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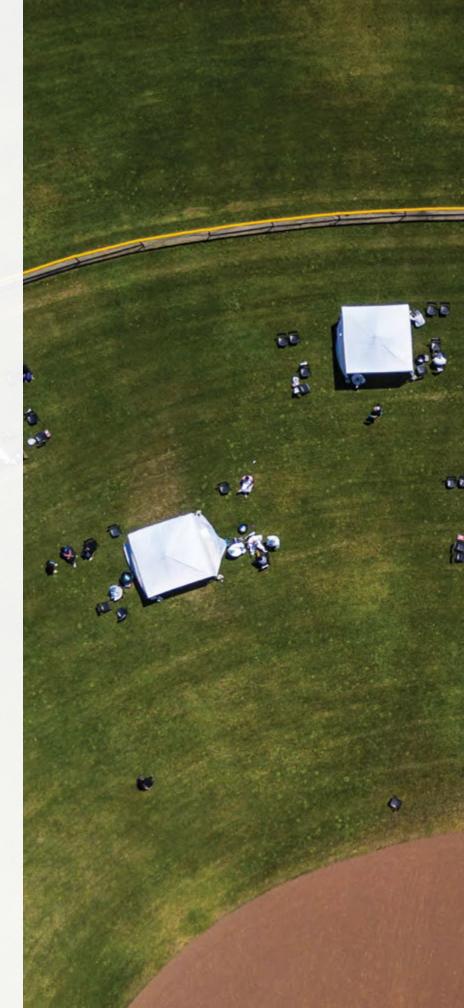
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# Meeting This Moment

These are not normal times, and this is not a normal issue of UCSF Magazine.

We have dropped our usual roundup of breakthroughs in science and medicine to devote every page to the pandemic. By now, you've likely consumed volumes of information about COVID-19, but I am confident the unique perspectives, deeper context, and important lessons learned in these pages will broaden how you think about this disease.

We activated UCSF's COVID-19 command center on February 2, Super Bowl Sunday, which was very early compared to the rest of the country. We admitted our first case the next day; it was thought at the time to be one of the first documented cases of community transmission in the U.S. It was clear then that our institution, our state, and our country were headed into trouble, and that UCSF would have an important leadership role to play.

In those early days, it quickly became clear to us that the incapacity to test at scale was one of UCSF's (and the country's) greatest weaknesses. Joe DeRisi, PhD, a top virologist and legendary problem-solver, came to me and said that he and the Chan Zuckerberg Biohub, which he co-leads, could contribute in a major way. I was thrilled but a little bit skeptical given all the hurdles that were aligned against such an effort. The unlikely story of how his team and a cadre of UCSF graduate students managed to build what Bloomberg called "the COVID test lab that could save America" starts on page 22.

In 1982, at the beginning of the HIV/AIDS pandemic, I arrived at UCSF as a postgraduate student. I witnessed the University rally in much the same way we have in recent months,

pivoting many of its labs and clinics to face a new disease that no one knew anything about. That crisis changed our clinical culture, and many of UCSF's leaders today "grew up," so to speak, during that time. It has influenced our collective thinking about what it means to be a public university and our role in the public health space.

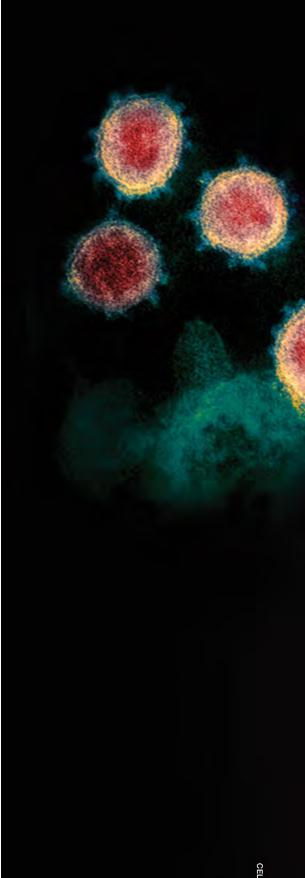
Ten years from now, when we look back to today, I know we will see something similar. The graduate students running COVID testing in the Biohub; the young trainees and health care providers on the front lines; and our students, who found creative ways to volunteer at the very moment they were also asked to adapt to online learning - all these remarkable individuals will find their careers transformed by this moment.

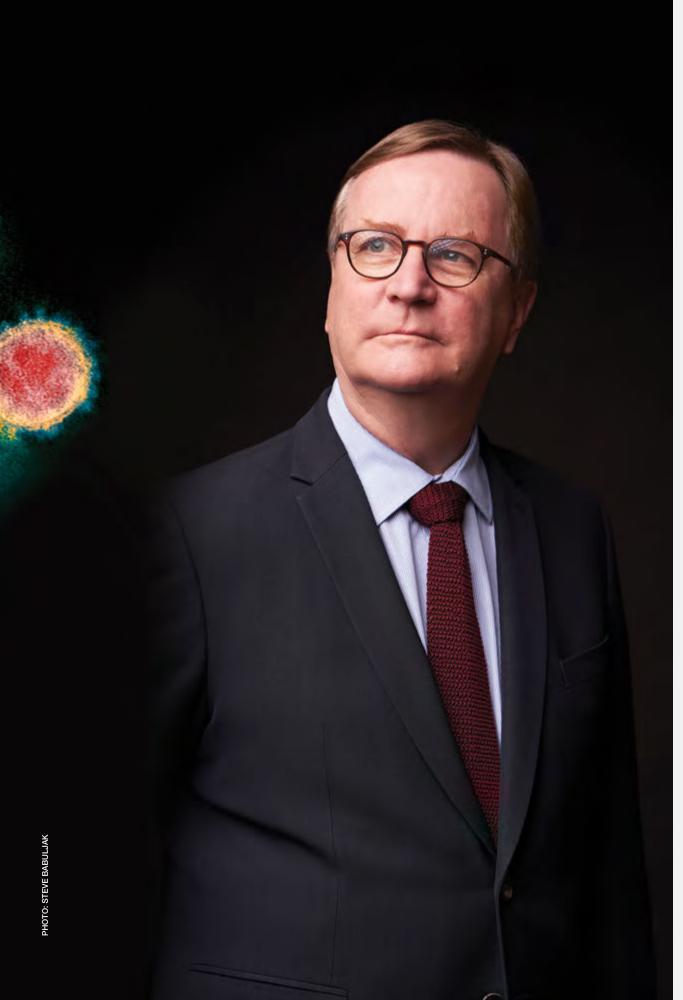
The can-do culture, the confidence that they can make a difference, and the instinct to act boldly to support the community will be lifelong lessons for them - much like HIV forged life lessons for those of us who were at UCSF in the 1980s during our own formative years.

As chancellor, I could not be more proud of how our community has risen to face this pandemic. The frustrations, the uncertainties, the risks, and the tragic losses of this moment are burdens every one of us must carry, but I trust that in these pages you will find some measure of wisdom, hope, and inspiration.

Sam Hawgood, MBBS

Arthur and Toni Rembe Rock Distinguished Professor





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# They Called Us Heroes

We were just doing our jobs.

Contributors: Ariel Bleicher; Allison Bond, MD; Katherine Conrad; Susan Godstone; Ann Brody Guy; Anne Kavanagh; Mika Rivera; and Beth Tagawa



## The ICU Nurse A Huge Responsibility

Kelly Timothy, RN, an intensive care nurse on UCSF's COVID-19 wards, cares for some of the Bay Area's sickest patients – and their families. In her own words, she describes how UCSF transformed its ICUs for COVID-19 patients, and why she's proud to be doing essential work.

I've been a critical care nurse for more than 10 years. I like the frenetic, fast-paced environment. ICU nurses have a heightened sense of what's going on around us. You see somebody walking fast down the hallway, and you know something is wrong. If a patient is very sick, a whole swarm of nurses will converge in their room.

A lot of our ICUs are so big that they cover multiple floors. I work in the medical-surgical ICU on the ninth and 13th floors of the hospital at Parnassus Heights. Those floors are where many of our COVID patients go if they need to be intubated and put on a ventilator. It's hard to convey how insanely different the space is now. Visitors are very limited. Until recently, nobody was coming in for elective procedures. It feels like a much smaller place.

The other thing that's really strange is that all the doors in the entire unit are shut. When the hospital began preparing for a surge

of COVID patients back in February, the facilities staff converted all the patient rooms in our ICU into negative-pressure rooms. These are rooms that, when the doors open, the air sucks in, which helps keep virus particles from getting out. The only way to maintain that is by shutting the doors.

Often, it's just me in a room with a patient. If they're really sick, they might have five or six different teams of providers working with them, but most of those providers can't come into the room because we can't have people constantly going in and out and using up PPE. Instead, I communicate with the other providers through a closed glass door. It's super-loud in the rooms because of the intense HEPA air filters, so I'm writing a lot of notes and shouting through the glass.

Once we opened up the hospital to transfer patients, we started



Kelly Timothy, captured via FaceTime in her San Francisco home on June 10 at 11:15 a.m.

because he was intubated for over 30 days. I took care of Ron almost every shift for an entire month. We did a daily Zoom call with his family. He was heavily sedated, but they just wanted to see him and talk to him. I can only imagine what it's like to have a family member who's very ill, and you have no control. Often, these families are told that their loved one has a very high likelihood of dying. Talking with them and supporting them is a tremendous responsibility.

to get extremely sick COVID patients from other hospitals.

They can take a really, really long time to get better. Some-

There was one patient, Ron Temko, who made the news

times they end up intubated for weeks and weeks.

In a sense, I got to speak more with Ron's family than I did with him. He probably doesn't even remember most of our time together. But just seeing the dedication of his family and of all the people who were trying to contact him, I thought, "He must be the coolest guy."

