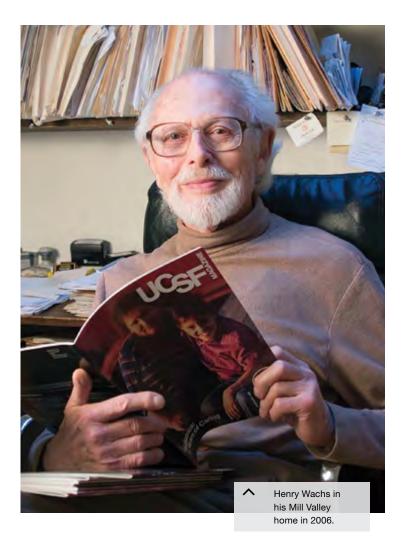


The first issue of *UCSF Magazine* was published in May 1978 and featured one of the first uses of UCSF's now-iconic logo. The publication and the logo were both designed by Henry Wachs, a persuasive and pragmatic trailblazer whose design work reflected an insightful worldview and garnered dozens of awards. Wachs died in December at the age of 102.

In developing a logo for UCSF, Wachs faced a complex challenge. Long before branding was commonly acknowledged as an important element in universities' success, UCSF leaders recognized the need for a cohesive and distinctive identity. The university had long existed as a loose confederation of its component parts, with a list of names and programs that had been continually evolving since 1873.

As Jeff Miller, a past editor of this magazine, wrote in an obituary for Wachs:

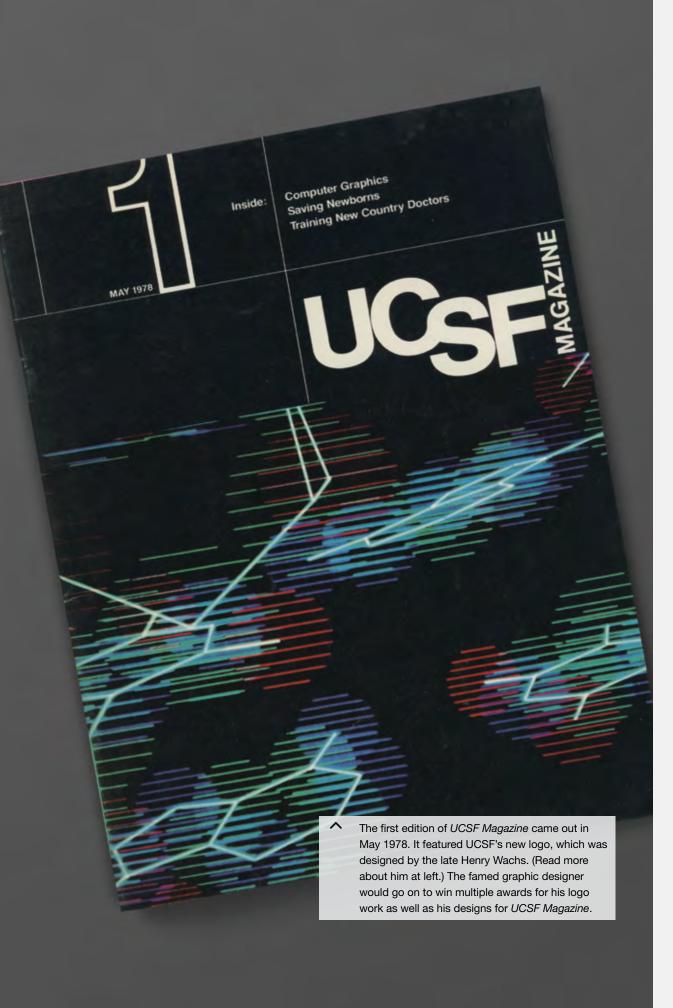
"Wachs' solution was to create a logo that was politically astute, distinct, and bold enough to capture the energy of an institution that in the early '70s was bursting with scientific ambition. His now-classic, stairstep, UCSF logo ... was a monogram that offered a nod to hierarchy (with UC on the top) and a bow to the distinction of the San Francisco campus (with SF on the bottom).... The sinuousness of the letters,



particularly the fusion of the 'C' and the 'S,' suggested that UCSF was on the move."

Wachs believed passionately in the university's public-science mission, and he was both reflective of the time and place and deeply aspirational about where the institution was headed. I see these same traits among UCSF's brilliant minds today, and it is a legacy we are proud to carry on in the pages of this publication.

Sam Hawgood, MBBS Chancellor, UC San Francisco Arthur and Toni Rembe Rock Distinguished Professor



#### **UCSF MAGAZINE**

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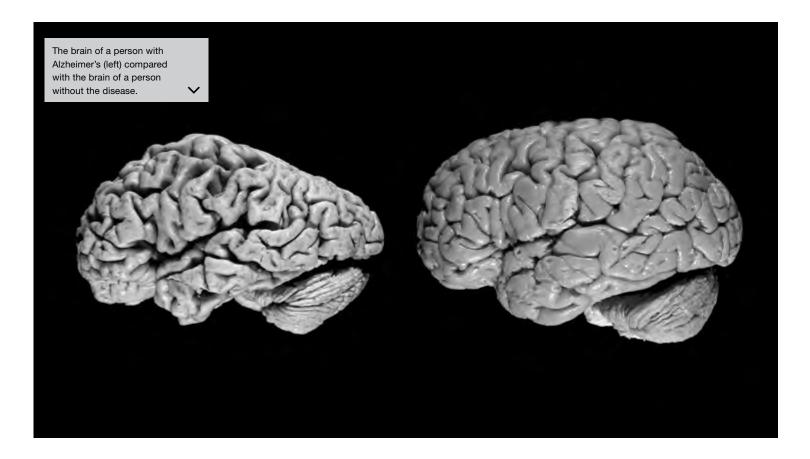
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#### Al Provides Early Warning of Alzheimer's Disease

#### Reviews of brain scans detected the disease six years before a diagnosis

Using a common type of brain scan, UCSF researchers have programmed a machinelearning algorithm to diagnose early-stage Alzheimer's disease about six years before a clinical diagnosis could be made - potentially giving doctors a chance to intervene earlier.

"One of the difficulties with Alzheimer's disease is that by the time all the clinical symptoms manifest and we can make a definitive diagnosis, too many neurons have died, making it essentially irreversible," says Jae Ho Sohn, MD, MS, a resident in the Department of Radiology and Biomedical Imaging.

Sohn trained the algorithm using nearly 2,000 images from a massive public data set of PET



Jae Ho Sohn. resident in the **UCSF** Department of Radiology and Biomedical Imaging

(positron emission tomography) brain scans of patients who were eventually diagnosed with either Alzheimer's disease, mild cognitive impairment, or no disorder. Eventually, the algorithm learned which features are important for predicting a diagnosis of Alzheimer's disease.

"This is an ideal application of deep learning, because it is particularly strong at finding very subtle but diffuse processes," says Sohn.

The algorithm was then tested on two novel data sets. It was able to detect 81 percent of the patients who developed Alzheimer's disease in one data set and 100 percent in the other. It made these predictions on average almost 76 months before the patients received a conclusive diagnosis.

Sohn says the next step is to apply the algorithm to larger, more diverse data sets, from different hospitals and countries. If that step is successful, the process could become a much-needed tool for neurologists to help patients get treatment sooner.

## Closing in on a Cure for Type 1 Diabetes

Stem cells show promise as potential insulin factories for patients

UCSF researchers recently made a major breakthrough in the effort to develop a cure for type 1 diabetes, by transforming human stem cells into mature insulin-producing cells.

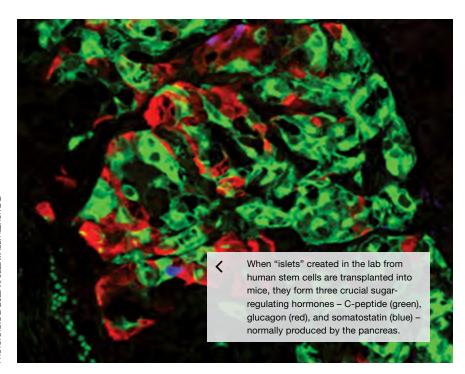
Patients with the disease can manage it with regular shots of insulin to compensate for the inability of their pancreas to produce this sugar-regulating hormone. But injected insulin cannot substitute for the fine glucose control provided by the pancreas, which is why patients who require insulin injections often experience serious health consequences like kidney failure, heart disease, and stroke.

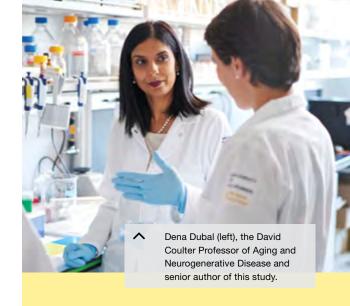
"This is a critical step toward our goal of creating cells that could be transplanted into patients with diabetes," says Matthias Hebrok, PhD, the lead author of the new study and the director of the UCSF Diabetes Center.

Hebrok and his colleagues, led by postdoctoral fellow Gopika Nair, PhD, focused on beta cell development and islet formation – the physical process by which certain cells separate from the rest of the pancreas and form the so-called islets of Langerhans, which produce insulin. In the lab, the beta cells responded to glucose more like mature insulinproducing cells. When transplanted into healthy mice, these lab-grown "islets" secreted appropriate amounts of insulin within days.

Hebrok's team is now using the CRISPR gene-editing tool to make these cells transplantable into patients, without the need for immunosuppressant drugs. They're also screening drugs that could protect a patient's remaining beta cells and reboot pancreatic insulin production.

"Current therapeutics like insulin injections only treat the symptoms of the disease," Nair says. "Our work points to several exciting avenues to finally finding a cure."





#### What is the Secret to Female Longevity?

Around the world, women outlive men, in sickness and health, in war and peace. In most animal species as well, females live longer than males.

Scientists at UCSF have identified a possible genetic mechanism for this highly durable phenomenon: the second X chromosome present in females.

The researchers gave mice four different combinations of chromosomes and gonads: the two found in nature - XX with ovaries and XY with testes - and two others created in the laboratory - XX with testes and XY with ovaries.

The mice were genetically identical except for their sex chromosomes. But even when everything else about them, including their environment, was the same, those with two X's survived longer on average. When two X's were combined with ovaries, the mice lived to the furthest edges of the mouse life span.

"This suggests that the hormones produced by female gonads increase life span in mice with two X chromosomes, either by influencing how the mouse develops or by activating certain biological pathways during their lives," says Dena Dubal, MD, PhD, an associate professor of neurology and the study's senior author.

There is ample scientific literature to suggest a protective effect from having a second X chromosome. In females, half of the XX pair is randomly silenced, or turned off, in every cell of the body. So in cells with defects, the healthy X can compensate for the unhealthy X. "When things go wrong in aging, having more of the X chromosome, along with its diversity of expression, could be really beneficial," Dubal says.

## Staying Awake During Spine Surgery Speeds Recovery

Nearly four in five Americans struggle with low back pain at some point in their lives. For those who need surgery, a traditional spinal fusion under general anesthesia can take at least four hours and require a hospital stay of three to four days, as well as postoperative IV painkillers.

UCSF now offers awake spine surgery, which takes half the time and typically has patients out of the hospital within 24 hours. "The procedure is changing my practice," says neurosurgeon Praveen Mummaneni, MD, co-director of the UCSF Spine Center and the Joan O'Reilly Professor of Spinal Surgery. "I can get my patients

through their surgery much more quickly."

UCSF is one of the first major medical centers in the U.S. to offer awake spine surgery; Mummaneni, also a resident alumnus, began performing the procedure in the spring of 2018.

The key to the new approach is a long-acting, local anesthetic called liposomal bupivacaine. The anesthetic is injected into muscle in the low back before the incision is made and provides pain relief for 72 hours. "This means we're not giving postoperative IV narcotics anymore," says Mummaneni. "And it's allowed us to cut the hospital stay by two-thirds."



#### Harnessing CRISPR to Fight Obesity

A new version of the CRISPR gene-editing system developed at UCSF has shown potential for treating obesity and other diseases caused by genetic mutations.

A study by Nadav Ahituv, PhD, a professor of bioengineering and therapeutic sciences, targeted two genes involved in controlling appetite: SIM1 and MC4R. Most people have two operational copies of both genes. In some people, though, one of these copies is damaged - a condition called haploinsufficiency. In the form of the condition involving these two genes, people are able to absorb only half the usual amount of protein and thus are constantly hungry and unable to control their food intake.

The Ahituv lab used CRISPRa (the "a" is for activation) to coax a single functional copy of either SIM1 or MC4R to produce extra protein to regulate hunger in haploinsufficient mice. The remaining functional gene copy produced enough of the missing protein that mice that received the treatment did not become obese.

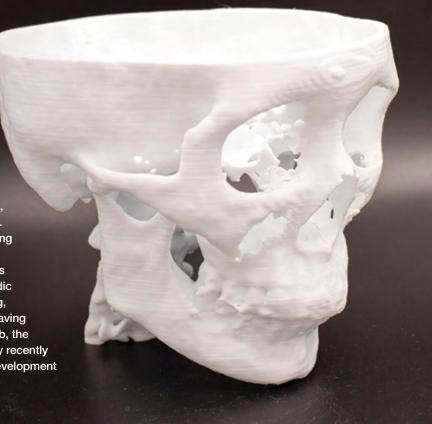
The research opens up the possibility of using CRISPRa to treat other haploinsufficient diseases, such as epilepsy, cancer, kidney diseases, and many others. "The advantage of CRISPRa for human therapies is that it doesn't make permanent edits to the genome," says Ahituv. "There are no genetic scars and, as such, there is less of a danger of offtarget effects."

3D replicas of patients' anatomy help clinicians plan surgeries, design devices, and train students

Orthopaedic surgeons at UCSF are making the most of the 3D-printing revolution. The technology allows them to quickly and cheaply create precise models of patients' bones from traditional 2D scans. Increasingly, surgeons and their trainees use these models to plan and practice operations. The ability to see, hold, and rotate a replica of a patient's anatomy can give them new perspectives that might otherwise be invisible on a flat screen.

