first job was at Rady Children’s Hospital in San Diego, where he eventually became chief of pharmacy.

He credits UCSF with instilling in him a patient-centered professionalism that has molded his three decades as a pharmacist, educator, and leader.

“I got so much out of my years at UCSF,” he says. “Being in that amazing environment gave me the skill set to do what I do today.”

One year ago, Schell was appointed director of pharmacy at Sharp Grossmont Hospital. He continues to educate pharmacists-in-training, including mentoring undergraduates. Communication, he believes, is essential to success.

“When I started at Sharp, I met with each employee to let them know that my job was to help them obtain the tools they need to do their work,” he says. “If I’m doing my job right, my staff is happy, and our patients are getting the best care possible.”

UCSF ALUMNI IN ACTION

In the 2014-15 fiscal year, School of Pharmacy alumni and friends made donations totaling $5.7 million to UCSF.

John Young, BS ’54, has continually supported the School of Pharmacy, including making a planned gift in the form of a charitable IRA rollover. Young credits UCSF with helping him build a 44-year career that spanned work in small-town drugstores, major chains, and top executive positions.

Kenneth Schell, PHARMD ’84

Hometown: New Shrewsbury, N.J.

Now: Vista, Calif.

Position: Director of pharmacy, Sharp Grossmont Hospital; clinical professor, UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences

Hobbies: Science fiction; model trains; exercise; fencing; hanging out with his wife, Janice
NAPOLEONE FERRARA, MD, Postdoctoral Alumnus

UCSF Lab: Reproductive Endocrinology Center
Hometown: Catania, Italy
Now: San Diego, Calif.
Position: Senior deputy director for basic science, UC San Diego Moores Cancer Center; Distinguished Professor of Pathology, UC San Diego School of Medicine
Hobbies: Motorcycles, photography, studying ancient history

Napoleone Ferrara has drawn inspiration from many medical mentors throughout his career, but his first influence was his maternal grandfather, a science teacher in Catania, Sicily. Growing up there, the young Ferrara was fascinated by his grandfather’s house full of books on the natural sciences.

Following his gut as well as his deep scientific curiosity, Ferrara isolated some enigmatic follicular cells in the pituitary gland. He discovered that the cells produce a master regulator of angiogenesis, or blood vessel growth. His discovery of vascular endothelial growth factor would touch millions of lives.

NEW THERAPIES: In 1988, Ferrara joined Genentech and worked his way from fellow to senior scientist over 24 years. In the process, he developed ranibizumab, which has helped prevent blindness from age-related macular degeneration in half a million people worldwide. He also developed bevacizumab, used to treat colon cancer and other cancers in hundreds of thousands of patients.

“Some very fortunate circumstances brought me to the university,” says Ferrara, who calls UCSF one of the most prestigious institutions in the world. “UCSF is a great place for exploration, where you can follow your gut and discover possibilities with many collaborators.”

"These disorders have striking similarities, relying on the same mediator, the same types of molecules,” Ferrara says. He continues his research on the regulation of angiogenesis and potential clinical applications at UC San Diego, side by side with the many young scientists he now mentors.

ALL IN THE FAMILY: Ferrara has received numerous awards, including the inaugural Breakthrough Prize in Life Sciences in 2013 and the prestigious Lasker-DeBakey Clinical Medical Research Award in 2010.

However, the Alumni Excellence Award holds a special place.

“I was honored to be selected,” he says. “UCSF is where my work began, and it’s a privilege to be a part of its alumni family.”

UCSF ALUMNI IN ACTION

Of UCSF’s 60,219 alumni, 9,173 are current, former, or volunteer faculty members.

Erik Ullian, PhD ’97, UCSF associate professor of ophthalmology, was awarded funding this year from the Paul G. Allen Family Foundation to investigate how to grow mature human brain cells in the laboratory. Ullian will collaborate with David Rowitch, MD, PhD, UCSF professor of pediatrics.
“Once you’re part of UCSF, you never really leave.”