After more than 40 days in our ICU, Ron was transferred to UCSF's Mount Zion hospital to recover for a couple weeks. I got to work there the day he was released. The last time I'd seen Ron, he'd been struggling to stand up. That day, he just hopped out of bed and said, "Look what I can

do!" He looked great; he looked just like a regular person. It made me so happy because we really did not think he was going to make it. I thought, "This is what we do this work for."

I pushed him out of the hospital in a wheelchair. I knew his family was waiting for him, but I was not expecting a crowd. When we came out, people were cheering and waving signs. Ron gave this whole speech. It was really cool and gratifying to be a part of that.

I know it sounds like a cliché,

but I'm really proud to be a nurse at UCSF during this crisis. I've been watching the medical grand rounds on Zoom, where our leaders talk about how everyone is responding – like how our grad students are running COVID-19 tests for all of California and how we're sending teams to help out in New York City and the Navajo Nation.

I love hearing those stories because they make me feel part of a close-knit community. At times, UCSF can feel like this huge, intangible thing. Now I see the interconnectedness, how we're all contributing to this greater goal.

It sounds like we're going to be taking care of COVID patients for a very long time. But to be quite honest, I've felt lucky to be an essential worker. I'm able to be useful. I feel like I've developed my skills specifically for this moment.

#### The Fresno ER Doc Healing the San Joaquin Valley

In a region where doctors are in short supply and poor health is widespread, UCSF Fresno emergency medicine physician Kenny Banh, MD, fights both COVID-19 and inequity.

UCSF Fresno is the biggest provider of care for underserved populations in the San Joaquin Valley. How many patients does your hospital's emergency department serve? I work at Community Regional Medical Center (CRMC), UCSF Fresno's biggest partner hospital. Our emergency department sees about 115,000 patients a year. To put that in perspective, UCSF's largest teaching hospital sees about half of that volume. We're the only Level I Trauma Center between LA and San Francisco.

In early April, CRMC erected triage tents to prepare for a surge of COVID-19 patients. How did that play out? Our cases never spiked, but they have grown incrementally. COVID is now an everyday diagnosis.

What are some of the health problems in the valley that make COVID-19 especially dangerous? We have high asthma rates, which are tied to poor air quality. Valley fever, a fungal lung disease, is also pretty prevalent. Imagine if coronavirus knocks out half your lung capacity. If you don't have full capacity to begin with, you might not have the reserve to survive.

COVID-19 is hitting the Latino population hard. Are you seeing that in the ER? If you look at hospitalizations, the percentage of Latino patients is fairly high. If you look at what I call the "worried well" - the people who walk into the ER who think they might have been exposed - they are predominately not Latino. It's a systemic issue. In general, our Latino and African American community members are disproportionately working hourly jobs that don't offer sick leave or health insurance. For them, how is finding out if you are positive for COVID a good thing? I'm not saying it's right. We should be testing, but it's a real issue.

You have a plan to improve access to testing. Can you tell me about that? If you look at a map of Fresno, most testing sites are in well-off districts. Drive-through clinics, for example, which are well intentioned, exclude people who don't drive or who can't use an

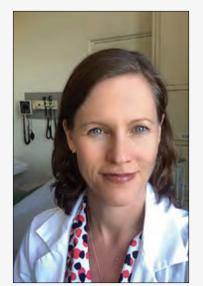


Kenny Banh, captured via FaceTime in the Community Regional Medical Center's COVID-19 evaluation unit on June 9 at 2 p.m.

app in English to schedule an appointment.

I run a free mobile health care clinic, which we had to shut down when the coronavirus hit. Now I'm trying to get funding to convert it to a mobile testing clinic for at-risk populations: our Latino and African American communities, our undocumented farmworkers, and our homeless community.

You're also the father of three young boys. How are you holding up? People are always wondering if I'm OK. I'm great, because this is why I went into medicine - to take care of really sick patients. Frontline doctors get recognized all the time, and I'm grateful for that. But I'll tell you who my health care hero is: a janitor at my hospital. This guy works like a machine. He turns over rooms, he flies around scrubbing floors. He's working for barely above minimum wage, and he's laying his heart out for it. He's the one keeping me safe.



Annie Luetkemeyer, captured via FaceTime at Zuckerberg San Francisco General Hospital on June 9 at 5:15 p.m.

#### The Clinical Trial Leader Searching for the Silver Bullet

It's a rare day when Annie Luetkemeyer, MD, puts in fewer than 12 hours at Zuckerberg San Francisco General Hospital. A UCSF physician-researcher, Luetkemeyer previously helped advance effective HIV drugs and a cure for hepatitis C. She is now leading clinical trials of promising therapies for COVID-19, including the antiviral drug remdesivir and convalescent plasma, and will soon be running vaccine trials. "Clinical trial participants are the unsung heroes in medicine, certainly in the COVID epidemic," she says. "It was remarkable that despite being sick and scared, many patients said, 'All right, I want to participate, even if this study may not help me, so I can help others."

#### **The Volunteer**

#### Lending a Hand in the Navajo Nation

The small city of Gallup has only 3% of New Mexico's population but, as of mid-July, nearly one-fourth of the state's COVID-19 cases. Alicia Catanese, RN, a surgical charge nurse, joined a UCSF Medical Center team in April and spent two months helping the Gallup Indian Medical Center cope with its COVID surge. The facility serves the nearby Navajo Nation reservation.

What is the situation like there? From the time we arrived, we have been going, going, going. That really shows you what kind of clinician you are, but there's also an understanding of the big picture: that we're here to help and to serve this community. That was the driving force behind our coming here.

How is it different from working at UCSF? This is a very small, community-based hospital. They don't have the resources that we have, so they have to send out a lot of their more critical patients to Albuquerque or Phoenix, to larger hospitals.

At UCSF we're one of the top hospitals, so we usually receive a lot of patients. Being on the receiving side is very different from sending people out. When we don't have something we need, I'm like, "Oh no, we don't have that!"

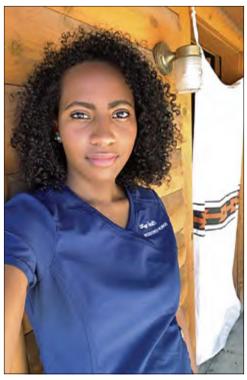
But the local staff knows the flow. They're so incredibly skilled. They know exactly what the patients need and when we just can't offer it here.

What else is different? You're catering to a different community, learning what that means.

Part of that was learning how they deal with death. They have a four-day process to complete burial ceremonies. They believe after four days a person's spirit has left the body.

It really puts things into perspective when we send people to Albuquerque. If the patient doesn't make it, the family has to travel there to receive the body. If it's not within the four days, then that really shatters their coping process. Knowing that furthered my empathy.

The Navajo Nation has been a COVID-19 hot spot. What's the protocol when people come to the ER? The first two weeks, we were just testing, testing, testing. Some people would be asymptomatic but had possible exposure from family members. We were giving everyone a mask to go home with. If they



Alicia Catanese, captured via FaceTime at the Gallup Indian Medical Center in New Mexico on June 10 at 1:15 p.m.

were symptomatic, we would send them to a nearby hotel or motel to self-quarantine.

What have you learned about the community that you're serving? They have a lot of pride in themselves and in their community for being the original people here. It helps me understand their history a little better. Just sitting with them and listening to their stories helps me understand a lot of the disparity and tragedy that they've had to endure over the years.

Anv other lessons vou've learned? I love being here. I really do. It's been such a joy and an honor, in this really crazy, tragic time, to still be able to serve and love people really well. This is why I became a nurse. I always tell my patients, "I feel like I'm learning so much more here with you in this space than maybe I'm giving to you." They tell me, "No, no, no. You're giving. You're giving everything." It's a very two-way, shared relationship. It's inspiring.



Faranak Fattahi, captured via FaceTime in her lab in UCSF's stem cell building on May 15 at 11 a.m.

#### The Stem Cell Biologist Cracking the Gender Mystery

Faranak Fattahi, PhD, has seen the numbers: In China, 1.7 times as many men as women have died from COVID-19. In Italy, 1.8 times as many. In Thailand, almost three times as many. Why? Fattahi, who grew up in Iran and is now a UCSF Sandler Fellow, has a hypothesis and data to back it up. Her team has found evidence that male sex hormones such as testosterone may increase the risk of COVID infection, and they've identified FDA-approved drugs that show promise against the disease. "All around the world, researchers are coming together to look for a solution," she says. "We're eventually going to find it."

### **The Custodian**Order Out of Chaos

When his bosses asked for volunteers to work inside UCSF Medical Center at Mission Bay during the coronavirus pandemic, senior custodian Abraham "Abie" Stillman raised his hand. For the past few months, he's been sweeping, scrubbing, and sanitizing the wards and waiting rooms at the eye of the COVID-19 storm, providing an invaluable service that keeps the hospital humming and those within it safe.

But Stillman doesn't think of himself as a hero. In his own words, he shares his reflections on essential work, why he finds satisfaction in cleaning up, and what he would like from the public instead of another thank-you.

During the seven months I've worked at UCSF, my assignments have changed a few times. When I first started, I would clean the child care center and the fitness center and sometimes office spaces. When the COVID-19 pandemic started, my supervisors said they needed volunteers to clean the hospital. I told them I would do that to gain experience cleaning different types of places and to be on the front lines.

When I go in to work, I get assigned a certain area in the hospital to clean. I sweep, I take out trash, I clean toilets, and I clean places such as exam rooms, offices, and clinics.

I feel relatively at ease and safe. The reality is that the risk of being exposed to infections, such as COVID-19, is an inherent part of this job because we are in a hospital setting, and quarters get close at times. But we follow safety protocols, like wearing masks, and try to keep a safe distance from each other. I personally take as many precautions as I can, and thankfully I feel like I have enough protective equipment.

Lately, my assignment has been cleaning the infusion ward, where people with cancer receive injections of medicines like chemotherapy. Just knowing that those people need us custodians in order to be able to receive their treatments – knowing that I am there with my team, making sure that the area is safe and clean and sanitized and functioning – makes me feel really good.