Pediatric cardiologists, maxillofacial surgeons, radiologists, dentists, and prosthetists are also beginning to incorporate 3D-printed anatomical models in their work. Research teams, too, are using 3D prints to design and prototype new medical devices. The technology is also gaining steam with students through training offered at UCSF's Makers Lab.

Adoption of 3D printing at UCSF and its affiliate care centers is surging thanks in part to Edge Labs, founded by UCSF orthopaedic surgeons Aenor Sawyer, MD; Alexis Dang, MD '04; and Alan Dang, MD '06. Edge Labs offers on-site 3D-printing services, which is saving clinicians time and money. In addition, Edge Labs, the Makers Lab, the Division of Pediatric Cardiology, and the Department of Radiology recently formed the Center for Advanced 3D+ Technologies to spur the development of on-site 3D printing and visualization technologies.



**FACULTY IN THE MEDIA** 

- As a researcher, it's fascinating and a great opportunity. As a clinician, it's worrisome."
- The problem here is not a lack of willingness to work.... It's a society that... doesn't have an adequate safety net, especially for our senior citizens."
  - ▲ Margot Kushel, MD, director, UCSF Center for Vulnerable Populations, on the increasing number of people over age 50 who end up homeless and living on the street in the San Francisco Chronicle
- [After just three minutes], patients said things like 'Wow, I feel better,' 'I feel less anxious,' 'I feel calm, cool and collected."

## How Do We Achieve Excellence?



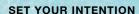
Gurpreet Dhaliwal, professor of medicine

Gurpreet Dhaliwal, MD, is a nationally acclaimed "master diagnostician." During grand rounds, he often impresses large audiences of medical professionals by unraveling complex medical mysteries with deductive reasoning. Also the site director of the internal medicine clerkship at the San Francisco VA Medical Center (and a UCSF

resident alumnus himself), he regularly teaches clinical reasoning to medical students and residents, too.

Here, Dhaliwal shares some tips for achieving excellence in medicine or beyond.

By Susan Godstone



Aim to master all the core skills of your field, but choose one area in which to truly excel, and commit yourself to that specialty.

#### TAKE ON ADDED **CHALLENGES**

Seek extra work. Dhaliwal says some people might ask, "Why do I always need to keep presenting myself with more problems?" But over the long term, continually challenging yourself will shift your performance from good to great.

Put yourself in front of as many realworld cases as possible to add to your brain's catalog of experiences. Take on extra assignments, learn from your colleagues' cases, moonlight, and be relentless in the learning you extract from each experience.

#### **ALWAYS BE LEARNING**

Analyze the moves of exceptionally talented players in your field. Great athletes and chess players study how, move by move, epic contests were won.

Pursue final outcomes. In medicine, this often means hunting down what happened to a patient after they leave your care. The brain needs to know how a story ends in order to do better next time.

As soon as you learn something new, the brain begins forgetting. You can counter this by teaching what you've learned to others - or teaching it back to yourself.

When you find you were wrong, examine your mistake rather than reacting emotionally.

#### **DEVELOP SELF-AWARENESS**

Becoming aware of your biases and we all have them – is critical to learning and decision-making. Cognitive biases are shortcuts that the brain takes to assess the probability of various outcomes, but they sometimes lead to poor decisions.

Monitor your thinking process. Doing this is not natural, and it takes great effort and vigilance. "In medicine, thinking is our most important procedure," says Dhaliwal. "When you step back and analyze your own thinking, you develop knowledge, wisdom, curiosity, and humility. We need doctors to have all of these in abundance."



### Overcoming Drug-Resistant Cancers





Sourav Bandyopadhyay, associate professor of bioengineering and therapeutic sciences

Patients battling lung cancer face a wily disease. Standard treatments often lose their effectiveness after less than two years. But now, UCSF scientists have demonstrated the effectiveness of a combination drug therapy that halts the growth of drug-resistant lung cancer cells in the lab.

Physicians have long sought to treat cancer by blocking the signals that promote tumor growth. In many cases, however, cancer cells develop resistance to these treatments. A research team led by Sourav Bandyopadhyay, PhD, an associate professor of bioengineering and therapeutic sciences, found that drug-resistant lung cancer cells continue to grow by using an alternative signaling pathway — and that using a second drug to block the alternative signals can thwart the drug-resistance.

Specifically, the second drug blocked an enzyme called Aurora kinase that promotes cancer cell growth. Previously, Bandyopadhyay's lab had showed that an unrelated group of drug-resistant breast cancers could also be successfully treated by adding Aurora kinase-targeting drugs to existing therapies. The findings could aid in developing more effective treatments for lung and other cancers.



#### The Orchid and the Dandelion

Is your child hardy and resilient or more sensitive and fragile? UCSF pediatrician Thomas Boyce, MD, has spent nearly 40 years studying the human stress response, especially in children. In this new book, he explores how most kids tend to be like dandelions, able to cope with stress and adversity, but a minority are like orchids, extremely sensitive to their environments. Boyce shares how - given supportive, nurturing conditions - orchid children can thrive. Read: bit.ly/ucsf-read-s19



#### Breakthrough

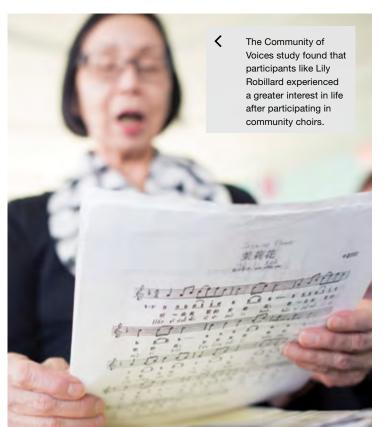
This documentary, about "a renegade scientist's visionary quest to find a cure for cancer," features immunologist James Allison, PhD, a residency alumnus and a former member of the UCSF and UC Berkeley faculties. Allison overcame many obstacles en route to his discovery of the immune system's role in defeating cancer - work that won him a 2018 Nobel Prize. Narrated by Woody Harrelson, the film includes interviews with several current UCSF researchers, including Max Krummel, PhD, who as a graduate student in Allison's UC Berkeley lab led several of the key studies recognized by the Nobel.

Watch: bit.ly/ucsf-watch-s19



#### The Nocturnists

A cardiologist recounts a nerve-wracking emergency medical encounter in North Korea. A hospitalist shares her frustration over caring for a homeless patient who would rather be on the streets. A chief resident describes his first code blue. Created and hosted by UCSF physician and resident alumna Emily Silverman. MD, this podcast and live event series is a forum for doctors to "share stories of joy, sorrow, and self-discovery." Listen: bit.ly/ucsf-listen-s19



#### Community Choir Participation Lifts Spirits

An innovative study of community choirs for older adults found that singing in a choir significantly improves participants' emotional well-being.



Julene Johnson. professor of nursina

Many older adults experience social isolation and depression, which previous studies have shown can exacerbate poor health. "There's a need to develop novel approaches to help older adults stay engaged in the community and also stay connected," says lead author Julene Johnson, PhD, associate director of the UCSF Institute for Health and Aging.

The study, Community of Voices, aimed to assess whether engaging older adults in the arts could improve their mental and physical health. The

researchers followed participants who sang for six months in one of 12 choirs. While there were no substantial differences in participants' cognitive or physical outcomes, their loneliness decreased and their interest in life improved significantly. Enthusiasm for the program was so great, in fact, that the 12 choirs continue to perform well after the study's end.



#### Haircuts Plus Health Care

UCSF doctors are training barbers in Oakland and San Francisco to aid in the fight against heart disease, especially among African American men.

The effort was the brainchild of Kenji Taylor, MD, MSc, whose father passed away suddenly from a heart attack. His story is not uncommon. African American men have the highest rates of hypertension and hypertension-related death of any demographic group. Taylor's father, who likely suffered from undiagnosed hypertension, had never seen a doctor because he was uninsured and mistrusted the medical system.

Out of that experience came the Cut Hypertension Program (cuthypertension.org), which trains barbers as health coaches who provide screenings, education, and referrals to primary care providers.

Barbers Joseph Peters (seated) to the and Terell Kennedy learn to test and counsel clients for high blood pressure at Benny Adem Grooming Parlor in Oakland.

"Being able to go out to the barbershop is a great way to not only start a conversation about hypertension but also show African American men that

they can have trusting relationships with health care providers," says Taylor, who is chief resident in family medicine at UCSF.

### How a Gene Mutation Reduces the Need for Sleep

It's every overachiever's dream: a gene mutation that allows them to function normally on just four to six hours of sleep a night.



Ying-Hui Fu, professor of neurology

In 2009, UCSF neurology professor Ying-Hui Fu, PhD, discovered a mutation in the gene *DEC2* in a family of natural "short sleepers" – people who go to bed at a normal time (between 11 p.m. and midnight) but wake up naturally at 5 in the morning. "These are not people who've trained themselves to wake up early. They're born this way," says Fu.

A new study in mice by Fu's lab reveals how the DEC2 mutation seen in human short sleepers may allow them to thrive on just a few hours of sleep. The researchers engineered mice to have the same mutation in the *DEC2* gene seen in human short sleepers. They discovered that DEC2 helps control levels of orexin, a hormone involved in maintaining wakefulness. The mutation seems to work by partially releasing the brakes on orexin production.

The DEC2 mutation is very rare, but there are other gene mutations that act on different pathways to cause natural short sleep. Fu is studying these genes with the goal of better understanding sleep and its impact on our health.

## It's About Living, Not Dying

Steven Pantilat, MD '89, is chief of UC San

Francisco's new Division of Palliative Medicine, an international expert in the field, and a lover of poetry that speaks to the heart. A line from a Mary Oliver poem inspires his work: "Tell me, what is it you plan to do / with your one wild and precious life?"

Bv Anne Kavanagh

#### What is palliative care?

It's medical care focused on improving the quality of life for people with serious illnesses. If you're facing heart failure, cancer, dementia, ALS, or another such disease, we can help you live as well as possible for as long as possible. Palliative care is not about dying but, rather, about living.

#### Are there any other misconceptions?

That you have to choose between quality or quantity of life. Palliative care helps you have both. Much of what we do is talk with people about what values and goals they hold most dear. People care about many things in addition to a cure. Patients hope to be at a child's wedding, for example, or visit their hometown one more time. We help them achieve the things that matter most to them - even while they're receiving chemo, surgery, or other treatments. It's not either/or.

#### What does palliative care involve?

A team of expert nurses, social workers, chaplains, and doctors work together to address all the issues that really matter to patients. I tell my patients, "You have an oncologist to take care of your cancer. Our focus is on you as a whole person: to relieve your symptoms; to help you make good decisions; to support you and your family emotionally, psychologically, practically, and spiritually."



#### How is UCSF advancing the field?

Last year, we started one of the first divisions of palliative medicine in the country. We've trained teams from over 250 institutions. We're leading a national network of 124 palliative care teams nationwide. We now have data on over 200,000 patient encounters that will help us research and improve care. We've come a long way, yet there's still much for us to learn.

#### Why is demand growing, and how are you preparing?

Doctors and patients are increasingly recognizing the benefits of palliative care. People want care that helps them live as well as possible for as long as possible. Once people learn what palliative care is, they want it. So we're training experts to meet this growing demand. We have one of the largest fellowship programs in the state, and we also train nursing students, medical students, and residents. We want all clinicians to know the basics of palliative care: how to manage pain, shortness of breath, and nausea and how to talk to patients about the things that matter most to them.

#### What have you learned from patients?

People appreciate honesty. It takes courage to face reality, but doing so can help people make the most of their time. Being diagnosed with a serious illness is devastating and can throw your life into chaos. But if we face the reality of the situation together, we can help people make good decisions about their care and make the most of their time. One of my patients had advanced lung disease and severe pneumonia but wanted to see her daughter get married – in 10 months in the Napa Valley. We didn't give her false hope. We said, "You've got to do it now." Three days later, her daughter came to the ICU in a beautiful wedding gown, her fiancé in a tuxedo. They pinned a corsage on the mom's hospital gown. Our chaplain officiated. There wasn't a dry eye. It was a beautiful wedding that she might otherwise have missed.

#### Is it tough to have these conversations?

We often find that patients feel great relief after having an honest, caring conversation about death and dying rather than skirting the issue. Which is not to say it isn't sad. The patient is sad. The clinician is sad about having to give hard news. But people with serious illnesses have typically already thought about the possibility of dying — that's what makes serious illness so scary. When it's done with kindness and compassion, it's often a relief. I tell patients it's like being dealt a hand of cards. We can wish we had a better hand, but we have to do our best with the cards we have.

#### What helps you through the sadness?

The satisfaction of helping people, of making a difference. There are also moments of real joy, even amid the sadness. One of my patients just died, and his wife shared a letter our social worker helped him craft to his family. The last line is "My one regret is that I don't know how *Game of Thrones* ended." It is so sweet and sad. I now think of him every time I watch an episode.

Steven Pantilat is the Kates-Burnard and Hellman Distinguished Professor of Palliative Care.