Although technically retired, Nancy Byl stays active, teaching at UCSF, caring for patients, doing research, serving on medical boards, and traveling around the world for bicycle tours, most recently in France and Sicily. She dearly values her mobility, having spent decades as a physical therapist helping people recover from impairments caused by aging, injury, and illness.

“I’ve taught people to support and stabilize their bodies and to stay healthy so they can enjoy life to the maximum,” she says. “And I try to do that too.”

**COMMITMENT TO HER CRAFT:**
Inspired by a volunteer stint at Sacramento’s Mercy General Hospital while in high school, Byl earned a bachelor’s degree in physical therapy from UCSF. After working at hospitals in Oakland and Stockton, she earned a master’s degree in public health from UC Berkeley.

Byl’s commitment to reach beyond the clinic to do research, teaching, and community service motivated her – after practicing for 20 years – to earn a PhD from UC Berkeley and San Francisco State University’s Joint Program in Special Education. She later became chair of the UCSF Department of Physical Therapy and Rehabilitation Science.

**THE FUTURE OF MOBILITY:**
Byl’s work focuses on understanding neuroplasticity and retraining the nervous system following Parkinson’s disease, stroke, and spinal injuries, as well as disabilities associated with focal hand dystonia in musicians. She has also tested new assistive technologies that increase strength and mobility, from bodyweight-supported treadmills to wearable robotics.

“A lot of exciting things are happening with rehabilitation robotics,” Byl says. “Imagery and virtual reality techniques can help a patient’s brain relearn tasks. Then we can use assistive technologies to help them become ambulatory.” Online consultations also are becoming more feasible, she adds, as wireless technologies allow therapists to monitor patients remotely, minimizing in-person visits and reducing costs.

**UCSF FOR LIFE:**
UCSF honored Byl’s many accomplishments with the Alumni Excellence Award. Her husband, UCSF head and neck surgeon Frederick Byl, MD ’64, accompanied her to the ceremony. The couple has been associated with UCSF for more than 50 years. Two of their three children, plus two sons-in-law and a daughter-in-law, are UC graduates.

“The university has been very good to me – as a student, researcher, department chair, and now as an emeritus professor,” she says. “Once you’re part of UCSF, you never really leave.”

---

**NANCY NIES BYL, BS ’63, MPH, PHD**

**UCSF Graduate Program:** Physical Therapy  
**Hometown:** Sacramento, Calif.  
**Now:** Oakland, Calif.  
**Position:** Professor and chair emerita, UCSF Department of Physical Therapy and Rehabilitation Science  
**Hobbies:** Antique cars, tennis, skiing, cycling
The Big Cheese

Walking through San Francisco’s Ferry Plaza Farmers Market on a Saturday, you wouldn’t think it unusual to run into your doctor sniffing peaches, eyeing lettuces, and squeezing tomatoes – though catching your physician selling cheese might come as a surprise. Not, however, if he’s David Jablons, MD, who leads a thriving research lab that develops novel therapies for patients with lung cancer, mesothelioma, and other thoracic malignancies. In 2003, after years of dreaming about farming in West Marin, the UCSF professor and chief of general thoracic surgery and his wife, Tamara Hicks, bought a 160-acre farm in Tomales, Calif., and Toluna Farms was born. Sheep and goats now roam the former cattle ranch, and their Tomales Farmstead Creamery produces award-winning cheeses.
Spread the cheer!

From tackling the toughest cancers to helping patients beat the odds like never before, there’s no place like UCSF.

This season of giving, consider a gift in tribute to the people of UCSF, whether a caregiver who touched your life or a professor or mentor who inspired your passion for health and wellness.

To make your gift, please use the attached envelope or visit makeagift.ucsf.edu/magazine
A young patient being treated for leukemia at UCSF Benioff Children’s Hospital San Francisco shares a hug with her favorite nurse.

JUST FOR KIDS: Read about how UCSF pharmacists are making cancer drugs for children more precise, limiting their toxic effects – PAGE 26.