I enjoy making order out of chaos. If there is a mess or if a space isn't looking right, it gives me peace and satisfaction to make it orderly. If I can see that an area now looks clean, and I've made a difference, that's rewarding to me. I also enjoy the camaraderie I have with the other employees and our ability to come together to accomplish a task.

Society wouldn't last a day without custodians because of the buildup



Abie Stillman, captured via FaceTime in the Rutter Center at UCSF Mission Bay on June 9 at 3 p.m.

"I don't consider myself a hero; it's just not how I think of myself." of waste and debris and contamination. So I know we are essential, but I don't consider myself a hero; it's just not how I think of myself. It makes me feel uncomfortable when people say "Thank you" to me just for doing my job. I don't want more recognition or praise. What I wish is for the general public to continue to practice social distancing. That would be much appreciated, so that eventually we can all get back out there in the real world.

After I've been cleaning all day, I usually go for a bicycle ride. These days, I've been getting off of work at 1:30 a.m. I usually hop on my bike around 2 a.m. and go for a long ride. I usually listen to metal while I'm riding; Judas Priest is my favorite. Almost nobody is out at that time of night. It gives me a chance to review how my day at work went and to enjoy the quiet of the city streets. I like unwinding and getting the endorphins going. It's just good to have some time away from work and all of the problems going on in the world.

Cleaning my own place when I get home is not always what I want to do. In fact, sometimes my partner and I let the cleaning go because we get busy. I am a bird owner, and the birds are quite messy; they get into everything. We had three birds who all met

tragic ends, so right now we have just one: a green-cheeked conure named Squeaky. She's resilient and very personable. She stays in her cage when my partner and I are not there, but when we are home, she is free to fly.

I am from San Francisco originally, and I am really stoked to be working here in the city at UCSF. Overall, I feel I am in a really good space. Everyone I work with at the hospital takes extreme pride in making sure everything is sanitized and clean, and it's really fun to enjoy the spirit of togetherness we all share. We are joking and jiving, we are trash-talking, and we all want to do a good job. It sounds cheesy and corny, but I have seen it to be true: Everyone is there to put in a full day's work. There's a feeling that we are all in this together.

#### The Hospitalist Creating a Human Connection

While the sickest patients go to the intensive care unit, hospital-based internists like Sajan Patel, MD, provide supportive care - monitoring oxygen and vital signs - to the many other hospitalized COVID patients. Patel, an assistant professor of medicine, recounts in his own words how the complicated emotions of caring for the Bay Area's first COVID-19 patients changed his ideas about what supportive care means.

It was early February, around Super Bowl Sunday, when we were starting to see the writing on the wall that, Hey, this is coming. Are we prepared for it? We were trying to focus on our patients, but COVID was the huge elephant in the room. The general feeling in the hospital was anxiety and wondering When is it coming?

On February 5, I got a text about my patient assignments that said, "You're going to get the COVID patients." In general, I'm pretty even-keeled. Part of being a hospitalist is you go to the patients, you just take it as it comes. But there's nothing - nothing in my life, in my medical career that prepared me to get that news. In medicine, you usually have at least some clinical knowledge or experience with the diseases you treat.

The number of U.S. patients that were identified at this stage was just 12. Seven were hospitalized, and I was going to care for two of those. So you can imagine the amount of knowledge at this time. We knew they had to be in isolation. We were practicing airborne precautions, which means wearing an N95 mask or a protective helmet called a PAPR (which stands for powered air purifying respirator). But gosh, we didn't know if the virus can stay on your hands for a long time, if you can bring that home.

The emotions of it were intense and a bit overwhelming. We'd heard stories about people, includ-

ing health care workers, getting pretty ill, which was unnerving. And that weekend my father was going to be visiting - he's 60-plus. In my head, I had to say, Can my dad still come out? What's going to happen to my partner I live with? It's that fear of just not knowing what you are getting into. There's this brand-new disease that we had so little knowledge about, and there was so much folklore out there. For guidance and support those first two days, I leaned heavily on my leadership. They huddled with me every day. There's the nurses, facilities work-



Sajan Patel, captured via FaceTime in the respiratory isolation unit at UCSF Medical Center at Mount Zion on May 16 at 2 p.m.

"I've accepted that I will likely get COVID "

> Patel wrote in a Facebook post in March. The post went viral and has since been shared 25,000 times.

ers - we'd huddle with them every day. I would chat with the hospital incident-command team, with departments of health. I appreciate that our colleagues have been very measured in saying, "Let's look at the data." With COVID, there's a lot of fear. But at UCSF, we've had a group of leaders saying, "Let's be thoughtful about this."

After days one and two, that crippling fear and anxiety were melting away because of the support I was getting from leadership, feeling more comfortable donning and doffing PPE, and just getting more familiar with the disease.

A huge part of that was just the human connection I built with the patients. That's been the most salient, important, and powerful part of this whole thing. I began to stop thinking of this as "I'm treating COVID." It broke the anxiety when I realized, this is what I do -I take care of people. Bringing it back to the patients helps you find your true north.

For example, we've been getting video conferencing working for patients to preserve PPE and minimize exposure for frontline workers. What I found, what's maybe the most powerful moment, is when I connect with a patient over Zoom and they see my face for the first time.

Because, as you can imagine, they don't know what their doctors and nurses look like because everybody's in this gear. And they're isolated from their families.

All that makes for an intensely dehumanizing experience for patients. So one of the things we can do, not only as doctors but also as humans, is give that back to them.

So that is one of the highlights of my day - just calling them over Zoom and saying, "Hey, this is what I look like." One of my patients said, "It's healing and humanizing to see your face.... I hope when I see you at Safeway I can recognize you."

#### The Emergency Medicine Chief The Hospital's First Line of Defense

In mid-March, UCSF Helen Diller Medical Center erected military-grade shelters where members of the Emergency Department could isolate suspected COVID-19 patients for triage before they even entered the hospital. It was just one of countless initiatives led by UCSF's chief of emergency medicine, Maria Raven, MD, MPH.

How has the Emergency Department handled safety? We've had many iterations of PPE, but we've always been a bit ahead of the curve. Before the shelters went up, we had patients in hallways or being rolled in by paramedics, and they could have been spreading respiratory droplets everywhere, right? So we made it so every single person, even our clerks, wore a mask and eye protection at all times.

Very early on, we also prohibited visitors in the Emergency Department. Probably in mid-March, I saw an elderly family member of a patient walking through our hallways, and I thought, Wait, we can't have elderly visitors in Emergency – they're at risk for getting this.

I remember just saying, "OK, make some signs, put them up. Here's what they're going to say. Laminate them."

And then we did it more formally - UCSF actually made really nice signs for us. A week later, when the San Francisco Health Department ordered hospitals to close to visitors, the incident-command team was like. "Can we see your signage?" But we just did it. It was the right thing to do.

So you went rogue? Well, in reality what we did was take action when we felt it was needed, without asking permission - sort of an "act-now, ask-later" situation.

That makes sense. You are that first point of contact. I feel very protective of our faculty and all of our providers and staff, because we really are the front line for the hospital.

By the time someone is admitted, the staff largely knows if they have COVID, or at least if they're highly suspected for COVID, and they go into an isolation room. But when people come into the ED, we don't know if they have the virus. You could be coming to us with a stroke or we could be intubating you for something else, and yet you could have COVID.

That puts us in a very high-risk situation -



Maria Raven, captured via FaceTime in the UCSF Helen Diller Medical Center Emergency Department's crash room on June 12 at 9:49 a.m.

basically our entire ED is like the inside of an isolation room. So, just before the shelters went up, we made a decision (this was another time we didn't ask permission) to have all of our providers in full airborne gear - gloves, N95 masks, and eye protection - for their entire shift. Patients also wear masks.

Has testing improved safety? Early on, we had to take many, many steps to even get a test. We had to call infection control, who would call the Department of Public Health, who would call the CDC. We had a lot of possible cases, but we could only test people who were sick enough to be hospitalized.

We had to come up with really clear instructions for people we released who might have COVID - they needed to self-quarantine. It was confusing for patients and upsetting for providers. Now that we have so much more control over the testing, since UCSF really developed its testing capacity, it feels much better.

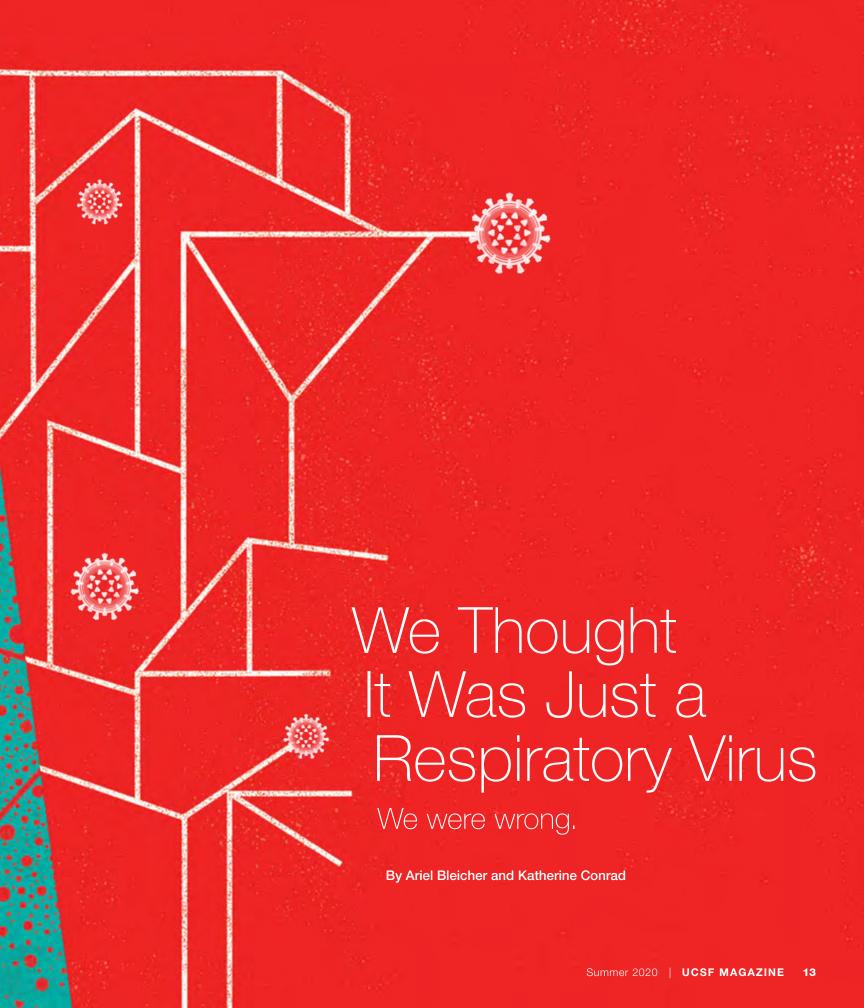


Joseph Kidane, captured via FaceTime in his apartment near UCSF's Parnassus campus on May 15 at 1 p.m.