## Powering the People Behind Palliative Care

#### **Inspiring the Best Bedside Care**

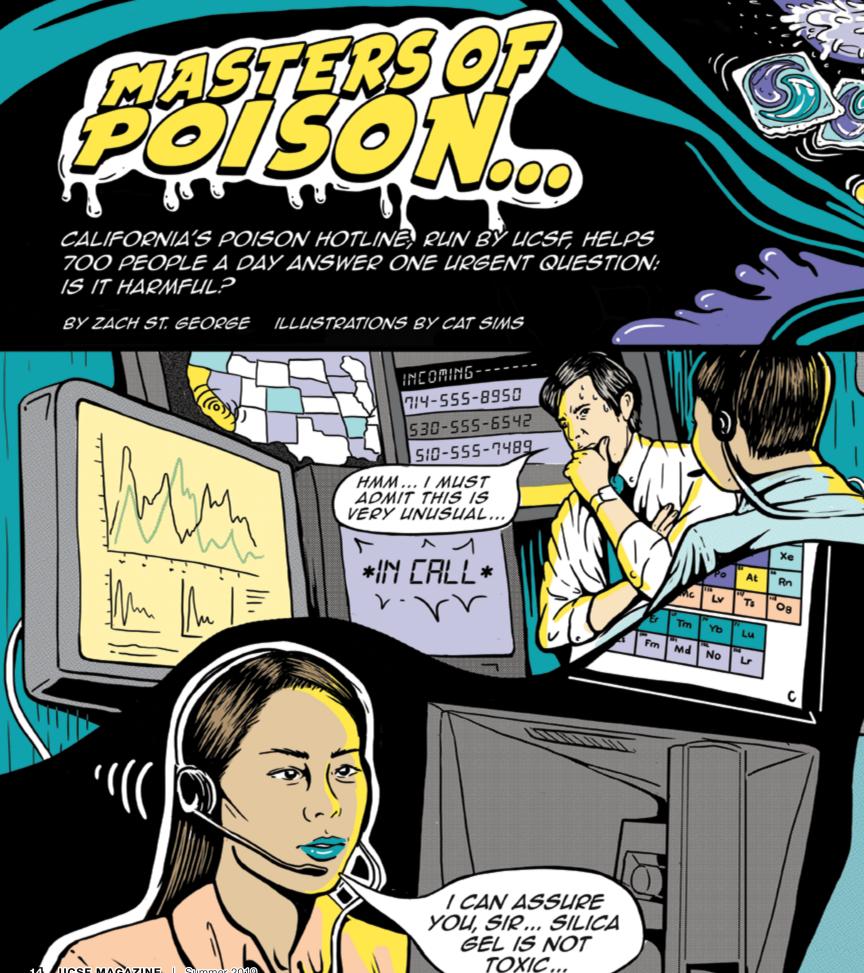
"So much of palliative care happens at the bedside, with nurses," says Susan Barbour, BS '79, MS '86, a clinical nurse specialist. Barbour and her colleagues have trained more than 500 UCSF nurses in how to manage symptoms and communicate effectively with those facing lifethreatening illnesses. These nurses have gone on to champion palliative care in their units, and many have instigated projects to improve care. "It's a grassroots effort," she says. One of their human touches: Bereaved families from the ICU now receive a card signed by everyone who cared for their loved one.

#### **Helping Clinicians Develop Resiliency**

Even the most dedicated clinician can experience burnout from the daily deluge of suffering and loss. Denah Joseph, an ordained Buddhist minister, trained psychotherapist, and palliative care chaplain at UCSF, teaches physicians and other caregivers how to be resilient. One of the most powerful ways, she says, is to develop "prosocial" skills – learning to cultivate awe, joy, appreciation, generosity, and compassion for oneself and others. "And community," Joseph adds. "Sharing and talking is the number-one intervention for burnout. Connection is protection."

#### **Bolstering Communication Skills**

"Health care professionals are trained to share a lot of information, but we are not trained to respond to emotions or talk about the big picture," says Wendy Anderson, MD, a palliative care physician at UCSF. She's also a faculty member at VitalTalk (VitalTalk.org), a nonprofit that teaches evidence-based skills for communicating with the seriously ill. All kinds of practitioners even longtime physician-leaders - are flocking to VitalTalk trainings, where they practice how to share serious news and tailor care plans to patients' unique needs. Anderson says these tactics can help clinicians get to the heart of a matter quickly and answer the most important question of all: "What do I need to know about you as a person to best care for you?"



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THE PHONE RINGS. BEN TSUTAOKA PICKS UP. "POISON CENTER," HE SAYS. THE CALLER IS A TEACHER, SHE'S WITH A STUDENT, HE WAS CHEWING ON A GEL PEN, AND IT EXPLODED ...







Ben Tsutaoka, PharmD, is a UC San Francisco associate clinical professor of pharmacy. He's worked in the San Francisco division of the California Poison Control System (CPCS) for 19 years, answering phones. If you call the toll-free Poison Help hotline, at any time, on any day, from anywhere in California, you'll reach CPCS. (The system also has divisions in Sacramento, San Diego, and Fresno/Madera, all administered by the UCSF School of Pharmacy.) Maybe you've talked to Tsutaoka. He and the other four dozen or so CPCS poison experts field about 700 calls a day. One call every couple of minutes, on average.

Most callers are members of the public (parents or siblings or nannies or teachers), but almost a third are medical personnel (nurses or doctors or emergency responders). The callers' predicaments run the gamut: They got bug spray in their eyes. Their sister took too much Prozac. Their baby swallowed the metal ball from a toy maze. Their patient appears to be in the throes of an opioid overdose.

Some people call because they're genuinely scared. Others call just for reassurance. When a clinician calls, it's usually to get an expert opinion on an unusual or difficult case. But really, everyone calls because they - or more often someone they're with - has ingested, inhaled, or otherwise come into contact with a suspect substance, and they urgently need to know: How bad is it? What should they do?

All day long, the calls toggle between mundanities and neardisasters – with lots of people worrying about matters that really aren't problems, mixed in with a few genuine emergencies, some of which may herald the start of a poison epidemic. To listen in on these calls is to witness a strange reflection of the world - one in which the things we eat and drink and use and depend on every day suddenly seem out to kill us. It's a stark reminder of the dangers of modern life, including the rise of opioids, the emergence of e-cigarettes and synthetic marijuana, and the candy-like appearance of single-use deteraent pods.

But the CPCS also represents a cause for hope: evidence that our fears are often exaggerated, that despite life's hazards, we are safer and more resilient than we think.

#### THE ART AND SCIENCE OF ANSWERING PHONES

The phone rings again. Sandra Agustin, PharmD, answers. She's a recent hire. She sits catty-corner from Tsutaoka in the San Francisco division - a well-worn room ringed with desks, located a couple of blocks from Zuckerberg San Francisco General Hospital (ZSFG). Along one wall is a shelfful of textbooks: Pediatric Dosage Handbook, Poisonous Plants of California, and Goldfrank's Toxicologic Emergencies. On a table sits a display case of medicines paired with candy look-alikes. "Labels tell which is which," it warns, "but most kids can't read between ages 1 and 6."

A man is on the line. He's breathing heavily. He was out running errands when his wife called him, frantic. She'd just stepped out of the shower and saw that their 3-year-old son had eaten some thyroid pills. Could be as many as 20, the man says.

Agustin asks what brand the pills are, how many micrograms, and when the boy ate them. The man doesn't know, doesn't know, doesn't know. He calls his wife and patches her in. Levothyroxine, 175 micrograms, 10 minutes ago. Agustin taps on her calculator, using the kid's estimated weight to determine the toxicity of the dose. Likely poisonous, she concludes. "It's a good idea to take him to the emergency department," she tells the parents.

This scenario is many callers' worst nightmare. Most of the time, though, callers are relieved to learn they have nothing - or very little - to worry about. "People are so grateful when we can tell them that," says Rais Vohra, MD, the medical director for CPCS's Fresno/ Madera division and a professor of clinical pharmacy and emergency medicine at UCSF Fresno. In addition to assuaging callers' fears, CPCS estimates it saves Californians upward of \$90 million per year in unnecessary medical costs - about seven times its annual budget. A call, after all, is a lot cheaper than a trip to the emergency room.

But, of course, emergencies do happen.

Another call. A woman, panting with exertion.

She's out on the street, hurrying to the house of her 15-year-old sister. The teen takes Prozac for depression, the woman says, usually two pills a day. She'd just eaten five at once. (Or maybe more. CPCS toxicologists know that people who are suicidal sometimes lie about how many pills they've taken.) "Was this on purpose?" Agustin asks.

"I don't know, you tell me," the sister says. Like, would someone do that by accident? It's as if she doesn't want to say it out loud that maybe her sister was trying to kill herself."

These calls – in which the person on the line is breathing hard, in which a life all of a sudden has taken a horrible turn - are hard to listen to. Your heart quickens, your palms sweat. Just listening. Can you imagine, you think, can you even imagine?

But after Agustin gets off the phone - after she's sent the sisters off to the hospital for help - she's cool, collected, not sweaty at all. Part of the job, she says.

The job, as one might imagine, requires a deep understanding of human physiology plus an encyclopedic knowledge of substances both dangerous and innocuous. Poison experts must be able to recall and synthesize this information quickly and relay it in a way a caller can understand. "It's a steep learning curve," says Justin Lewis, PharmD '09, the managing director of CPCS's Sacramento division and a UCSF associate clinical professor of pharmacy. "Poisoning isn't something they teach to a significant extent in pharmacy school."

Just as important, he says, you must be able to convey confidence and empathy and stay calm under pressure. Getting your message across can take some persistence. About half of the calls to CPCS concern children under age 5, and although their exposures are often benign or only mildly toxic, it can be hard to convince a panicked parent that the things they think are harmful actually aren't.

Take, for instance, silica gel packets. These little moistureabsorbing pouches are one of the most common causes of calls to CPCS. They come tucked in countless products, from electronics to dried seaweed. They're often labeled "DO NOT EAT." But that's because silica isn't food, Tsutaoka explains, not because it's toxic. Decades ago, when he was studying to become a pharmacist, he

was surprised to learn this. He went home and ate some packets, just to be sure. "They're crunchy," he recalls. But nothing happened. "So then I was a believer."

The trickiest calls tend to come from health care professionals. "The calls that stick out are the ones where the patient is actively dying," says Serena Huntington, PharmD '11, the managing director of CPCS's Fresno/Madera division and a UCSF assistant clinical professor of pharmacy. "The doctor is on the phone with you, and they're wanting to know what kinds of quick antidotes they can give."

The phone rings yet again. A nurse is calling from an emergency room. Tsutaoka takes it. It's about a 19-month-old boy, the nurse says. He got into a bottle of chemotherapy pills and ate an unknown quantity. How does CPCS advise treating him?

Tsutaoka types the name of the drug, Xeloda, into an online database of toxicological information and scans the articles. "Interesting," he says. "Hmm." He tells the nurse he'll call her back. He's never had a case involving this drug before, he says. "It's something kids don't usually get into."

He huddles with the division's managing director and two onduty physicians who are here to help in situations like this. They believe the exposure isn't immediately life-threatening, but it could become so as the medicine works its way through the boy's system. Best to play it safe and give the boy Vistogard, an antidote. One of the physicians says he'll follow up with the nurse so that Tsutaoka can get back to the phones.

#### THE DOSE MAKES THE POISON

Another call. A mom. Her kid had put his finger on the counter where she had cut up some raw chicken, and before she could stop him, he had stuck his finger in his mouth. She doesn't know what to do.

"I know it's horribly dangerous," she says.

Not really, Tsutaoka tells her, in the very kindest way. It's actually pretty rare to get infected with E. coli or Salmonella, he says. Watch the kid closely, and if he gets diarrhea, give him some Pedialyte.

Agustin is on the phone with another mom. Her daughter was spraying her keyboard with cleaning solution, and some of the spray went in her glass of water. She didn't notice until she drank some of it. "She's hysterical," the mom says. She sounds embarrassed. Her daughter is a college student. "I think it's more about stress."

Agustin is understanding. If the daughter had gotten a full glug of the cleaner, that might be a problem, she reasons out loud. But half a misting, diluted in a glass of water? "I don't expect her to have any symptoms," she tells the mom.

It's not always easy to figure out what's poisonous and what's not. Look up "poison" in Merriam-Webster and you'll learn it's "a substance that through its chemical action usually kills, injures, or impairs an organism." This definition, though, is so broad as to be nearly worthless. "What is there that is not poison?" wrote the Swiss physician Paracelsus in the 16th century. "All things are poison and

nothing is without poison. Solely the dose determines that a thing is not poison." In other words, all substances are potential poisons – aspirin, glass cleaner, even table salt – but we usually encounter them in benign amounts. Pop an aspirin. Wash a window. Sprinkle some salt. At some level, there's a toxic dose, sure, but where exactly is the line between safety and danger?

For most of human history, poisons came primarily from the natural world – plants, fungi, minerals, animals. Common toxic exposures therefore remained more or less the same for millennia. Among them were arsenic, cyanide, mercury, opium, lead, mushrooms, and alcohol. Starting in the early 20th century, however, homes across the developed world filled with new medicines, cleaners, pesticides, and other synthetic products – fruits of the burgeoning science of chemistry.

By 1955 in the U.S., 250,000 different trade-named substances flooded the market. Accidental child poisonings had become a crisis, causing more than 400 deaths a year. With little knowledge of what the new products contained and how they affected the body, clinicians found it difficult to both treat exposures and warn the public about them.

It was against this landscape that poison centers emerged. A pharmacist named Louis Gdalman established the first one at St. Luke's Hospital in Chicago in the 1930s. Illinois pharmacists Anthony and Natalie Burda recount its history in the journal *Veterinary and Human Toxicology*. Initially, they report, Gdalman just advised the hospital's own staff. But soon he was taking calls from across the city. "Louis was called day and night," his wife recalled to the Burdas. "He never refused a call." He recorded what he learned about poisons, doses, and antidotes on small cards, thus creating the country's first (albeit crude) toxicological database.

Gdalman's model spread quickly. By the late 1970s, more than 600 poison centers dotted the U.S. They helped initiate public awareness campaigns, educating parents about poison hazards and advocating for child-resistant packaging. As a result, even as the population boomed, child poisoning deaths dropped – to fewer than 50 a year today.

However, isolation and disorganization plagued the early centers. Each had its own phone number and methods of operation – some more sophisticated than others. "A lot of them were just little pieces of hospitals or pharmacies," says Stuart Heard, PharmD '72, CPCS's executive director and a UCSF clinical professor of pharmacy. Often, poison center employees had little or no expertise in toxicology, he adds.

The American Association of Poison Control Centers, established in 1958, pushed for consolidation and standardization. In California, the number of poison centers shrank from more than a dozen in 1980 to just four in 1997, when the California Emergency Medical Services Authority united them under the CPCS moniker. At the time, the four centers – housed at ZSFG, at the UC Davis and UC San Diego medical centers, and at Valley Children's Hospital in Madera – had different cultures and procedures, says Lee Cantrell, PharmD, the managing director of CPCS's San Diego division and a clinical professor of pharmacy at UCSF and UCSD. "Each site was its own kingdom, more or less."

After winning a contract bid, the UCSF School of Pharmacy took over administration of the CPCS, merging the four divisions into one statewide service. While some regional flavor remains (San Diego has particular expertise in snakebites, for instance, and Northern California in mushrooms), they now work "like one big call center but spread out," Heard says. Today, no matter where you are in California, you can call the same number and know you are getting the same quality of service.

#### EXPOSING NEW THREATS

All morning at the San Francisco division, the room hums as students and fellows follow up with people who had called earlier, learning how things turned out. Education is a large part of CPCS's mission, Heard says. UC pharmacy and medical students can choose to do a clerkship at a CPCS division as one of their clinical rotations. Three of the four divisions also serve as training sites for post-residency fellowship programs in medical toxicology – the science and practice of diagnosing, managing, and preventing poisonings.

Now it's mid-afternoon. The doldrums. Calls slow to a trickle. The volume will pick up again around 4 p.m., when people start getting home from work and school.

The tide of calls ebbs and flows with the rhythms of daily life but usually holds steady throughout the year. On occasion, though, a tsunami strikes.

Sometimes the surge merely reflects a new societal fear. In September 2001, after letters containing anthrax spores were mailed to several politicians and media outlets, killing five people and infecting 17 others, calls poured into CPCS. "The whole country just went crazy thinking that anthrax was everywhere," Heard says. "Our role was to reassure them that was highly unlikely – that the white powder they found in their kitchen was just something they spilled."

A similar wave of calls followed the literal tsunami that, in 2011, destroyed a nuclear power plant in Fukushima, Japan. Many Californians worried that radioactive debris would make its way across the Pacific to the state's coast. Dozens of people called CPCS asking where to find potassium iodide, an over-the-counter compound that can protect the thyroid from radiation damage. Other people called because they had taken too much potassium iodide; in an attempt to protect themselves from poison, they'd poisoned themselves.

Other times, an influx of calls signals a new poison hazard, allowing CPCS to quickly identify the threat and alert the public. A few years back, for example, Raymond Ho, PharmD '04, the San Francisco division's managing director and a UCSF associate clinical professor of pharmacy, was working the phones when he started getting suspiciously similar calls from several hospitals around the city. Kids were arriving at emergency rooms with glazed eyes, lethargic and vomiting. Nobody knew what was happening. But some of the clinicians had a suspicion, which CPCS toxicologists confirmed: The kids were stoned. CPCS briefed the city's public health department, which investigated. It turned out the kids had all been at a *quinceañera* party, and somebody had set out a tray of cannabis-infused gummies.

One of the largest and scariest poison outbreaks is still ongoing. It started in 2015. That fall, a man showed up at ZSFG looking like he'd overdosed. His pupils were tiny, he was having difficulty breathing, and he appeared to be heavily sedated. He insisted he'd only taken a Xanax, an antianxiety drug. Toxicologists at CPCS's San Francisco division had the man's pills tested and found they were laced with a high dose of fentanyl, a synthetic opioid 100 times stronger than morphine. They immediately notified public health officials. "We suspected we were just seeing the tip of the iceberg," says Craig Smollin, MD, the division's medical director and a UCSF professor of emergency medicine.

Sure enough, hospitals across the Bay Area and Central Valley began calling CPCS regarding similar cases. People were buying, either on the street or online, what looked like common recreational drugs or pharmaceuticals - Xanax, OxyContin, methamphetamine but were actually much more potent counterfeits. "We were able to surveil the outbreak and team up with our colleagues in the health department to get the word out to the community," Smollin says. While synthetic opioids are still a growing problem, those early warnings likely saved lives, he says. "It makes me feel we're doing something really important."

Recently, CPCS has also begun taking a more active role in helping to combat opioid use disorder, which causes tens of thousands of deaths per year nationwide. "We said, 'How can we leverage our expertise to help mitigate this epidemic?" says Kathy Vo, MD, an assistant medical director of CPCS's San Francisco division and a UCSF assistant professor of emergency medicine. Through a pilot program under the California Department of Health Care Services, emergency clinicians can now call CPCS to get advice on administering buprenorphine. This opioid alternative treats withdrawal and helps patients stay off heroin and other riskier opioids, thus preventing overdoses. But because starting patients on buprenorphine in emergency departments is a relatively new practice, emergency providers may feel uncomfortable doing so.

"So we're here to hold their hand," Vo says.

#### A REASSURING VOICE

It's late afternoon now. Tsutaoka and Agustin are nearly done with their shifts. A new team of specialists has arrived.

The phone rings, and Leslie Lai, PharmD '18, answers. The caller is distraught. Her 4-year-old son was snacking on some dried seaweed, she says, and then suddenly he was spitting out something white and granular. Lai can hear the boy screaming. "It looked like tapioca," the mom says. The boy had eaten a packet of silica gel beads.

"They're not toxic," Lai tells her.

They're not?

No.

The mom sounds bashful. "I just panicked," she says. "I think I scared him." The kid's screams hit a new register. "She says it's okay," the mom tells him. "It's okay. It's all right." The boy stops crying, and the mom hangs up.

The phone rings again.

#### TO CALL OR NOT TO CALL

ABOUT 80 PERCENT OF CALLS TO THE CALIFORNIA POISON CONTROL SYSTEM ARE MADE FROM HOMES. HERE'S WHAT DRIVES MANY OF THESE CALLS AND WHAT THE PUBLIC SHOULD KNOW.

#### BUTTON BATTERIES

Besides being a choking hazard, these can cause serious burns. Seek medical help immediately.

#### CANNABIS EDIBLES

Don't induce vomiting. Marijuana typically isn't life threatening, but small children may need hospital care. Call Poison Control for advice.

#### **GLOW STICKS**

The chemicals in them may irritate the skin or throat but usually don't cause serious harm. Rinse the affected area, and if symptoms worsen or persist, call Poison Control.

#### HAND SANITIZER

Eye exposure isn't a problem, but swallowing it can be. Again, best to call Poison Control.

#### LAUNDRY PODS

Just a bite can be deadly. Call 911 immediately.

#### MEDICATION

Depending on the type of drug, even a single pill can be hazardous. Call 911 if the victim is shaking, unconscious, or having difficulty breathing. Otherwise, check with Poison Control.



The mechanical legs press forward, rhythmic and powerful. Clad in an exoskeleton that looks like mechanical armor. 12-vear-old Dilan Horwitz could be mistaken for a superhero - an assessment that wouldn't be entirely wrong.

A year ago, Dilan was an academically gifted sixth grader and the star catcher on his Little League team - with a seemingly minor nut allergy. Then last July, while on a family vacation in Croatia, he suddenly collapsed after an apparent allergic reaction. Within minutes, he had stopped breathing and had no pulse. "He went from being perfectly fine to fighting for his life, just like that," recalls his father.

At a nearby hospital, an MRI revealed a grave prognosis: Oxygen deprivation had resulted in severe brain damage. Dilan was transported straight from Croatia to UCSF Benioff Children's Hospital

Oakland, where he spent two months tackling hours of daily physical, speech, and occupational therapy.

His therapy included regular sessions in the exoskeleton, a wearable robot equipped with computerized sensors and motors. This innovative technology helps patients regain stability and relearn how to coordinate their movements, which is important for Dilan, who now struggles to control his body.

Back home in Fremont, Dilan has emerged with a new ambition: to become a physical therapist. "It's possible I might not be a professional baseball player," he jokes.

But Dilan hasn't given up on sports. In March, he took to the field with his Little League team - a bit shaky but walking proudly on his own.

- Beth Tagawa

Physical therapist



## THE UCSF GUIDE TO HEALTHY HAPP EATING

We talked to dozens of experts, and they agree: No fad diets. No superfoods. No shame. Here are 12 tips for getting it right.

Chopping garlic and onions helps release anticancer enzymes, but heat stops this process. So wait 10 to 15 minutes before tossing them in a hot pan.

Many other tough, leafy greens become more bioavailable and easier to digest when cooked, making them more nutritious than when raw. But eating raw greens like spinach and kale is still better than eating none at all!

Roasted potatoes have double the glycemic index of boiled potatoes. While this makes for better flavor, it also raises blood sugar faster - something you want to avoid if you're worried about diabetes or cardiovascular risk.

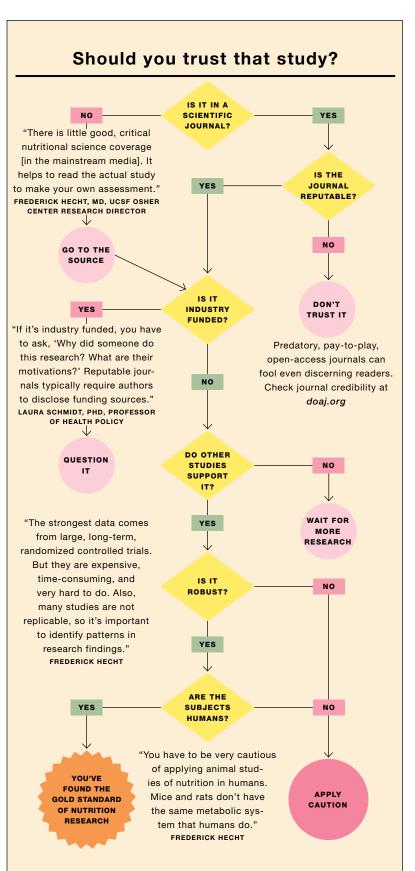


## Start with Skepticism

We all want easy answers, but nutrition science is an imperfect and evolving field. The food research in our newsfeeds is often overhyped and misinterpreted or skewed by human error, scientific bias, and weak methodology. And when it is wrong, the stakes are high.

Take the '80s advice to follow a low-fat diet. It triggered a billion-dollar industry of low-fat, high-sugar food with little nutritional value (remember SnackWell's cookies?) and contributed to a public health crisis marked by skyrocketing rates of diabetes. "Telling people to follow a low-fat diet without paying attention to what was in that diet was one of the worst public health mistakes of the last 30 years," says Frederick Hecht, MD, the Osher Foundation Professor and director of research at the UC San Francisco Osher Center for Integrative Medicine. "We as a field have made huge mistakes. We need to better convey the limitations of current science when providing advice."

Our best advice to you: Take every piece of nutrition advice with a grain of salt.



Companies excel at using healthysounding but meaningless buzzwords to get you to buy their products. They know this "health halo" can trick our brains into thinking their products are better for us than they really are. Of course, the best way to avoid this deception is to skip packaged foods altogether. But if you must buy the box or bottle, look for the facts behind the hype.

RICH IN VITAMIN C We know from UCSF's Truth Tobacco Industry Documents archive that tobacco companies marketed sugary kids' drinks as healthful by touting their added vitamin C. Some of these same brands still use Big Tobacco's playbook to hook kids on their drinks. The truth is, vitamin C in a bottle of colorful sugar water is still, yep, unhealthy sugar water.

#### HIGH IN ANTIOXIDANTS

Antioxidants are chemicals that zap "free radicals" - molecules that can damage cells. Although antioxidants in their natural packaging inside fruits, veggies, and whole grains do help fight chronic disease, there's very little support for added antioxidants providing similar health benefits. In fact, some studies found they were actually harmful to health.

#### ALL NATURAL

The "all natural" claim was invented by marketers. Although it sounds close to "organic," it actually has no universally accepted definition. so products labeled "all natural" could contain hormones, pesticides, and all kinds of other bad stuff.

#### ORGANIC

Although the "organic" label tells you that at least some of the ingredients were produced without conventional pesticides, fertilizers, hormones, or antibiotics, it doesn't mean the packaged item is healthy. Organic junk food is still junk food.

#### **GLUTEN FREE**

This FDA-regulated claim is important for people with celiac disease (an autoimmune disorder) who can't tolerate gluten, a protein found in many grains. However, "gluten free" doesn't mean "good for you," especially if the product is full of sugar, salt, and fat.

#### INGREDIENTS

As a general rule, look for simpler, shorter lists with ingredients you recognize. If you see lots of names that look like they belong in a chemistry textbook, it's probably a less-than-healthy product.



#### SKIP THE SUPPLEMENTS?

Supplements are big business. But unless you know you have a specific nutritional deficiency, supplements could be doing more harm than good. We just don't know.

Unlike prescription medications, the FDA has few regulations for supplement manufacturers. In fact, supplements are considered safe by the FDA until proven otherwise.



U.S. take dietary supplements



50,000 supplements are on the market today over 12x the number available 25 years ago



#### \$11.6 billion

is the predicted global market by 2024 for the fast-growing sector of "brain health" supplements

"It's not that all supplements are bad," says Joanna Hellmuth, MD, MHS, a neurologist at the UCSF Memory and Aging Center. "It's just that there are no protections

in place at the moment to inform the consumer one way or the other."



More than half of Americans are on at least one prescription medication, and most of our homes are bursting with over-the-counter pills, ointments, and syrups. It turns out, however, that your kitchen pantry and fridge are also key – as long as you fill them with the right stuff.

That's why UCSF family physician Daphne Miller, MD, not only asks all her new patients to bring in their vitamins and prescriptions, but also dives into what she says really matters: "We talk about what they eat."

Miller, who spent years traveling and researching the healthiest regions around the globe, wrote her first book, The Jungle Effect, on the traditional diets and recipes that had kept those communities healthy for generations. In the process, she came to see the dramatic link between certain diets and a striking lack of chronic diseases, including heart disease, depression, diabetes, colon cancer, breast cancer, and prostate cancer.

The "food-as-medicine" movement Miller represents is hardly new. But recent studies by the renowned UCSF food-policy expert Hilary Seligman, MD, MAS '06, and her collaborators have begun to rigorously evaluate outcomes of programs through which doctors "prescribe" increased access to healthy foods. In 2017, the UCSF team found that sick patients who got special meals for six months suffered less depression, were less likely to make trade-offs between food and health care, and were more likely to stick with their medications. (See "Understand the Impact of Food Insecurity" on page 30.)

While the effectiveness of such programs

needs more study, researchers from Tufts University have calculated that providing insurance coverage for healthy food to patients could prevent as many as 3.3 million cardiac conditions and save more than \$100 billion in health care costs.

What's more, the idea of fighting chronic disease through diet has already entered the mainstream. And perhaps no disease is more closely associated with "food as medicine" than cancer. According to UCSF integrative oncologist Donald Abrams, MD, nearly half of all cancer patients pursue popular diets, such as the alkaline, Paleolithic, ketogenic, vegan, or macrobiotic regimens, in the hope of improving their survival and preventing a recurrence.