#### The Medical Student Finding Ways to Serve

After shelter-in-place orders shuttered academic institutions across the country, medical student Joseph Kidane collaborated with hundreds of his UCSF peers to form a COVID-19 volunteer workforce. They secured safety gear for health workers, created a video to educate the public about the coronavirus, and helped quarantined hospital patients make video calls to family and friends. "This pandemic is affecting everyone, and no one's immune to it," he says. "But I think of all the frontline health care workers and their tremendous efforts and sacrifices, and it makes me feel a lot more courageous about my future endeavors."







In late January, when hospitals in the United States confirmed the presence of the novel coronavirus, health workers knew to watch for precisely three symptoms: fever, cough, and shortness of breath. But as the number of infections climbed, the symptom list began to grow. Some patients lost their sense of smell and taste. Some had nausea or diarrhea. Some had arrhythmias or even heart attacks. Some had damaged kidneys or livers. Some had headaches, blood clots, rashes, swelling, or strokes. Many had no symptoms at all.

By June, clinicians were swapping journal papers, news stories, and tweets describing more than three dozen ways that COVID-19, the disease the coronavirus causes, appears to manifest itself. Now researchers at UC San Francisco and around the world have begun taking a closer look at this dizzying array of symptoms to get at the disease's root causes. They are learning from people inside the hospital and out; people on the brink of death and only mildly sick; people newly exposed and recovered; people young and old, Black, brown, and white. And they are beginning to piece together the story of a virus unlike any known before.

#### How infection sets in

Viruses lead a curious purgatorial existence of being neither fully alive nor dead. Enveloped in a protein cloak, a virus consists almost entirely of genetic material – DNA or RNA, the blueprints for all of life. But it can't reproduce on its own. To survive, it must break into a cell and co-opt the cell's gene-copying machinery.

The novel coronavirus, an RNA virus named SARS-CoV-2, has become notorious for its skill at breaking and entering human cells. Its tools of choice are the protein spikes protruding from its surface – a feature that distinguishes all coronaviruses. The spikes of SARS-CoV-2 are the crème de la crème: By the luck of the evolutionary draw, they are able to easily grab hold of protein gates on human cells known as ACE2 receptors and, like jackknives, pry these gates open.

"You can think of an ACE2 receptor like a docking site," says Faranak Fattahi, PhD, a UCSF Sandler Fellow. When the coronavirus pandemic hit San Francisco, Fattahi repurposed her laboratory to study this key receptor, which normally

Spikes on the virus's surface act like jackknives to break and enter human cells.

plays a role in regulating blood pressure. "When the virus lands on it," she says, "it initiates a molecular process that brings the virus inside the cell."

If you're exposed to SARS-CoV-2 – say, from a cough or sneeze – the virus will likely first encounter ACE2 receptors on cells in your nose or throat. But these receptors also populate your heart, gut, and other organs. Fattahi's team has found evidence suggesting that male sex hormones such as testosterone may increase the number of ACE2 receptors that cells produce, which could help explain why SARS-CoV-2 seems to wreak greater havoc on men than women and why kids rarely get sick. "The fewer ACE2 receptors, the less risk of infection – that's the idea," she says, adding that this hypothesis for the disease's gender gap is only one of several.

Once inside a few initial host cells, the virus sets them to work churning out copies of itself. Within hours, thousands of new virus particles begin bursting forth, ready to infect more cells. Although SARS-CoV-2 is less deadly than the original SARS virus, which emerged in 2002, it replicates more rapidly. Also unlike SARS, which primarily infects the lungs, SARS-CoV-2 replicates throughout the

airway, including in the nose and throat, making it highly contagious – like the common cold.

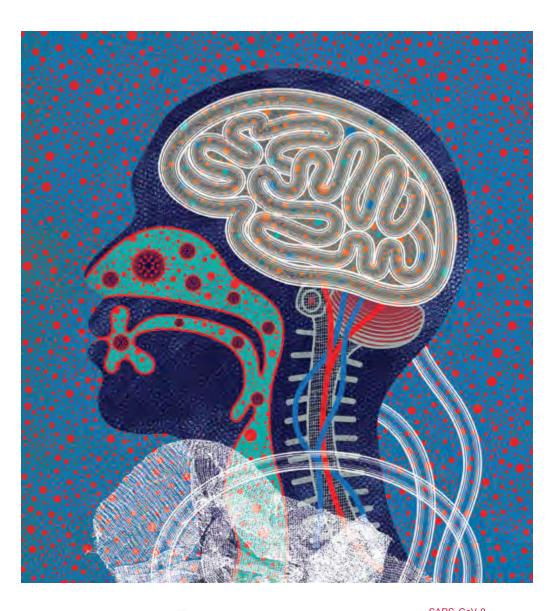
However, infection with SARS-CoV-2 usually doesn't feel like a cold. Fewer than 20% of infected people who eventually show up at a hospital report having had a sore throat or runny nose. During the first few days of being infected, you're more likely to have a fever, dry cough or, peculiarly, lose your sense of smell or taste.

Most likely, though, you won't feel sick at all. When UCSF researchers tested people for SARS-CoV-2 in San Francisco's Mission District, 53% of those infected never had any symptoms. "That's much higher than expected," says Monica Gandhi, MD, MPH, a UCSF professor of medicine with expertise in HIV. Surveys of outbreaks in nursing homes and prisons show similar or even higher numbers. "If we did a mass testing campaign on 300 million Americans right now, I think the rate of asymptomatic infection would be somewhere between 50% and 80% of cases." Gandhi savs. Millions of people may be spreading the virus without knowing it, she points

out, making asymptomatic transmission the Achilles' heel of efforts to control the pandemic – and highlighting the importance of universal masking.

"The majority of people who have COVID-19 are out in the community, and they are either asymptomatic or only mildly ill," says Sulggi Lee, MD, PhD, a UCSF assistant professor of medicine. When the coronavirus pandemic hit San Francisco in early March, Lee conceived a study to investigate why. She scrambled to assemble a team and procure funding and equipment. She borrowed a colleague's mobile clinic – a van outfitted with an exam table and a phlebotomy chair – so that her team could drive around the city, collecting samples from infected people. Lee hopes data from the study, called CHIRP (COVID-19 Host Immune Response Pathogenesis), will show how people's immune systems respond as SARS-CoV-2 starts to gain a foothold in their bodies.

"A lot is riding on that initial response," she says. If Lee and her collaborators can figure out the biological processes that allow some infected people to stay relatively well, they can perhaps use that knowledge to prevent others from falling severely ill.





SARS-CoV-2 replicates throughout the airway, making it highly contagious, like the common cold.

"It's pretty compelling data that maybe we're not dealing with a hugely aggressive virus."

- Max Krummel, PhD

#### Battling in the lungs

True to its name, SARS-CoV-2 (which stands for severe acute respiratory syndrome coronavirus 2) is first and foremost a bad respiratory virus. If your immune system doesn't defeat it at its landing site in your nose or throat, it will advance down your windpipe, infiltrating the cells lining your lungs' branching air tubes. At the tubes' ends, tiny air sacs called alveoli pass oxygen to your blood. As the virus multiplies, the alveoli may fill with fluid, shutting down this critical gas exchange. Your blood-oxygen level may drop and, typically about six days into an infection, you may start feeling short of breath.

What causes this mayhem? "Some of it is definitely caused by the virus itself," says Michael Matthay, MD, a UCSF professor of medicine who has studied acute respiratory diseases for more than 30 years. Inevitably, a fast-replicating virus will kill or injure many of the lung cells it infects; the more cells it infects, the more ruin it will leave in its wake.

But SARS-CoV-2 doesn't appear to be a savage destroyer of cells. Although it's too early to know for sure, the virus's fatality rate seems to be roughly 10 times that of the flu. "You would think that's because it's just a killing machine," says Max Krummel, PhD, UCSF's Smith Professor of Experimental Pathology and chair of the Bakar ImmunoX initiative. So far, however, the science suggests otherwise.

"One of the weirder things about this new coronavirus is it doesn't seem to be incredibly cytopathic, by which we mean cell-killing," Krummel says. "Flu is really cytopathic; if you add it to human cells in a petri dish, the cells burst within 18 hours." But when UCSF researchers subjected human cells to SARS-CoV-2, many of the infected cells never perished. "It's pretty compelling data that maybe we're not dealing with a hugely aggressive virus," Krummel says.