However, writing in the online journal *Oncology*, Abrams and his co-authors caution that these diets can introduce nutrient insufficiencies or even eliminate foods proven to be beneficial for cancer prevention and general health. They point out that most of these diets have positive aspects, but that physicians should encourage dietary changes that emphasize the positive features of these popular diets while correcting for their faults (see sidebar).

The bottom line? Whatever you have in your medicine cabinet, what's on your grocery list matters, too.

#### **Dietary Rx**

Cancer-nutrition advice from integrative oncologist Donald Abrams, MD, avoids the pitfalls of popular diets. The rest of us could benefit as well.

#### MORE FRUITS & VEGGIES

Eat five to nine servings of produce a day (more vegetables than fruits).

#### BUY ORGANIC

Buy organic produce if possible and your budget allows.



#### THINK CRUCIFEROUS

Eat cruciferous vegetables (broccoli, cauliflower, brussels sprouts, kale, etc.) every day.

#### THE WHOLE CHICKEN

Buy organic chicken and go easy on the eggs.

#### NO SOGGY VEGGIES

Don't overcook vegetables - steam, blanch, or stir-fry them.

#### EMBRACE SOY

Eat unprocessed soy (tofu, soy beans, soy milk) but not processed soy like fake cheese or meats.

#### THINGS TO AVOID

Limit meat consumption and avoid processed meats and refined sugar.



Incorporate turmeric into your diet as an anti-inflammatory.

STRESS LESS!
Stress and lack
of sleep affect
your brain in

similar ways.

After a restless night, do you find yourself craving a bagel or muffin or even a donut? The problem is neurological, says Aric Prather, PhD, an associate professor of psychiatry who studies how sleep affects health.

Sleep-deprived brains do a poor job regulating appetite and impulses. Studies show that when we're tired, we crave not just more foods but also those that are higher in fat, sugar, and salt – foods we know are bad for us but are evolutionarily primed to love. Prather's lab recently found, for example, that people who sleep five hours or less a night drink 21 percent more sugary drinks than people who sleep at least seven to eight hours. So don't blame your lack of willpower when you're blearily facing the fridge. Instead, consider ways you could get more shut-eye. Understand that this is your brain on too little sleep:

The executive system quiets, lessening its suppression of impulses to eat.

Hormone imbalances in the **hypothalamus** amplify feelings of hunger while dampening feelings of fullness.

Reward centers
become more active,
making comfort foods
even more desirable.

5

#### **Ditch Weight-Loss Diets**

Deny yourself. Lose weight. Feel great. That's what every fad diet promises. But science tells us otherwise, says Ashley Mason, PhD, a UCSF assistant professor of psychiatry. Dramatically restricting calories, she says, changes our brains and bodies in ways that make it easier to pack on the pounds – a biological reality that is no match for willpower. So while extreme dieters can lose weight in the short term, they gain most of it back within a few years. What's more, weight loss isn't the only yardstick with which to measure our health. If your goal is wellness, you're probably better off ditching diets altogether, Mason says. Instead, focus on improving the quality of your food by buying whole ingredients (think produce, nuts, and other foods that don't need labels) and cooking at home.

KEEP YOUR SMILE HEALTHY:



Some foods and drinks help fight cavities, says dentistry professor Sheila Brear, BDS. Here are a few to try (and a few to avoid):

Eat hard cheese at the end of a meal and after dessert.

Chew gum 5-10 minutes after a meal, which stimulates cavity-thwarting saliva.

**Drink tea,** which combats tooth decay.

Avoid juices and snack foods like chips. When consumed frequently between meals, they can cause tooth decay as much as sugary candies because they're high in carbohydrates, a form of sugar.



Want to fend off disease and have more energy? Try eating within an eight- to 10-hour window, says guest expert Satchin Panda, PhD, a professor at the Salk Institute, an adjunct professor at UC San Diego, and a worldwide expert on circadian rhythms research. Here's why:



#### ORGAN CLOCKS

Almost every organ has a circadian clock, a 24-hour internal timing system that tells our systems when to wake, sleep, eat, and perform other functions. A growing body of research suggests that for optimal health, we need to abide by these innate rhythms.

#### REST IS BEST

Our metabolism's circadian rhythm primes us for food intake in the daytime. The pancreas cranks up insulin secretion, for example, and the gut prepares to absorb nutrients. Then, just as the brain needs sleep, our digestive organs need downtime to repair and rejuvenate.

#### DISRUPTION AND DISEASE

Shift workers often experience circadian rhythm disruption, and correlation studies worldwide show that this can predispose them to obesity, diabetes, and heart disease and increase their risk for cancer and depression. Panda has also shown that mice who ate within an eight- to 12-hour window did not succumb to disease – even though they were fed a high-fat, high-sugar diet.

#### OUT OF WHACK

Eating late can cut into the time our stomach, liver, intestines, and other organs need to cleanse, which is about 12 to 14 hours. Even that handful of nuts before bed can take four to five hours to digest.



AVOID GUT "JET LAG"
Panda says it's also
important to choose
and stick to a consistent eating window,
every day, so the
body knows when
to expect food.

## **Practice** Mindful **Eating**

For all the time we spend buying, preparing, anticipating, and seeking advice about food, we give surprisingly little attention to eating it.

"Eating is most often unconscious and automatic," says Elissa Epel, PhD, a UCSF professor of psychiatry. We eat while driving, while watching TV, while browsing our phones or checking our email.

What if we just, well, ate? "What people find when they focus on the experience of eating is they actually feel more pleasure and more satisfaction. And they are less likely to overeat!" Epel says. Mindful eating teaches us to appreciate the lima bean or the broccoli floret; it shows us we can savor a slice of pie and not yen for another. But can it really make us healthier?

Epel and Frederick Hecht, MD, director of integrative medicine research, and their UCSF colleagues are finding that the answer is yes. In a clinical trial of 194 obese adults given guidance on diet and exercise, those who also received mindfulness training ate fewer sweets and reported significantly less compulsive eating than those who didn't get the training. A year later, the mindfulness group had greater increases in HDL ("good") cholesterol and greater decreases in blood sugar and triglycerides (blood fat) - all markers of improved metabolic health.

"Just being aware can have a profound effect on eating behavior and risk for diabetes," says Rachel Radin, PhD, a postdoctoral scholar who helped analyze data from the trial. Awareness includes noticing not just how foods taste, smell, look, feel, and sound, but also what we believe and feel about them. When we open the refrigerator, do we feel pangs of hunger - or are we just bored?

Andrea Lieberstein, MPH, a mindfulness instructor and consultant for the UCSF study, says "You're learning to check in with yourself in the moment. This allows you to make the conscious choice to eat in a way that is both pleasurable and guilt-free."

STEPS	FOR	MINDFUL	EATING:*

STEPS FOR MINDFUL EATING:					
PAUSE	REFLECT	ENGAGE	CHECK		
Take a breath	Consider how	Enjoy your food	Tune in again to		
before eating.	your food got to	with all your	your level of hun-		
Observe any	you and who	senses. Notice	ger and fullness.		
thoughts or emo-	helped make	its colors,	Consider how		
tions. Be aware	it. Feel a sense	textures, fla-	taste and enjoy-		
of how hungry	of appreciation	vors, scents,	ment change		
or full you feel.	or gratitude.	and sounds.	over time.		

\* Adapted from Well Nourished by Andrea Lieberstein



Are you a

stressfreeuc.org

/healthstudy

to join a study of

meditation and

mindful eating.

#### Feast with Family

It's no secret that sharing home-cooked food is healthier and cheaper than dining out. But did you know that family meals impart mental and emotional benefits, too? For instance, studies link regular family meals to lower rates of depression and eating disorders, higher self-esteem, and better academic performance among kids and teens. So go ahead - gather your loved ones around the table and let the connection and conversation flow.

## Get Kids to Love Healthy Eating

New parents: follow Katie @babyledweanteam



"My teacher told us that sugar causes you to get a disease where you're going to need a shot every day. I don't want a shot, so I'm not going to eat my ice cream."

That's the lesson the 5-year-old daughter of Sara Buckelew, MD, MPH, brought home from kindergarten one day. Buckelew, medical director of the Eating Disorders Program at UCSF Benioff Children's Hospitals, says it's just one example of the unintentional messages embedded in how we talk about food. Rather than expressing shame or negativity, "we should be sending messages about the importance of variety and nourishing your body," she says.

#### "The problem is that dessert is now occurring all day long, every day."

"I'm all for dessert, as long as it's recognized as a treat and something special," says nutritionist and researcher Andrea Garber, PhD, chief nutritionist for the Eating Disorders Program at UCSF Benioff Children's Hospitals. Garber emphasizes that it's not good for parents to be too restrictive, since children whose parents apply more external controls have been shown to eat significantly more sweets than other kids when their parents are not present. "Those control strategies backfire with our kids, and they backfire on us."

"Sometimes it's important to have a slice of apple pie. You're human, and it's great to share this experience with the people you love and enjoy this moment."

Darya Rose, PhD '10, UCSF neuroscience alumna and healthy-lifestyle author, blogger, and podcaster, says that framing different foods as "good" or "bad" sets up a destructive dynamic that relies on willpower. "And when you're using willpower, eventually you're going to lose. When you realize that there are all these valid reasons

Find Rose's recent TedX Talk "Get Healthy Without Dieting" at bit.ly/ucsf-rose to eat different foods - including grandma's pie - it can help break down that food moralizing and establish a healthier relationship with food," she says.

Advice from Katie Ferraro, MPH, an associate clinical professor of nutrition in the UCSF School of Nursing, a specialist in baby-led weaning, and a mother of seven children, including quadruplets and infant twins:

#### Strive for variety

Research shows the more textures and flavors kids are exposed to early in life, the greater food acceptance they'll display down the road.

#### Try to start early

Some flavor compounds are transmitted through breast milk. If a mother mixes up her diet while breastfeeding, the baby's future palate may benefit.

#### Model diverse tastes

Data show picky eaters tend to come from households where parents have limited variety in their diet. Broadening your food horizons will

encourage your kids to do the same.

#### Consider baby-led weaning

Starting at 6 months, infants have the capacity to feed themselves. If you combine selffeeding of solid foods with purees, your child will experience myriad textures, tastes, and foods and develop the ability to listen to their own hunger and fullness cues. Evidence shows this weaning strategy is just as safe as spoonfeeding as long as parents have received proper instruction.

#### Try and try again

Some babies need to try a new food about 10 to 15 times before thev'll like or accept it. Try offering the same foods prepared in different ways - boiled, roasted, baked, broiled.

#### Prepare for setbacks

Some degree of picky eating is inevitable, starting around age 2.

#### Cook with your kids

Start as young as you can. Have them mix, chop, sprinkle, stir. If they help prepare a meal, they will be more inclined to eat it.





## **Understand** the Impact of **Food Insecurity**

You may or may not be the healthiest eater. But most people at least have access to healthy options: a supermarket in their neighborhood; reliable transportation to get there and back; and the disposable income to afford fresh, whole foods.

For more than 40 million Americans, however, the choices are different. Parents choose to skip meals so their kids can eat. Elders choose between paying for medications and paying for groceries. Cheap, processed, packaged foods are often their only choice - and many of these are so unhealthy that they lead to entire communities of people who are both malnourished and obese.

Government food-aid programs and community food pantries play an important role in addressing such food insecurity, but they are ill-equipped to make fresh and healthy foods more available. However, another approach is showing promise: "food pharmacies" that provide patients with free, nutritious groceries during clinic visits, as well as guidance on nutrition, recipes, and cooking that are tailored to patients' specific medical needs.

According to Hilary Seligman, MD, MAS '06, a nationally recognized expert on the intersection of food insecurity and health, such programs can improve health and lower medical costs. "Your mother probably taught you that nutritious food makes you healthy. But for a low-income household, affording these foods turns out to be not so easy. Here is where food pharmacies might step in and make a big difference - both in helping people stay healthy and in reducing costs of care," says Seligman.

UCSF is engaged in addressing food insecurity beyond the walls of the clinic as well. In 2015, Seligman launched EatSF, a program that provides free vouchers for fruits and vegetables to low-income individuals and families. The program has provided produce to more than 10,000 people in San Francisco and has become a national model for creating equitable local food systems.

"My goals for EatSF are big, but the model is quite simple," says Seligman. "We are supporting economic activity in underserved neighborhoods and making fruits and vegetables available in the city's food deserts. At the same time, we are reducing food insecurity and improving health."

For more information on EatSF visit: eatsfvoucher.org

"I always assumed people who were getting food stamps would be like those you see on the streets in San Francisco," says Molly, a UCSF student who uses the Basic Needs & Food Security for Students program. "And I know a number of other classmates who use government assistance. It's changed my mindset about what food insecurity is."

#### HELPING STUDENTS ACCESS HEALTHY FOOD

Food insecurity among college students is a growing problem nationwide, driven largely by the spiraling costs of higher education. Across the University of California, 44% of undergraduates and 26% of graduate students report experiencing food insecurity. To destigmatize this reality and assist struggling students, UCSF launched the Basic Needs & Food Security for Students program. Here's how it helps:

#### 600

UCSF students receive CalFresh benefits, the food-assistance program formerly known as food stamps.

#### 320

students per week "shop" at UCSF's Student Food Market, which distributes free, fresh produce and other food.

of UCSF students have downloaded a UCSF app that connects them to food left over after catered campus events.

Researchers are discovering that soil with a rich diversity of microbes - lots of laborers carrying different nutrients leads to the most nutrition-packed food.



# Embrace the Future of Food

These trends just might shape what and how we eat in the years ahead.

#### Personalized nutrition

Nutrition, it turns out, is incredibly idiosyncratic. Culture, environment, genetics, body composition, and the gut microbiome all play roles in how individuals process calories and nutrients. The variables are daunting, but a data-driven future promises to show each of us how we, and we alone, should eat.

Even today, oncology dietitian Natalie Ledesma, MS, is using personalized testing to advise patients in her private practice. She tests her patients' blood, urine, hormones, and stool and even looks at their genome before making suggestions. When it comes to this approach, she says, "I am going to push the envelope. I think we will continue to personalize nutrition regimens more and more, and genomics will become a more commonly used nutritional tool."