The bigger provocation, he suspects, may be your own immune system. Like any pathogen, SARS-CoV-2 will trigger an immune attack within minutes of entering your body. This counterstrike is extraordinarily complex, involving many tactics, cells, and molecules. In a UCSF study called COMET (COVID Multi-phenotyping for Effective Therapies), Krummel and other scientists have been observing this immune warfare in more than 30 people admitted to UCSF hospitals with COVID-19 and

other respiratory infections. "What we're doing is looking at patients' blood, their genes, and the secretions from their noses and lungs, and we're asking, 'What's your army? What's your response strategy?"

An early analysis of COMET data, Krummel says, suggests that the immune systems of many hospitalized patients mobilize differently – and more aggressively – against SARS-CoV-2 than against influenza viruses, which cause the flu. Their lungs are ravaged, these data suggest, not by the virus alone but by the detritus of an immunological battle gone awry. This rogue immune response could explain why, around day 11 of a COVID-19 infection, patients often develop a severe pneumonia known as acute respiratory distress syndrome, or ARDS.

Ultimately, COMET seeks to find COVID-19 therapies that can rein in an overeager immune system in order to prevent or treat ARDS. But that

feat won't be easy, says Carolyn Calfee, MD, MAS '09, an ARDS expert, UCSF professor of medicine, and co-leader of the study. Too much or the wrong kind of intervention, she explains, could cripple a person's immune system to the point where it can't clear an infection. "It's a fine line between therapeutic and deleterious," Calfee says. "We're trying to find that balance."

Typically, people who die from COVID-19 ARDS die around day 19. Reported rates of mortality have varied widely, with the highest rates being where the pandemic has hit hardest, overwhelming hospital resources and staff. At UCSF hospitals – due to the city's early shelter-in-place orders, which prevented an initial surge of COVID-19 cases – so far only nine of 86 critically ill patients have died.

"The good news is that we've been doing clinical trials of best-care practices for ARDS since 1998," Matthay says. Thanks to research by him and others, for example, clinicians have long known which ventilator settings result in the fewest deaths and how to flip patients onto their stomachs – a technique known as proning – to best help them breathe. If public health measures can keep hospital admissions low so that frontline providers can make good use of the skills and knowledge they already have, we may find that we have less to fear from SARS-CoV-2 than we thought.

On the other hand, the virus behaves in ways that are still mysterious.



The virus's fatality rate seems to be roughly 10 times that of the flu.

#### Heart failure

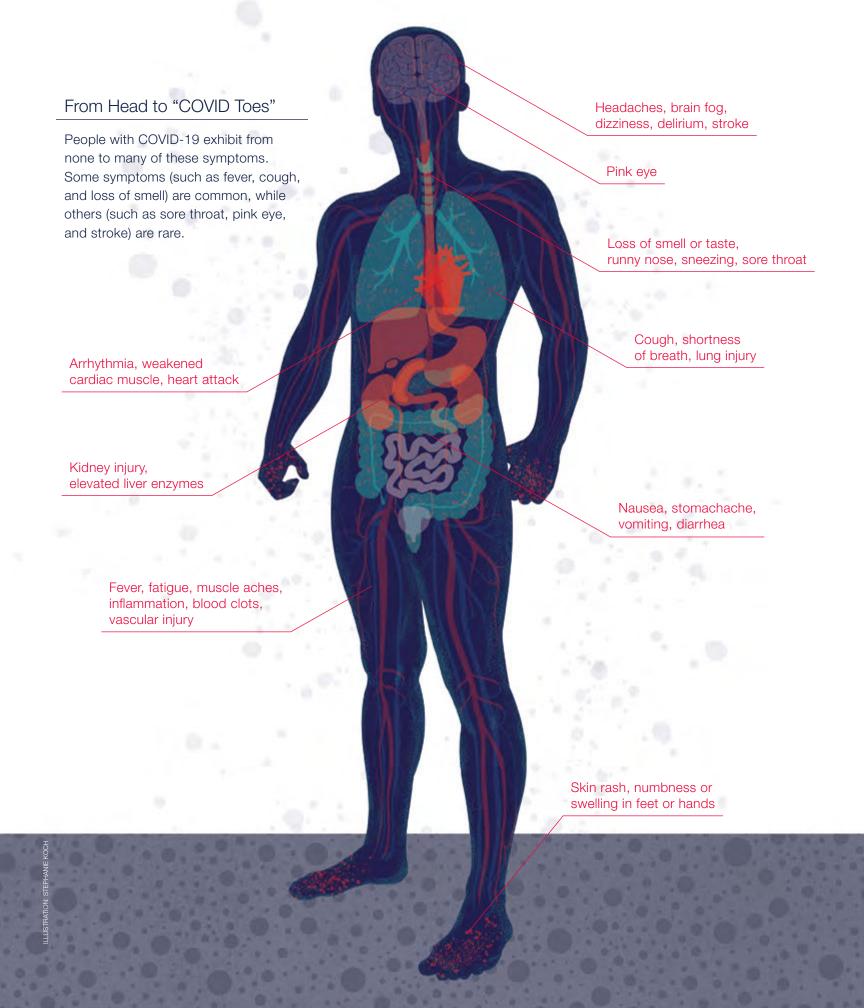
In April, Susan Parson, MD, a Bay Area medical examiner, made a startling discovery. For nearly two months, officials had believed that the first people in the U.S. to die from COVID-19 had died of respiratory failure in Washington

state in late February. At the time, the U.S. Centers for Disease Control and Prevention limited testing to people who had respiratory symptoms and had recently traveled to China or otherwise been exposed to the virus. Those restrictions, however, turned out to be misguided.

As a medical examiner for California's Santa Clara County, Parson had done a routine autopsy on a 57-year-old woman named Patricia Dowd, who had died suddenly at home on February 6. In Dowd's tissues, Parson found the cause of her death: SARS-CoV-2. But the virus hadn't wrecked Dowd's lungs. In fact, she had only mild pneumonia. Instead, SARS-CoV-2 had ruptured her heart.

Meanwhile, epidemiologists began learning that preexisting heart disease and related conditions put people at greater risk of suffering and dying from COVID-19. "We're finding that many patients who have more severe forms of the illness are obese, they are diabetic, they are hypertensive," says cardiologist Nisha Parikh, MD, a UCSF associate professor who specializes in population health research. Such risk factors, she says, are unusual. "They're not ones that really stood out in prior epidemics."

Clinicians, too, were seeing surprising numbers of COVID-19 patients develop heart problems – muscle weakness, inflammation, arrhythmias, even heart attacks. "We're not used to respiratory viruses



having such dire consequences on the heart in such apparently high numbers," says cardiologist Gregory Marcus, MD, MAS '08, UCSF's Endowed Professor of Atrial Fibrillation Research. Many patients whose hearts acted up also had failing lungs. But others had no other symptoms or, like Dowd, only mild ones.

Since March, Marcus has co-led one of the largest community surveys to better understand the spread of SARS-CoV-2 and its myriad effects. The study, dubbed COVID-19 Citizen Science, has so far enrolled more than 27,000 people; anyone with a smartphone can participate. Marcus plans to also start collecting data from wearable devices, including Fitbits and Zio patches, which wirelessly monitor heart rhythms. "There may be large numbers of people who are suffering from cardiovascular effects of COVID-19 in the absence of other symptoms." Marcus says. "I'm worried we're missing those cases."

It stands to reason that SARS-CoV-2 affects the heart. After all, heart cells are flush with ACE2 receptors, the virus's vital port of entry. And, indeed, laboratory experiments suggest that the virus can enter and replicate in cultured human heart cells, says Bruce Conklin, MD, a professor of medicine and an expert in heart-disease genetics at UCSF and the Gladstone Institutes.

But Conklin doesn't think SARS-CoV-2 necessarily kills heart cells outright. Rather, in the process of copying itself, the virus steals pieces of the genetic instructions that tell the heart cells how to do their job. "It's hauling away and hijacking stuff that's necessary for the heart to beat," he says. He is currently testing this hypothesis using human heart cells grown in gallon tanks in the lab of Todd McDevitt, PhD, a bioengineer at UCSF and the Gladstone Institutes.

It's also possible, however, that an infected person's own immune system may do the majority of the damage in the heart, as it appears to do in the lungs. "The heart probably gets infected by a lot of other viruses, and they don't have a lethal effect," Conklin says. "What makes this one different?"

Most symptomatic cases of COVID-19 are mild. 80% 15% 5% Non-Severe Severe Critical

#### Stranger things

Toward the end of March, as San Francisco began to warm up, Sonia got cold feet. She put on wool socks and turned up her heater. Still, her feet felt frozen. Three days later, her soles turned splotchy purple. Red dots appeared on her toes. At night, her cold feet itched and burned. Walking hurt. And she was exhausted, napping through afternoon Zoom meetings. "It was so bizarre," says Sonia, a San Francisco resident. A week later, her symptoms were gone.

"Yes, COVID," wrote Lindy Fox, MD, a UCSF professor of dermatology, replying to an email describing Sonia's case. Sonia wasn't surprised. Anyone, like her, who's been following news of the pandemic has probably heard about "COVID toes," a painful or itchy skin rash that sometimes pops up in young adults with otherwise mild or asymptomatic cases of COVID-19, "It looks like what we call pernio, or chilblains," Fox says, "which is a pretty common phenomenon when somebody goes out in cold weather - they start to get purple or pink bumps on their fingers or toes."

Many people with rashes like Sonia's don't test positive for COVID-19, Fox says, which has made some clinicians skeptical of the connection; when patients have both, it's just a coincidence, they believe. But Fox doesn't think so. For one thing, "the time of year is wrong," she says. "Pernio usually shows up in the dead of winter." Even more compelling, dermatologists around the world are "getting crazy numbers of calls about it," Fox says. "In the last three weeks,

I've had somewhere between 10 and 12 patients. Normally, I have four a year."

And it's not just dermatologists who are adding their observations to COVID-19's ever-expanding symptom list. Gut specialists are finding that 20% to 40% of people with the disease experience diarrhea, nausea, or vomiting before other

20%-40% of people with COVID-19 experience diarrhea, nausea, or vomiting before other symptoms.

symptoms, says gastroenterologist Michael Kattah, MD, PhD, a UCSF assistant professor. If you swallow virus particles, he says, there's a good chance they will infect cells lining your stomach, small intestine, or colon. As in the lungs and heart, these cells are studded with vulnerable ACE2 portals.

Especially disconcerting, Kattah says, is how long the virus seems to persist in the gut. About 50% of patients with COVID-19 have virus particles in their stools, often for weeks after their nose swabs test negative, he points out. Laboratory studies show that these particles are often still alive and can infect cells in a petri dish. Whether fecal transmission occurs between people, however, is an open question. If the answer is yes, people recovering from COVID-19 may need to stay guarantined even after they feel well, and the rest of us will need to be as meticulous about bathroom hygiene as we've become about handwashing and mask-wearing.

Other specialists are also raising flags. Neurologists worry about reports of COVID-19 patients with headaches, "brain fog," loss of the sense of smell, dizziness, delirium, and, in rare cases, stroke. Nephrologists worry about kidney stress and failure. Hepatologists worry about liver injuries. Ophthalmologists worry about pink eye. Pediatricians, meanwhile, worry about a peculiar COVID-related inflammatory syndrome that's showing up in kids and young adults.

# "There's a lot of smoke. We need to figure out where the fire is coming from."

- Michael Wilson, MD

Researchers are still sorting out the causes for this constellation of effects. If you come down with a particular symptom, is it because the virus is attacking your cells? Because your immune system is overreacting? Or just because you're very sick? In any severe illness, for example, the kidneys must work extra hard to filter waste and control nutrients and fluid; if overtaxed, they may begin to fail. Similarly, cognitive problems can result from increased blood toxins due to stressed kidneys or from low oxygen due to respiratory distress. "There's a lot of smoke," says Michael Wilson, MD '07, MAS '16, the Rachleff Distinguished Professor at UCSF's Weill Institute for Neurosciences. "We need to figure out where the fire is coming from."

Recently, there's been speculation that some of COVID-19's seemingly disparate symptoms may stem from trouble in the blood. Blood clots, for example, are showing up in cases of COVID-19 frequently enough for clinicians to take notice. "There's something unique about the coagulation system in these patients," says nephrologist Kathleen Liu, MD '99, PhD '97, MAS '07, a UCSF professor of medicine. In car-

ing for COVID-19 patients on dialysis machines, she's been surprised to see blood clots block dialysis tubes more than usual. Clotted tubes are common, she says, "but this is extreme."

That may be because, as growing evidence suggests, SARS-CoV-2 can infect cells in the walls of blood vessels that help regulate blood flow and coagulation, or clotting. If true, this behavior could explain some of the virus's weirder (and rarer) manifestations, such as heart attacks, strokes, and even "COVID toes."

"Our vasculature is a contiguous system," says cardiologist Parikh. "Thus injury in one area, such as blood vessels in the lungs, can set off clotting cascades that affect multiple organs." Some of that trouble likely results from inflammation triggered by the immune system, she points out, although another culprit may be the body's RAAS, or renin-angiotensin-aldosterone system, a hormone system that controls blood pressure and fluid balance. Because RAAS involves ACE2 receptors, Parikh suspects it may become disrupted when the virus infects cells through these receptors, thus triggering coagulation and other downstream effects. Her lab is now studying this system in COVID-19 patients to better understand how SARS-CoV-2 infection affects it.

Inevitably, some ailments may turn out to be red herrings. During a pandemic, when people are flocking to hospitals with infections,

Evidence suggests SARS-CoV-2 can infect cells in the walls of blood vessels that help regulate clotting. clinicians will also see a rise in other health problems, simply by the rules of statistics, points out S. Andrew Josephson, MD, the Francheschi-Mitchell Professor, chair of UCSF's neurology department, and a member of the Weill Institute for Neurosciences. "If the prevalence of infection is high, then almost any condition – a broken leg, if you will – you might conclude is associated with COVID-19."

"As clinicians, we want to get information to our medical community and to the public as quickly as possible," Josephson says, "but we have to be cautious about not making too big a deal of a little blip."

#### The long tail

As with any infection, how long a bout of COVID-19 lasts varies from person to person. If you're ill enough to need critical care, you can expect the disease to take at least a few weeks to run its course. In some cases, symptoms persist for months. For a typical milder case, though, you should feel better within a couple weeks.

At that point, the question foremost on your mind will be: Am I immune? There are now more than a dozen antibody tests on the market, but most are unreliable, according to UCSF research. And even the best tests can't tell you whether you have enough of the right kinds of antibodies to protect you against reinfection. "There is a lot of hope and belief that we'll have an antibody test that actually informs us of immunity, but we're not quite there yet," says Chaz Langelier, MD, PhD, a UCSF assistant professor of medicine who is working to improve diagnostic tools for COVID-19.

What we have in the meantime are a lot of unknowns: If you do become immune to SARS-CoV-2, when and how does that occur? Will you gain immunity from a mild or asymp-

tomatic case, as well as a severe one? How long will that immunity last?

"The answers will have huge implications for social distancing and masking and for getting the economy back up and running," says Michael Peluso, MD, a clinical fellow who came to UCSF three years ago to help fight HIV. Now he's co-leading a new study called LIINC (Long-term Impact of Infection with Novel Coronavirus), which is enrolling people who have been infected with SARS-CoV-2 and will follow them for two years. Besides illuminating changes in immunity over time, LIINC is investigating chronic effects of infection on the immune system, lungs, heart, brain, blood, and other parts of the body.

"I hope people will recover and immunity will be protective and longlasting, and that will be that," Peluso says.

It's what we all hope. We hope we will beat an infection swiftly – or, better yet, avoid the virus until there is a vaccine. We hope that if we do fall gravely ill, we will be cared for by the best providers and tended to by people we love. The reality, as we already know, is more complicated. And even if COVID-19 doesn't batter our bodies, the pandemic will surely leave scars – on our psyches, our livelihoods, our institutions, and our health – that we are only beginning to fathom. In truth, we don't know how our cards will fall, as individuals or as a people. Only time – and data – will tell.

# **How I Survived**

Exceptional care was crucial, but I'm painfully aware that privilege also pulled me through.

By F.T. Kola

n the morning of March 11, I stood behind the door of my apartment holding a backpack of overnight clothes and breathing heavily through a mask. Moments later, I heard the knock: two EMTs in PPE, who escorted me downstairs to a waiting ambulance. My mail carrier, busy in the lobby, was the only witness to my departure. As we passed her, a look of shock flashed across her face. I imagined her thoughts forming: This parade of masks, and gloves, and medical equipment - is this it? Is this the virus? It felt like the establishing shot of a movie: the infected being removed from their homes.

Just hours before, I had learned that I was positive for the novel coronavirus. The doctors thought I needed to go to the hospital. The night before, I had spent terrified hours wracked by chills so intense I thought my teeth would break. Five days earlier, on a Friday evening, I had developed a mild fever, which worsened. Over the weekend, self-isolating and confused. I had veered between moments of feeling fine and wondering if whatever it was had gone away, to being unable to do simple tasks like unloading the dishwasher without needing to lie down.

The following Monday morning, I called the health center at Stanford University, where I am a fellow. Over video, the doctor said she thought she could hear pneumonia as I spoke. Given my status as a diabetic, she was concerned. She ordered chest X-rays and tests for flu and COVID-19, which she was able to do only because Stanford had developed its own test. I was lucky - I had not been to Wuhan or Italy, so I did not qualify for a public test. I had only been, I told the doctor, to a friend's wedding in Florida the last week of February. Like thousands of other Americans, I had moved through packed

airports and sat on overbooked planes (diligently handwashing and wiping down my seat, which experts had said would keep us safe). Everywhere that weekend in Miami, there were crowds, and somewhere during that time, the virus had passed silently between us.

After all, February and early March was a very different time in America. The phrase "social distancing" was not yet in the public lexicon. Widespread community transmission of the virus seemed like a threat on the horizon; we did not know that it was already happening here. The ambulance carrying me drove through a bustling, business-as-usual San Francisco. Outside UCSF Medical Center, I lay strapped to a gurney while the staff debated whether I should be put into a tent recently set up for COVID-19 testing or go into the hospital building. People passed by with their lunches, Get Well balloons, and referrals. Lying there, I felt as though I was occupying a different time and space - as if I were some horrible harbinger of the future, an infected creature unnoticed in the midst of normalcy.

t would be weeks before the first stories T twould be weeks 25.5.1.1 trickled out of New York about how the coronavirus attacks every part of the human body, how it can necessitate amputations, how it can cause heart attacks or strokes. The little I thought I understood about the virus would turn out to be wrong; inside the hospital, in a negative-pressure room (which I had only previously heard about in coverage of Ebola), I told



"I thought about how strange it was that a tiny virus that had long lived quietly in a bat in China should have, within a matter of months, crossed an ocean and lodged itself in my lungs."

myself that young people rarely got seriously sick and were even less likely to die, that I was surely there only overnight. Instead, almost two weeks would pass before I went home.

An odd thing about COVID-19, in my experience, is that during the day, you feel almost fine, but at night, like a monster of legend, the virus roars to life. In the daytime, I asked my doctor about being discharged, or I pored over studies from Wuhan to try and anticipate the virus's course. But almost exactly at 5 p.m., my temperature would begin to rise. I'd be hit by terrible chills, and my ability to think anything beyond the most basic thoughts would fall apart. Life was day or night, normal or feverish. I didn't realize, either, exactly what was happening to my lungs, even as my blood-oxygen level progressively deteriorated. I went from occasionally needing supplemental oxygen to being hooked up to the tank constantly; from two liters to six liters to a prophylactic move to the ICU

so I could be ventilated immediately if necessary. To keep me calm, the doctor turned the monitors away so that I couldn't see the numbers. Mostly, when I contemplated my breathing, I thought about how strange it was that a tiny virus that had long lived quietly in a bat in China should have, within a matter of months, crossed an ocean and lodged itself in my lungs. I spent three days in the ICU, immensely fortunate that I never needed ventilation. I then spent another five days on a newly created COVID-19 ward, waiting for the fevers to gradually diminish and to be able to breathe "room air."