Integrative dietitian Danica Cowan, MS, agrees but notes that truly personalized nutrition is a long way off. "It's important to remember much of the science isn't there yet." For now, she says, "Rather than undergo lots of tests, most people will see far more benefit from simply eating more fruits and vegetables and a lot less junk."

#### MDs with culinary cred

Most primary care providers have relatively little training in nutrition, but that's beginning to change.

Training for medical students in "culinary medicine" is gaining ground nationally. The approach imparts skills ranging from cooking, shopping, budgeting, and label-reading to nutritional counseling and understanding food-assistance programs.

Nutritionist and professor Andrea Garber, PhD, helped pilot such a course at UCSF over the last two years, hiring professional chefs to guide students as they cook healthy meals, while also covering chemical and metabolic pathways and exploring case studies on nutrition and chronic disease.

What might a future with more kitchen-savvy doctors look like? Imagine primary care providers who ask patients about their shopping habits and cooking skills.

Replace conversations about saturated fat and cholesterol with real-world tips about vegetables and grains. Picture low-income patients receiving a map to their local food pantry. In this future world, obesity, diabetes, and hypertension rates all decline, and medical costs drop as well. And the doctors who learned to cook back in medical school? They're likely quite a bit healthier, too.

#### Sustainability

"Today we are in the late stages of a catastrophic meltdown in global biodiversity, unprecedented in human history, almost entirely driven by global demand for meat, fish, and dairy foods," says Patrick Brown, a UCSF postdoc alumnus who is the founder and CEO of the buzzy plant-based-meat startup Impossible Foods.

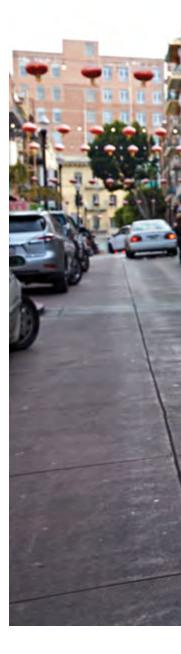
The fact is, the future of food itself is inextricably linked to the health of the planet. Environmental degradation threatens the healthfulness of foods; at the same time, food production inflicts incredible damage on the planet. And most ominously, climate change is certain to increase global hunger and reduce agricultural biodiversity in the next few decades.

Daphne Miller, MD, a UCSF clinical professor who founded the Health from the Soil Up initiative and teaches medical students about aligning agriculture and conservation with human health, suggests three steps for anyone who wants to eat more sustainably. "Step one: Just eat more vegetables, fruits, and whole grains – whole foods that are as unprocessed as possible. Step two is to choose foods that are produced in the United States," she says. Fewer food miles means a lighter footprint; it also supports more diversified, healthful agriculture in the U.S. Step three: Get curious about how your food is grown. While the "organic" label is a helpful guide, you want food grown in soil that has been enriched with cover crops and has not been overly tilled or treated with chemicals.

"The boundaries of health," she says, "extend beyond our bodies to the environment."



Mental Health on the Margins





A window into my world as a community psychiatrist in San Francisco

By Richard Feng, MD

here were strong hints from my very earliest years that I'd become a community psychiatrist.

I remember exploring San Francisco, where I grew up, yearning to understand the people and communities around me. Whenever I rode a public bus, for example, I'd wonder about the lives of my fellow passengers.

As I grew into my teens, I became increasingly aware of scores of inequities around me, of the daily suffering and pain experienced by those on the margins of society. It was hard to ignore the city's sizable homeless population, for example. I began to notice that kids in San Francisco who have barely learned to walk then have to learn to sidestep around human feces on the sidewalk, to stay away from hedges fouled with used syringes and broken glass, to avoid making eye contact with people on the street yelling angrily at no one in particular.

I also started to recognize that the individuals I saw all around the city were each a part of their own community. I come from an immigrant, working-class family, and early on I was able to appreciate my parents' individual efforts and their dedication to our family. Then, slowly, I began to also recognize that they were part of a larger community that predetermined, and in many ways limited, what we as a family were able to do. It was that awareness of the power of one's community, for good as well as ill, that drew me to community psychiatry.

A community psychiatrist is a rare bird. The field of psychiatry is intensely personal, with the patient-psychiatrist dyad at its core. The symbol of conventional psychiatry's professional identity is the therapist's couch – occupied by one patient at a time. In that context, psychiatrists agonize and ruminate over the particular travails of each person before them. Community psychiatrists, by comparison, likewise care deeply about the patients we treat, but we are also willing to shift our focus from the individual to the community and then back to the individual - back and forth, back and forth, just the way an optometrist switches lens during an eye exam. Another difference is that all psychiatrists - indeed, all physicians, no matter their specialty are trained to inquire about a patient's social history. But community psychiatrists see this knowledge not as background information, but as an active, dynamic aspect of an individual's lived experience. To us, in other words, a patient's social history is almost as important an entity in the context of treatment as is the patient him- or herself.

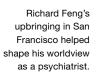
This worldview now informs my day-to-day work as a community psychiatrist with the San Francisco Department of Public Health. When I see a patient, I see both an individual and that individual's

societal and historical context. For example, when I meet with a 40-year-old woman who is struggling with depression, I see the influences of her family background, of her immigration experience, of her ambivalence about Western health care, of discriminatory government policies, of gender norms, of class dynamics, and of much more. I try to understand how all those factors interrelate. This is no abstract intellectual exercise. It is my job to take all these strands of this woman's life into account in trying to help her feel better. Sure, I recommend an antidepressant, but I also speak to her skepticism toward modern medicine, which has been shaped over generations, and I acknowledge the norms and dynamics within which she exists.

In my office, I have multiple chairs rather than a single couch. I try to have everybody (almost literally!) who has close ties to the patient in the room: family members; friends; a case manager; a therapist; a social worker; maybe even a parole officer, a guardian, an attorney, a housing rights advocate, someone from the clergy. The sense of collaboration generated by this roomful of people is my biggest joy.

My biggest frustration stems from the abundance of referral resources we have at our disposal. It's one thing to know where the closest homeless shelter is, but it's another to know which shelters accept women and children, which have short waiting lists, at which ones you need to start waiting in line several hours ahead to be assured of a bed – in short, which shelter is most suitable for a particular individual. The trick is to be able to recall exactly the right resource when a patient is sitting in front of you. And the really frustrating thing about having so many different organizations and resources is that while it's easy enough to refer patients here or there, it's also all too easy for patients to be shuttled around among well-intentioned individuals who keep shifting the responsibility for follow-through to the next person down the line.

Much of what community psychiatrists do is informed by raw experience, by the nitty-gritty details of actually caring for our patients. Every time one of my colleagues or I help a patient fight an eviction notice, for example, or sign up for an English class, or find a pharmacy in a safe part of town, we become a little savvier, a little more resourceful.







But at the same time, the day-to-day grind of focusing on our patients' compelling, individual needs has a downside. It can distract us from the big-picture issues that are an enormous factor in community psychiatry. I can spend hours on the phone going back and forth with a hospital in an effort to get one of my patients an inpatient treatment bed, for example. Yet in some ways I'm butting my head against a wall: the reality that there's a severe shortage of hospital beds for the sickest psychiatric patients. All those hours on the phone leave us no time to pause and think about, much less address, systemic issues like a lack of sufficient inpatient beds.

That's why I found my time in the UCSF Public Psychiatry Fellowship so affirming; it gave me a chance to get off the treadmill of my clinical training and examine big-picture issues. I'd spent eight years learning how to care for individuals. The fellowship allowed me to appreciate the equally powerful role a physician can play in the community. Although I was still in training, during my fellowship I worked as a staff psychiatrist at a community mental health clinic in Chinatown, gaining valuable firsthand experience. In addition, the public psychiatry residents participate in an intensive weekly seminar. Week by week, we focused on a different aspect of the community mental health system, learning from community leaders at numerous different organizations. We visited the county jail to learn about its mental health services. We rode along with law enforcement officers to learn about the mental health challenges they encounter. We also learned about the impact that legislation, funding sources, and various regulatory agencies have on our patients and our work.

Just as I was on the cusp of truly serving the communities I was longing to help, the fellowship served as a bit of a reality check. Every medical school applicant writes in their admissions essay that they want to "treat the underserved," but actually doing so isn't as easy as wanting to. Yes, I can accomplish a lot as an individual community psychiatrist. But my fellowship year made me aware that I still must work within a system, with multiple stakeholders, with countless restrictions and limitations on my clinical best judgment.

At the same time, the fellowship made me aware that there are incredible opportunities for collaboration within this system. Mental health is part of every major social issue of our time: housing affordability, criminal justice reform, economic inequality, you name it. We community psychiatrists have a chance to inject ourselves into discussions on countless consequential matters. That prospect simultaneously daunts me and inspires me on a daily basis.

Today, the feeling I get whenever a new patient walks into my office reminds me of the way I felt as a kid, when somebody boarded a bus on which I was a passenger: I may not quite know what to expect, but I feel curious and open all the same.

Richard Feng, MD, completed his residency in psychiatry and a fellowship in public psychiatry at UCSF. He is now an assistant clinical professor of psychiatry.

# Why We Need More Public Psychiatrists

Public psychiatrists – also called community psychiatrists – provide mental health care within the safety net, says Christina Mangurian, MD '03, MAS '15, who co-founded and co-directs the UC San Francisco Public Psychiatry Fellowship at Zuckerberg San Francisco General Hospital. "So think about it as the system of care where people who are uninsured or have public insurance, like Medicaid, can get psychiatric treatment," she explains. As treatment for mental illness gradually becomes less stigmatized, people with means can find care in the private sector, she notes. But there are fewer psychiatrists to care for the most vulnerable:

#### 40%

Proportion of psychiatrists who now work in private practices but accept only cash payments

#### 10%

Decline in number of psychiatrists working with public sector and even with privately insured populations between 2003 and 2013 Homeless individuals on the streets of the Bay Area represent the most visible public psychiatry needs, but they are just the tip of the iceberg:

#### 28,200

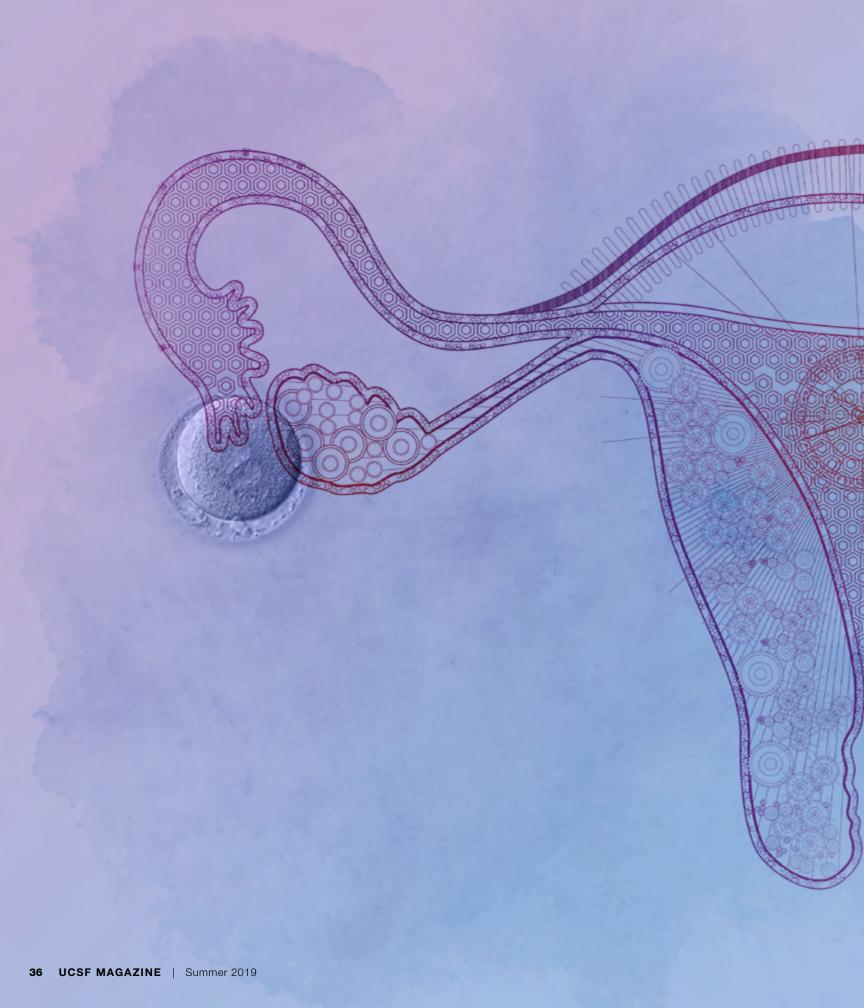
Estimated number of homeless in the nine Bay Area counties in 2017

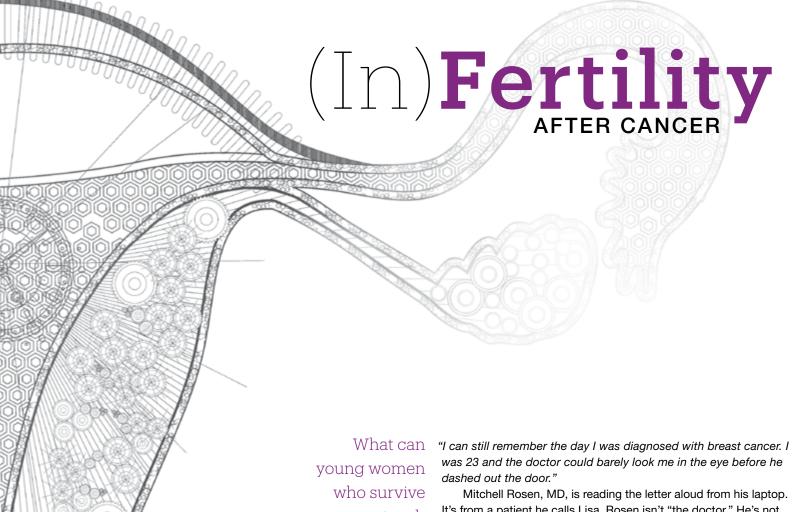
#### 45%

Proportion of homeless in Oakland who reported problems with psychiatric or emotional problems

#### 14%

Proportion of homeless in San Francisco and Alameda Counties who receive mental health services





young women
who survive
cancer teach
us about why
ovaries fail
decades before
other organs?