The experience of a COVID-19 patient is one of intense loneliness and isolation. For their own protection, doctors and nurses can't spend extended amounts of time in the room with you, so they do as much as they can in a single visit. This means hours of isolation in the negative-pressure room. Everyone you see is in layers of PPE; no one touches you ungloved or unmasked. No one you love is there to comfort you. You know that if you die, you will be without family or friends around you, and if you're on a ventilator, you will not even be able to say goodbye. I longed, very desperately, for my mother to hold my hand for the very specific feeling of her cool palms. I often fell asleep dreaming of it.

nd yet, I was constantly struck by the A extraordinary lengths to which the hospital staff went to establish a human connection through the isolation and layers of protection. These attempts may have seemed like small gestures, but they were so meaningful to me that they served as a psychological balm, a true feature of my treatment. The nurses brought me my favorite tea on their runs to Peet's. They gathered an array of lotions for me to sample (as if I were in a department store) when my skin grew irritated from the medical tape. They brought me magazines from their own homes when I had nothing cheerful to read. They ordered elaborate lunches to try to get me to eat, as I'd lost my senses of taste and smell. They called to check on me even after I'd been moved to another ward. Over my complaints of tiredness, they gently walked me around the room to keep my lungs working; this particular

intervention, I believe, helped keep me off a ventilator and may have saved my life. They wiped the sweat off my body in the early hours of the morning after my fevers broke, and they counted my breaths as I slept. I invoke the names of my nurses as if they were saints, which to me they were: Kuanie, Steve, Selena, Taik, Stephanie, and so many others who tended to me through fever and fear. Even the kind people who disinfected the COVID-19 ward daily - surely the least desirable assignment in the hospital - asked if I was OK, if I needed anything. It is an odd and painful thing to know that you are literally a biohazard, but they did their best to make me feel like a human. I came to see the work that the nurses, doctors, technicians, and staff did as the closest thing to radical love caring for someone you do not know, in their moment of sickness. Doing whatever you can to ease their discomfort, no matter how small, even as they pose a risk to you.

"I invoke the names of my nurses as if they were saints, which to me they were: Kuanie, Steve, Selena, Taik, Stephanie, and so many others who tended to me through fever and fear."

In late March, I was discharged into a San Francisco that felt like a different city: an empty hospital lobby, silent streets. At home, I took my first long shower in weeks. Then I stood at my open window and breathed in lungfuls of fresh air – thankful to be alive, dazzled to have made it. I survived due to an alchemy of intersecting factors – the care provided to me, including the wise monitoring and foresight of my many doctors, including Dr. Abhisake Kole and Dr. Erin Yao-Cohen at UCSF and Dr. Robyn Tepper at Stanford; matters of personal physiology; and, importantly, a range of socioeconomic privileges.

Over the long, continuing period of my recovery, that last feature – privilege – has painfully taken up more and more space in my mind. Daily, hearing the accounts of others who are sick with the virus, it seems like the defining feature of my experience. Illness often feels like a private thing – yet being sick with COVID-19 fully reveals that it is a

social matter too. It's been clear to me that my experience was an exceptional one. Others have been unable to access tests or have been turned away from hospitals when they were as sick as or sicker than I was. Hospital staff have been infected for want of PPE. I have received months of thorough and thoughtful aftercare at Stanford, so I have not been left to navigate the often confusing and stressful post-COVID landscape of my health alone; that's something I am able to do only because I have insurance, which also allowed me to deal with the considerable hospital bill.

I was able to self-isolate and social distance, and I did not have to work in unsafe conditions or risk exposure to the virus in order not to lose my income. I am not unhoused, or incarcerated, with very little agency when it comes to staying safe. While I share the same chronic illnesses that many other Americans of color disproportionately suffer from and that leave us vulnerable to the virus. I did not share a lack of access to treatment for those conditions prior to my infection, increasing my chances of survival despite them. I was not at the mercy of inequalities that have left Americans of color - in particular, Black and Indigenous Americans - to die at rates disproportionate to that of white Americans.

s I write this, the streets of San Francisco A are alive again – not with commerce but with protest, as Black Americans yet again demand the basic right not to die from state violence. We are at the intersection of two pandemics: the virus that came to us and the violent inequality that we have maintained and cultivated over centuries. The coronavirus is like a mirror: It reflects that inequality, in its exact forms and contours, right back at us. It has taught us the extent of our connections in its transmissibility and the extent of our responsibilities in the public health measures we have had to take. We can no longer ignore that what happens to our bodies - and whether we survive – is a matter of the society we shape, and not just our individual selves.

F.T. Kola is a Wallace Stegner Fellow at Stanford University, where she is working on her first novel.



# How to Build a COVID Testing Lab in Eight Days

As the United States' testing regime floundered in the early days of the pandemic, scientists at UCSF and the Chan Zuckerberg Biohub created from scratch a diagnostic lab that became a model for the nation.

By Ariel Bleicher



ON JANUARY 25, a man vacationing in Cambodia with his family went swimming in their hotel pool. After toweling off, he spiked a fever and was sent to a local hospital, where his nose and throat were swabbed and the samples were tested for a deadly virus ascendant in his hometown of Wuhan, China. By the following afternoon, the diagnosis was delivered: Cambodia's first case of COVID-19.

Officials whisked the samples off to scientists in Phnom Penh for further analysis. The hospital test had provided simple confirmation: *The virus is here*. But to understand its path and contain its spread, health experts needed details. How had the virus arrived? Was it the same as the strain storming across China? Or was it a related but different virus that had emerged independently?

Months earlier, before anyone had heard of COVID-19, the Phnom Penh lab had begun using a new system, introduced by researchers from the San Francisco-based Chan Zuckerberg Biohub, to answer those very questions. It consisted essentially of a commercial gene sequencer and sophisticated cloud-based software called IDseq, which identifies a virus or other pathogen from its genetic sequence. The Cambodian group was one of 11 international infectious disease laboratories using the technology to study diseases like dengue and malaria. But in late January, the Cambodian scientists turned their attention to sequencing the novel coronavirus newly landed at their door.

The sequencing data confirmed what everyone had suspected: The virus had indeed originated from the initial outbreak in Wuhan, having hitched a ride in the unsuspecting tourist. More profoundly, though, the speed and success with which the Cambodian lab executed the analysis



revealed to the Biohub team the power of their IDseq technology. Here was a tool that could minutely track - and thus help combat - what was quickly becoming a global pandemic.

"At that point, I thought that's what our priority would be - turning our eyes to other parts of the world to try to contain the fires there," says biochemist Joe DeRisi, PhD, UC San Francisco's Tomkins Professor and co-president of the Biohub.

"And then the fires came here."

BY LATE FEBRUARY, the Bay Area had begun bracing for its own surge of COVID cases. DeRisi was texting daily with Priscilla Chan, MD '12, mulling the right problem to tackle. Chan had met DeRisi during her student days at UCSF and had been impressed by his knack for rooting out the causes of mysterious infections – including the 2003 SARS epidemic and scourges that kill boa constrictors, cockatiels, and honeybees. So, in 2016, when Chan and her husband, Facebook founder Mark Zuckerberg, made a \$600 million gift to create the Biohub, with the goal of eradicating infectious diseases, they asked DeRisi to lead it. Now they wondered how they might help thwart the burgeoning COVID pandemic.

DeRisi assembled a small task force to brainstorm ideas. Then, out of the blue, his cell phone rang. "I almost didn't answer it because I thought it was a telemarketer," he recalls. It was actually Gavin Newsom, the governor of California. He wanted to know what DeRisi thought the state should do to avoid mistakes in its COVID response. More testing, DeRisi said, without missing a beat. If you want to make smart decisions about quarantining people or locking down parts of the economy, he told Newsom, you need to know where the virus is and who's infected. In other words, you need to be able to test a lot of people. "Otherwise you're flying blind," he told the governor.

The conversation got DeRisi thinking. Who was going to do all this testing? It was becoming clear that the federal government wasn't up to the task. The U.S. Centers for Disease Control and Prevention (CDC) already had a testing backlog, plus many of the test kits it was sending to states were proving defective. "The stark realization for me was there was no cavalry coming," DeRisi says. "The CDC wasn't going to ride in and provide tens of thousands of tests to Californians. Neither were the local health departments - they weren't powered to do it."

But what about the Biohub? They had the space to set up a lab, the scientists and engineers to get it going, a line of volunteers willing to do the work, and even a donor offering to pay for it. "What could we be doing that would be more important?" DeRisi asked himself. "Nothing."

There was just one problem. The Biohub didn't have a license to run a clinical lab. As a research center studying the biology of human diseases, the Biohub used tools and techniques similar to those of diagnostic labs. But while research labs are designed to foster innovation and experimentation, clinical labs prioritize consistency and regulation. Quality must be

"The stark realization for me was there was no cavalry coming." - Joe DeRisi, PhD

tightly controlled, documentation systems established, and tests validated. Converting a portion of the Biohub's research team into a clinical one wouldn't be trivial.

"We were trying to think outside of the box about what they could do," says Steve Miller, MD, PhD, the director of UCSF's clinical microbiology lab, which often partners with the Biohub on research projects. When COVID hit, Miller and his staff had started working around the clock to develop a viable diagnostic test and to gather the necessary equipment and supplies

in preparation for the hordes of patients expected to start flocking to UCSF hospitals. His team had the means to do maybe a few hundred tests per day - likely not enough to meet UCSF's needs, let alone the Bay Area's.