By Ariel Bleicher

Mitchell Rosen, MD, is reading the letter aloud from his laptop. It's from a patient he calls Lisa. Rosen isn't "the doctor." He's not even an oncologist. He considered becoming one after his brother died of cancer when Rosen was in college, but he knew he couldn't stomach the grief of regularly losing patients. Instead, he specialized in obstetrics and gynecology and went on to become director of the Fertility Preservation Program at the UC San Francisco Center for Reproductive Health, where he is an associate professor. The program, now one of the oldest and largest in the nation, has helped thousands of young people with cancer retain their ability to have children after treatment.

Fifteen years ago, however, when Rosen was just getting the program off the ground, few oncologists referred patients of childbearing age to fertility clinics, where they could choose to freeze eggs, sperm, or embryos before exposing their bodies to toxic cancer therapies. The risk of infertility was low, they were told. Only years later did they show up at the UCSF clinic – young survivors, mostly women, who had fought off cancer in their teens, 20s, or 30s and who were then struggling to get pregnant. Lisa was one of them.

"Once I was diagnosed and I asked about fertility treatments, a doctor advised, 'You are young. As long as you get your periods back, you'll be fine."

She had a lumpectomy, then six months of chemotherapy, which stopped her menstrual cycle. When she started to have periods again, she was relieved. But by the time she found her way to Rosen seven years later, she had all but given up hope of a child. She was 30 years old.

"Is it time to relinquish the dream of having a family of my own?" she wrote. She felt as if the ghost of her cancer had returned to mock her: "'I might not have taken your life, but I have taken something else.""

"This story was so emotional for me," Rosen says. He resolved to do everything he could to ensure that cancer patients like Lisa understood the real risks cancer treatments posed to their fertility and at least were given the option of fertility preservation. But what were those risks? Why and how – and to what extent – did young cancer survivors become infertile? No one knew.

In studying the problem over the past decade, Rosen has come to see it as an extreme case of reproductive aging – the decline in ovarian function that most women experience in their late 30s and early 40s. Cancer therapies, Rosen thinks, may cause this natural process to speed up, leading to the ovaries' early demise. If he's right, patients like Lisa may hold the key to an even greater enigma – one that is becoming increasingly salient as more women delay childbirth: Why do ovaries fail long before other organs?

#### A mysterious decline

Not until the Age of Enlightenment did people realize there is something unusual about ovarian aging. Before the early 1800s, most women died before reaching menopause. But as medicine and public health improved, life expectancy rose. This newfound longevity proved it was possible for organs – hearts, livers, brains – to last beyond a century. Ovaries, however, remained a stubborn exception. While the average American woman today will live to be 81, her ovaries will expire by age 51.

The explanation comes down to simple math. Contrary to male humans, who produce some 1,500 sperm every heartbeat during their entire lives, a female makes all the reproductive cells she will ever have before she is even born, at about 26 weeks' gestation. At their peak, these cells – immature eggs called oocytes – number around 6 to 7 million. As soon as they're created, however, the oocytes begin to die off. By the time a baby girl is born, no more than 2 million remain. By puberty, there are fewer than 500,000. With each menstrual cycle, some of the surviving oocytes – maybe 1,000 or so a month – begin maturing into adult eggs, but typically only *one* egg (or two, in the case of fraternal twins) leaves the ovaries to be fertilized. The rest of the maturing oocytes perish. Month after month, this attrition continues until the reserve of oocytes is nearly gone, signaling the start of menopause.

But this story begets a mystery: Why so much loss? How does it happen? And can it be stopped?

Rosen came to UCSF in 2002 as a medical fellow to help answer those questions. His mentor, Marcelle Cedars, MD – now the Laura

Ambroseno and Raffaele Savi Family Presidential Professor and director of both the UCSF Center for Reproductive Health and the Division of Reproductive Endocrinology – had a deep-seated interest in solving infertility. Cedars had come of age "on the coattails of women's liberation," she says. "Women of my generation were told, 'Get your career; fertility will always be there.' But it was a trap. The reality is, men and women are not equal in terms of time to have a family, and that became a very big issue for us." Although she was able to have children in her late 30s, she says, "lots of my peers could not."

Cedars sought to find genes and other molecular markers that could inform women how – and how fast – their ovaries were aging. Starting in 2006, her team enrolled 1,100 reproductive-age women

She felt as if the ghost of her cancer had returned to mock her: "I might not have taken your life, but I have taken something else."

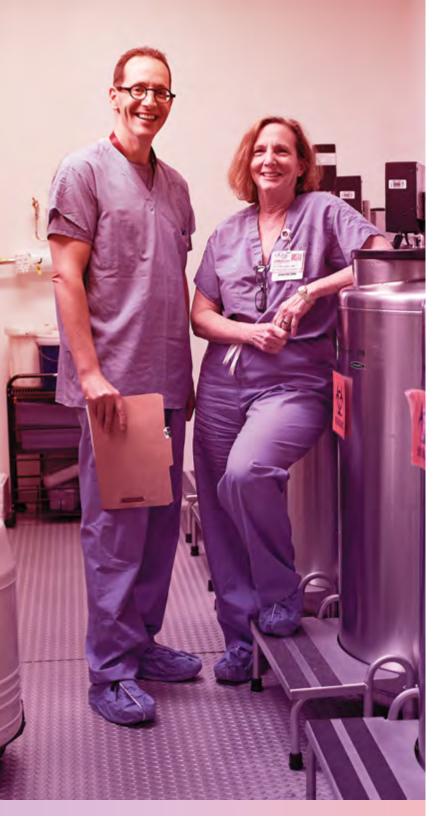
of diverse ethnicities in what came to be called the Ovarian Aging Longitudinal Study, or OVA. Still ongoing, the study remains one of the largest and longest-running of its kind. (Cedars' team recently expanded the study's scope to also explore the link between ovarian aging and cardiovascular disease. "We believe the ovary is a window into a woman's future health," she says.)

Meanwhile, Cedars and Rosen (who joined the UCSF faculty in 2005) were seeing more patients like Lisa – young women who had beaten cancer but were now facing the early loss of their fertility. Tests suggested that their ovaries had unusually low numbers of oocytes for their ages. Some patients had already started menopause. "This process that might normally be happening at age 41, it's now happening at, like, 31," Rosen says. "That was very puzzling."

He began to suspect that this accelerated decline in fertility was more common than oncologists knew. To confirm his hunch, he and his colleagues surveyed more than 1,000 women across California who had been diagnosed with cancer before age 40. As previous data had shown, fewer than 10 percent lost all function of their ovaries for good immediately after treatment. But Rosen's team found that many more patients got their periods back only to suffer infertility later in life. Among those who underwent chemotherapy for breast cancer, for example, nearly two-thirds were unable to conceive and more than a quarter reached menopause before age 45. Almost no one had been referred to a fertility specialist at the time of diagnosis.

For Rosen, the findings were a wake-up call. "As a medical community, we had been really underestimating the true impact these cancer treatments had on these women," he says. Between his teaching and his clinical duties, he drove around California telling





Mitchell Rosen and Marcelle Cedars, shown in the UCSF embryology laboratory, are working to solve the mystery of ovarian aging in order to predict — and perhaps even extend — a woman's reproductive lifespan.

Lisa's story to physicians, philanthropists, politicians who set health insurance policies – anyone who would listen. He wanted women like Lisa to have the information she did not – to know what they were up against and to be given a choice to do something (freeze their eggs, for example) before it was too late.

But Rosen had another motive, too: He wanted patients to come to UCSF. "I really thought we could take care of them the best," he says. More than that, he believed these women might help him decode the mystery of ovarian aging – not just for cancer patients, but for all women trying to plan for a family. "That's what I'm trying to figure out – whether we could predict when the reproductive window will end and know what's causing the problem," he says. "Then maybe we can fix it."

#### Cancer's double blow

Two months before she was supposed to be married, in December 2016, 31-year-old Stephanie Chuang woke up with a cough. The sound – deep and guttural – was so foreign, she immediately saw a doctor, who ordered a series of chest scans. The call came the next evening: "I'm so sorry, Stephanie; it looks like lymphoma."

"My heart dropped," Chuang recalls. "The thing I thought about right after my mortality was my fertility. I always knew that I probably wanted children. I didn't want cancer to rob me of that possibility."

A week later, after surgery and more tests, she met with Rosen. By then, he had expanded the Fertility Preservation Program to accommodate more than 200 referrals a year. He had also begun following many patients after their cancer treatments – tracking the health of their ovaries as they aged and seeing how their reserves of oocytes dwindled over time. Chemotherapy, he told Chuang, would likely cause her to promptly lose a large portion of her reserve, essentially inducing years of aging in just months.

The reason for that isn't entirely clear, Rosen says. But his and others' work at UCSF has led to a theory. Chemotherapy, he explains, targets fast-dividing cells. That includes cancers, of course, but also hair follicles and blood cells. Maturing oocytes, too, are likely victims because the cells surrounding them, which support their development into eggs, are growing rapidly. Chemotherapy probably kills most, if not all, of these ballooning balls of cells – called ovarian follicles. But the decimation doesn't end there. The sudden extinction of the growing follicles triggers new waves of oocyte maturation – a kind of overcompensation – thus forcing thousands of would-be eggs into the cycle of growth and death before their usual time.

Diana Laird, PhD, a UCSF associate professor of reproductive sciences, explains it this way: "You're withdrawing more heavily from your bank account, so you deplete your bank account faster." Laird has found evidence of this snowball effect in chemotherapy-treated mice. Her lab recently pioneered technologies to image the animals' ovaries in three dimensions so she can count oocytes directly – something that can't be done in humans. "It's a pretty profound loss



#### WHAT ABOUT EGG QUALITY?

A woman's ability to bear children – cancer or no – depends on more than the number of oocytes (reserve eggs) she has left. It's well known that as a woman's age goes up and her oocyte quantity goes down, so does oocyte quality. Around age 35, although a woman's ovaries may still harbor hundreds of thousands of oocytes, her probability of getting and staying pregnant has already begun to wane. By her early 40s, that probability is less than 10 percent.

Experts debate how the declines in oocyte quality and quantity are related. Marco Conti, MD, the director of the UCSF Center for Reproductive Sciences, maintains they are "two distinct events" that just happen to more or less coincide. Their causes – as well as potential diagnostic markers and treatments – are likely different, he suspects.

Unlike quantity, he points out, quality depends heavily on chromosomes - the molecular packages that hold a cell's DNA. When scientists look inside a woman's eggs, they tend to find more problems with their chromosomes the older she is. At age 42, for instance, an estimated 80 percent of oocytes have chromosomal defects bad enough to result in failed conception or miscarriage. Why that's the case is still an open question. One hypothesis blames the molecular machinery that organizes and rearranges chromosomes so that heritable traits can be passed from parent to child. Like an old car, Conti says, this machinery "may progressively become faulty with age."

Marcelle Cedars, MD, the director of the UCSF Center for Reproductive Health (CRH), likewise insists that "quality is not linked to quantity." But Mitchell Rosen, MD, who directs the CRH's Fertility Preservation Program, disagrees. ("We debate a lot," Cedars says. "That's part of the fun of working together and how we get to the right answers.") "There is a relationship," Rosen argues. "The whole world of fertility practices by it. When we see a patient, and there's a good ovarian reserve, we feel better. Why? Because we really do think it matters. The exact formula and how it works has yet to be determined, but we do see a connection between how many eggs are left in your ovaries and your ability to conceive."

Diana Laird, PhD, a UCSF associate professor of reproductive sciences, thinks this connection might originate at the very beginning of an oocyte's existence. She has discovered, for example, that in the ovaries of a mouse fetus, oocytes rearrange their chromosomes at different times and at different rates. The last oocytes to complete this early development also seem to be the last ones to later begin maturing into eggs in the adult mouse. In humans as in mice, she points out, it's those late bloomers that tend to have the most chromosomal defects. "Is it possible that some of those defects arose when a woman was in utero?" she wonders.

If that's true, it's also possible that cancer therapies – which appear to speed up oocyte loss – simply force the ovaries to use up their "good" eggs faster, leaving the "bad" ones behind. But that's just a guess, Laird says. "Once we find the mechanisms that are important in normal ovarian aging, then we can go back to the cancer case and ask, 'Is it similar or not?'"





that we see," she says. She speculates that a woman's ovaries might use some as-yet-unknown cellular signaling to choose which oocytes to mature and which to kill – and at what rates – and chemotherapy disrupts this communication.

Before starting her own chemotherapy, Chuang decided to have Rosen's team surgically extract her most mature follicles, fertilize the eggs with her fiancé's sperm, and freeze the embryos. They were able to save 13. "I felt this could be my only shot at possibly having my own biological children," Chuang says. "It gave me peace of mind just knowing those little guys were there."

Yet when she returned to the UCSF fertility clinic a year and half later - after her cancer was gone and her periods had returned - she was disheartened. Just as Rosen had predicted, her reserve of oocytes appeared to have shrunk significantly. She doesn't want to say how much. "Honestly, it still feels like a loss I haven't fully reconciled with," she says. "As a woman, I do feel a little 'less than.'" Even though she had the 13 frozen embryos as a back-up plan, she knew a baby wasn't guaranteed. Calculating success rates for in vitro fertilization (IVF) is complicated, but the chance of an embryo transfer resulting in a live birth tend to start around 40 percent for women younger than 35 and to get slimmer as women get older.

Chuang is now part of an ongoing UCSF study led by Rosen and clinical fellow Kaitlyn Wald, MD, to better understand the long-term effects of chemotherapy and radiation treatments on fertility. "We've discovered that women who do have cycles drop their [oocyte] volume about 50 percent," Rosen says. "What we don't know is what happens next. Do they continue to have the same rate of loss? Does it go up? Does it go down? If I knew that pattern, I could tell my patients, 'This is how much time you have left to have kids.' That would be extremely powerful."

### **Restoring hope**

Both Rosen and Cedars concede it will likely be years, if not decades, before they can definitively answer the questions every hopeful parent asks: Will I be able to have children? For how long? Understanding ovar-



Stephanie Chuang, creator of thepatientstory.com, is part of an ongoing UCSF study to better understand the long-term effects of cancer treatments on fertility.

## "Honestly, it still feels like a loss I haven't fully reconciled with."

ian aging will require not only close clinical observation but also deeper knowledge of women's reproductive biology. To that end, they say, they are fortunate to have collaborators like Laird and other basic scientists at the UCSF Center for Reproductive Sciences - including Marco Conti, MD, the center's director and UCSF's Fred Gellert Professor, and Aleksandar Rajkovic, MD, PhD, a professor of pathology and UCSF Health's first chief genomics officer - who are probing fertility's genetic and molecular underpinnings.

"Together, I think we'll solve the mystery," Cedars says, "although what we find may be very different from what we expect."

In the meantime, she and Rosen remind their patients that uncertainty, however unsettling, can also be cause for hope. Last December, two years after her diagnosis, Stephanie Chuang came home from vacation with her now-husband to find she was pregnant. Rosen had recommended the couple try conceiving naturally before resorting to IVF. "We weren't expecting anything, and then boom - a miracle baby," she says.

She believes she got lucky. "I don't know about the future," she says. "If we want more children, maybe it won't be so easy."

Lisa, too, found luck in the end. When she came to the UCSF clinic back in 2009. she'd already tried IVF three times, without success. But, Rosen says, "we made it happen for her." When she learned she was expecting, she sent him a letter:

"To simply say 'thank you' does not seem fitting in view of what you have done for us. You have not only helped us achieve a dream that was feeling like it was never going to come true but have helped restore our sense of faith and hope."



## **ALUMNI HUB**

#### The Passionate

Across the country and around the world, UCSF alumni are making waves in their fields and putting their passion, skills, and dedication to work in their communities. Meet five alumni recently honored in four UCSF: The Campaign

- The Dedicated
- The Compassionate

Alumni Award categories:

- The Innovators
- The Audacious

## Alumni

Join us to celebrate and reconnect next year. Mark your calendars for Alumni Weekend, June 5-6, 2020.

alumni.ucsf.edu

## Kimberly Topp, PhD, **Postdoc Alumna:**

Married to UCSF and loving it

Kim Topp was the first person in her blue-collar family to go to college, and the degree did not come easily.

in the 1970s, when it was still a nascent field. "I chose physical therapy specifically because we work hands-on with people and can have a positive impact on their mobility and quality of life," Topp says. One of her formative experiences was volunteering at a preschool

for children with autism and realizing the power of working one-on-one with someone in need.

Topp started her UCSF career as a postdoc in 1990; joined the faculty in 1993 as a member of the departments of Physical Therapy and Rehabilitation Science and of Anatomy; and "retired" in July 2018, following 25 years as a faculty member, 11 of them as chair of Physical Therapy. However, she's still active at UCSF, doing research and helping her successor as chair sometimes working remotely to avoid the 80-mile commute from her Aptos home.

"My very supportive husband understands that I'm married to UCSF," Topp says. No wonder she received a UCSF Campaign Alumni Award as one of The Dedicated. She uses the word "devotion" to describe her feelings for UCSF; her department; her field; and her patients, colleagues, and students. "UCSF is a phenomenal place," she adds, "and I love what I do."

During her tenure as chair, Topp expanded the department's offerings, spearheaded a doctorate in rehabilitation science and an entry-level Doctor of Physical Therapy program, created the interdisciplinary Clinical Skills Center, added physical therapy residencies and faculty practices, and strengthened the curriculum in anatomy.

"I'm very proud of having had 25 years of students in physical therapy and medicine," Topp says. "Now I see them reaching their potential in clinical care, advanced training, policy change, global health, and other areas."



#### Robert Ho, DDS '91:

## Taking care of people by caring for their teeth

Robert Ho has a knack for knowing what his patients really need – even when it has nothing to do with their teeth. A patient once paid him with a burrito for staying late to fix his very painful tooth. To another patient he said, "No payment is necessary; use the money to buy diapers for your newborn baby."

Ho doesn't see anything odd about his tactics. "What it comes down to is taking care of people," he says. "That's one of the values I received as a student from my mentors at UCSF: Develop lifelong relationships with your patients."

Ho was nominated as one of The Dedicated by students and colleagues who marvel at his zeal in teaching his students and caring for his patients.

An expert at dispensing fluoride and flossing directives, Ho is also one of those rare medical professionals who senses what people really need. Recently, he visited a longtime patient who was in the hospital fighting what appeared to be a losing battle with cancer.

"I came to schedule your six-month cleaning appointment," he told the man upon arriving at his bedside. Behind his oxygen mask, the patient broke into a wide grin. Six months later, he sat in the dental chair, getting his teeth cleaned and thanking Ho for bringing him and his family - hope.

"I share those stories with my students to inspire them, to remind them why we're doctors: to help people, first and foremost," he says. "To give back. I find great joy in that."

Ho comes by these instincts honestly. In 1975, he was 10 years old when Vietnam collapsed, and his family boarded a transport plane for the United States. With just \$200 in their pockets, the family of five landed in San Francisco to start their new life. The children learned English and earned good grades in school - Ho's were high enough to gain him admission to UCSF's School of Dentistry. Gratefully, he made the most of his opportunity. And he has always remembered his roots.

"As doctors, we struggle just like everybody else," he says. "These stories remind me of all the hardships I went through to become a doctor."



#### Luisa Buada, BSN '77, MPH:

## Creating healthier communities, one patient at a time

Calling Luisa Buada one of The Compassionate is surely an understatement in light of all she has achieved as an advocate for the underserved.

Buada has been instrumental in ensuring that residents of San Mateo County and the larger Bay Area region receive access to high-quality health care, regardless of their income or insurance status.

The daughter of a Filipino farm worker and a nurse, Buada has been a lifelong supporter of farmworkers' rights and health care for all. As a teenager, she witnessed the poor health conditions of migrant and seasonal farmworkers while volunteering with the United Farm Workers' Union alongside César Chávez. The experience spurred her to help improve those conditions.

Just out of nursing school, Buada founded Clínicas de Salud, a community health center and specialized clinic for Salinas Valley farmworkers. She also founded the Berkeley Primary Care Access Clinic and was integral in the establishment of LifeLong Medical Care, both of which offer much-needed health care services and programs to low-income populations.

Buada has served for the past 15 years as director of the Ravenswood Family Health Center in East Palo Alto, an organization that sees more than 17,000 adults and children annually - predominantly low-income, uninsured, and undocumented residents of Palo Alto, Belle Haven, and North Fair Oaks. Under Buada's leadership, Ravenswood has grown from 13 employees to more than 200.

In 2018, Buada received the California State Assembly Woman of the Year award in recognition of her public service to the 24th Assembly District.

"It is an honor to recognize Luisa for her extraordinary work in the 24th Assembly District," said Assembly member Marc Berman. "For more than three decades, Luisa has expanded access to health care for tens of thousands of residents who would not have care otherwise. With limited resources, Luisa is creating healthier communities, one patient at a time."



## **Andrew Plump, MD '95, PhD:**

## Unraveling the science behind heart disease

Andrew Plump will never forget the Saturday night in 1992 when he saw proof that he had indeed given heart disease to a mouse using genetically manipulated embryonic stem cells.

"The icing on the cake was that these mice developed atherosclerosis," Plump recalls. Until then, mice had never shown any evidence of the very human condition of heart disease. "My model became the gold standard for studying the genetics and pharmacology of heart disease."

Clearly a defining moment in his career, the experience at New York's Rockefeller University was both a hard-earned lesson in the rigors of science and the ultimate preparation for his future in drug development. It also led to Plump's nomination as one of The Innovators, as his work has had far-reaching impacts for his fellow scientists, as well as medical doctors and patients.

"If I knew at the beginning what I knew after the first year, I don't know if I would have ever chosen to experiment with stem cells and mice," he reflects.

"I was really trying to unravel disease biology, and in particular, cardiovascular disease, so I jumped in headfirst. I worked 16 hours a day. I learned and I learned and I learned. I failed and I failed and I failed. But eventually, I pushed the science forward."

On leave from UCSF at the time, Plump, who is also a resident alumnus, considers the University instrumental in guiding him toward his discovery. He calls the day he was admitted to UCSF's School of Medicine one of the proudest days of his life.

"This institution embraces diversity in a way that makes it great. It is the ability to stitch together not just science and medicine but science and medicine and policy and ethics and diversity to create an institution that really is leading-edge in terms of how we think of health care," he says. "I believe in a collaborative approach to medicine. I learned that at UCSF."

In the trenches, Plump also learned that the scientific process to find new drugs is a 10- to 15-year journey in its most accelerated form. But he calls that process his "sweet spot," and now, as president of research and development at Takeda Pharmaceuticals, Plump leads teams in discovering medical treatments that put patients first. "I discovered that what drives me is the potential to make a positive impact for patients," he says.



#### Linda Bernstein, PharmD '77:

## Blazing a trail mixing pharmacy and media

Harnessing the power of media to educate patients and professionals came naturally to Linda Bernstein – whether it was featuring medication tips on a cereal box or producing and hosting a pharmacist TV series.

A clinical professor on the UCSF School of Pharmacy's volunteer faculty and an expert in medication misuse, Bernstein knew what most people didn't about their medicines – and what they didn't know was hurting them.

"Media-based consumer and professional education became the thrust of my career," says Bernstein, who founded Vita Media Corp., a medical communications company. "As a media pharmacist, I could teach millions about medicines and living healthier lives."

Her decision was groundbreaking. The media regularly turned to doctors to explain medical mysteries – but pharmacists? Not so much.

Her inaugural project, *The Lub Dub Club*, a preschool heart health curriculum, was a hit. TV spots for KQED – featuring the Pickle Family Circus expounding on poison prevention, healthy eating, and exercise – followed.

Next, the woman UCSF named as one of The Audacious aimed her advice at adults. *In the Medicine Cabinet*, a Sunday radio program, ran for 10 years. KTVU aired 52 *Your Consumer Pharmacist* vignettes. Appearances on television morning shows followed. She was media spokeswoman for Safeway Pharmacy, sang kids' health tips on PBS, and wrote health columns and a book, *The Family Vacation Health and Safety Guide*. Her travel health tips even popped up on United Airlines' in-flight television service.

Eventually, Bernstein used media to teach pharmacists. When *Pharmacy Education on the Air* was first broadcast on Lifetime TV, more than 500 pharmacists called for continuing-education credit. "I knew I had struck a nerve," she recalls. More kudos followed. She, along with executive producer Eric Herfindal, PharmD '65, MPH, received the C. Everett Koop, MD, Award for best professional film at the 1994 International Health and Medical Film Festival for *Alzheimer's Disease: Current Concepts in Management*.

It was never easy, but Bernstein believed in herself and her work. "Plenty of doors closed in my face. But I knew these educational programs were of such value to patients and my profession that if I wanted to do it, I had to fight for it. It was as simple as that."





For months, the 78-year-old\* had been behaving strangely. Fearing the worst, his family consulted UCSF neurologist Georges Naasan, MD.

As told to Ariel Bleicher Illustrated by **Eleanor Davis** 

Georges Naasan, MD

**UCSF Memory and Aging Center** 

The patient was severely paranoid: He thought the hospital staff was out to get him. Most doctors would have diagnosed dementia, but I knew this wasn't your typical case.

HYDLUNTARY

Му bones hurt.

Food tastes bad.

You're not a real doctor!

> Dad is normally so sweet.

> > He tore up the intake form and ate it!

Testing was hard. Everything was a negotiation.

We need to draw some blood.

I'll only give you three tubes.

How about five?

The MRI and spinal tap results were unremarkable.

If it really is dementia, we'll take him back to Ohio to care

> for him - and say goodbye.

Killer immune cell

> Tumor antibody

Finally, after two weeks of searching, we found a molecule in his blood - an antibody - that suggested his immune system was attacking his brain.

This is very rare, but it can sometimes be triggered by cancer. We scanned the patient and found colon cancer.

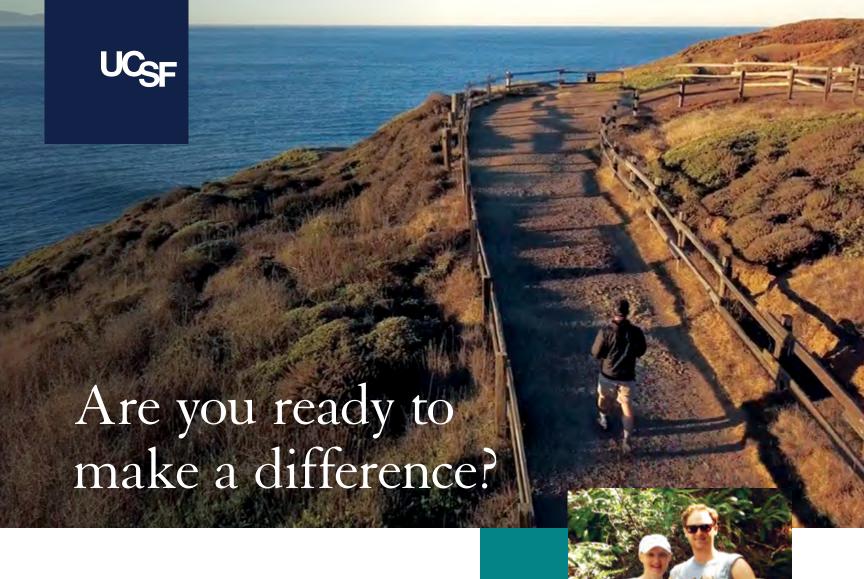
If we treat your father's cancer, his cognitive problems may go away.

Thank you for not giving up!

> Thank you for trusting me.







In May 2014, Karen Orofino lost a two-year battle with ovarian cancer. In the years that followed,

\$100,000 for ovarian cancer research at

UCSF, through hikes and bike rides that keep
his mom's memory alive. Thanks in part to his
efforts, a clinical trial is currently underway for a
test to detect ovarian cancer in its earliest stages.

#### Are you ready to help change lives?

You can inspire your community to advance lifesaving research and improve health.

Visit *together.ucsf.edu* and create a personal fundraising page to honor a loved one or to campaign for a cause that matters to you.