The Biohub team calculated they could easily achieve a per-day rate in the thousands, they told Miller, significantly boosting California's testing capacity - which, in the absence of national leadership, was (and still is) being filled by a patchwork system of commercial and public labs. But the team was hamstrung by the state's clinical licensing laws. So what to do? Maybe they could test people as part of a research study? No, because then study participants couldn't legally get their results. Maybe they could send positive samples to UCSF for

#### **JANUARY**

12/31/19: A pneumonia "of unknown cause" is identified in Wuhan, China

1/12/20: China shares the genetic sequence of the novel coronavirus with the world

1/26: California confirms its first case of COVID-19, the third in the U.S.

24

1/30: Scientists in Cambodia track the burgeoning outbreak using the Biohub's IDseq technology

1/30: The virus spreads to 18 countries outside China; WHO declares a global health emergency

1/31: The U.S. government issues a policy discouraging clinical labs from developing in-house COVID tests. eventually leading to widespread testing delays and shortages

#### **FEBRUARY**

2/6: The U.S. CDC begins distributing its own test kits to state-run health labs: the kits are later found to be defective

2/23: Cases surge in Italy, eventually shutting down the world's main nasal swab factory

2/29: The U.S. FDA announces a new policy enabling clinical laboratories to develop their own tests

2/29: UCSF laboratory scientists begin working on a test in-house





UCSF volunteers Paula Hayakawa Serpa (left) and Valentina Garcia examine patient sample tubes.

validation? No, that would be a logistical nightmare. Well, then, what if the Biohub simply got certified as a clinical lab?

"My original response was 'Oh, hell no,'" says Ed Thornborrow, MD, PhD, Miller's boss and the medical director for all UCSF clinical labs. California's licensing rules, he knew, were even stricter than federal guidelines. Meeting them under normal circumstances could take months, possibly a year – an unacceptable timeline. But he agreed to look into the possibility and concluded it was doable under two conditions.

First, California's health department would have to approve the Biohub as a temporary extension of one of UCSF's clinical labs. Check.

Second, the Biohub-turned-testing lab would have to be staffed by clinical laboratory scientists, licensed specialists who had completed months of postgraduate coursework and had passed an exam. "That wasn't going to happen," Thornborrow says. "These people are in short supply. You can't just go hire dozens of them on the spot; they're not out there." But hundreds of UCSF graduate students and fellows trained to do laboratory science were offering their labor. "If we were going to

get the Biohub lab off the ground, we would first have to get California to change the law," Thornborrow says.

And so, with help from the UC Office of Legal Affairs, they did. On March 12, the day after the World Health Organization officially declared a pandemic, Governor Newsom issued an executive order nixing the staffing restriction. Check, check.

Suddenly, the road to certifying the Biohub's COVID testing lab was clear. Now DeRisi and his team just had to build it.

AS SOON AS DeRisi heard about Newsom's order, he relayed the news to his task force. Its members were huddled in a conference room, still planning research projects. "Joe came in and said, 'OK, this is happening. We're going to transition over and do testing," recalls Emily Crawford, PhD '12, whom DeRisi and the other Biohub brass had appointed as the task-force lead. "I was shocked," she says. "I remember calling my mom late at night and being like, 'This is totally insane." Then she thought, *Bring it on*.

#### **MARCH**

**3/2:** The Biohub creates a COVID-19 task force

**3/4:** California declares a state of emergency

**3/9:** UCSF begins providing in-house testing but has only enough capacity to test its own patients

**3/11:** WHO declares a pandemic

3/12: Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, calls the U.S.'s testing response "a failing" 3/12: California Governor Gavin Newsom relaxes the certification requirements for clinical testing labs, giving the Biohub team the green light to begin building an extension of UCSF's clinical lab

**3/13:** President Trump declares a national emergency

**3/16:** Bay Area counties issue the first shelter-in-place orders in the U.S.

**3/18:** The Biohub's testing assay passes the final validation check for FDA certification

**3/20:** The Biohub team processes their first patient samples

3/22: UCSF and other major Bay Area medical centers call for donations of masks, gowns, and nasal swabs, setting in motion an outpouring of community and private-sector help to solve equipment shortages

**3/26:** The U.S. leads the world in COVID-19 cases, with more than 80,000

**Timeline legend:**National or global events

**UCSF** events

"The first thing I did was understand I could not be in charge of everything, because it's overwhelming and no one can do that," Crawford says. She asked Vida Ahyong, PhD '15, a research scientist at the Biohub who had spearheaded the IDseq project in Cambodia, to be her co-lead. Together, they recruited dozens of volunteers and organized them into subteams. One team would source supplies, another would oversee equipment, another would deal with patient samples, another would design the data system, another would manage lab waste, and so on. There were 13 teams in all. Everyone worked in pairs; that way, if someone contracted the virus, their partner could take over.

The teams jumped into action. "It was a mad push," DeRisi recalls. "Literally the lab was empty on March 12, and on March 13 we began carting in equipment from labs down the street at UCSF. It was raining, and there we were, hauling \$80,000 robots down the 16th Street bike lane."

By March 16, most of the pieces were in place. Under Miller and Thornborrow's guidance, the teams had worked out a protocol for handling patient samples. They had bought, borrowed, or built themselves machines for processing the samples - and had named them Batman, Woody, Milo, Nico, Cat, Beyoncé, J-Lo, and Shakira. They had stockpiled supplies for running the machines: gloves, masks, vials, trays, and chemical reagents. They figured they would need another week or two to make sure everything was working smoothly and get the paperwork off to the U.S. Food and Drug Administration (FDA) for certification. And then UCSF's chancellor called.

Since the start of the pandemic, Sam Hawgood, MBBS, had kept in close touch with DeRisi and the Biohub team, cheering them on and helping remove political obstacles. But as cases of COVID outside China swelled - first in Italy; then in Iran, South Korea, and Japan -Hawgood worried a wave would hit San Francisco before the testing lab was ready. "It was clear we were headed into trouble," he recalls. "I had an intense sense of urgency that we needed to do everything we could not to get overwhelmed; days mattered, even hours." Hawgood, UCSF's Arthur and Toni Rembe Rock Professor as well as its chancellor, urged DeRisi to speed up the timeline.

"At that point, we were all thinking we still had over a week left," Ahyong recalls. "Then it was, 'Just kidding, you have 48 hours." The next two days, she says, "were a very big blur. It was all adrenaline. Everyone was like, 'Who cares about sleep anymore? Let's get this done."

"There we were, hauling \$80,000 robots down the 16th Street bike lane."

- Joe DeRisi, PhD

It was nearing midnight on Friday, March 18 - only six days after they got the go-ahead to start building the testing facility - when they ran the final validation check to prove the lab met the FDA's criteria for certification. "We were sitting around with our fingers crossed," Ahyong says. "When the experiment finished and we saw the report, we literally jumped for joy." Two days later, they ran their first patient samples. "We were so tired. We were so happy.... We were live."

The jubilation didn't last for long. By April, the Biohub team had scaled up their operation and trained enough student workers to handle more than 2,500 tests a day. But hardly anyone was sending in samples. It was a busy day if they got more than 250. "For a few weeks, we were like, 'Well, we've built this, and nobody came,'" Miller says.

One reason was that the surge of hospitalizations everyone had expected didn't hit San Francisco, a fact that experts attribute to the city's early shelter-in-place orders. Yet they knew the virus was still circulating. Hundreds of thousands of residents were waiting to know whether they could safely go back to school or work. So why weren't they getting tested?

The answer, it turned out, was swabs. To test someone for COVID-19, you need a swab - basically, a long, sterile Q-tip - to sample their nasal passage for the presence of the virus. But swabs, the Biohub team learned, were in short supply. "We're talking about a global pandemic," Thornborrow says. "Every country in the world was having a mad rush on nasal swabs." Making matters worse, the outbreak in Italy had shut down the world's main swab factory.

#### **APRIL**

4/2: The Biohub lab scales up its testing capacity to 2,688 tests per day

4/2: The pandemic has sickened more than 1 million people in 171 countries

4/16: UCSF offers free testing to all California county public health departments, thanks to the Biohub lab and support from the Chan Zuckerberg Initiative

4/24: California averages 16,000 tests per day; Governor Newsom says the state will need at least 60,000 tests per day in order to reopen

4/26: The global death toll surpasses 200,000

#### MAY

5/12: California scales up its testing capacity to 35,000 tests per day

5/27: U.S. deaths surpass 100,000, far higher than any other nation

#### JUNE

6/4: The number of known cases worldwide grows faster than ever. with more than 100,000 new infections every day

6/28: COVID-19 has sickened 10 million people and killed more than 500,000

"It was baffling," says Madhura Raghavan, PhD, a UCSF postdoctoral fellow who helped build the testing lab at the Biohub. "We had all this expensive equipment, we had all this manpower, but we were limited by this tiny little swab."

So the UCSF and Biohub teams went in search of more swabs. Chancellor Hawgood got in touch with Marc Benioff, a longtime UCSF donor who, as CEO of the cloud computing firm Salesforce, had extensive business contacts in China. "Salesforce had boots on the ground in China going from factory to factory," Thornborrow says. "They'd send me pictures of package inserts or advertisements for swabs and ask me, 'Will this work?'" Eventually, they found some reputable suppliers and ordered hundreds of thousands of swabs to be distributed to hospitals, county health departments, and whoever else needed them.

Meanwhile, UCSF and the Chan Zuckerberg Initiative (CZI), the couple's philanthropic venture, announced that – thanks to the Biohub expansion – UCSF would provide free testing to all 58 county health departments in California. Fearing equipment shortages and backlogs at commercial labs, many health departments had issued restrictive testing guidelines and held back on community testing. After UCSF and CZI's announcement, however, more and more patient samples began showing up at the Biohub – and not just from hospitals, but also from nursing homes, homeless shelters, jails, prisons, and research teams surveying underserved or especially vulnerable communities. [See "An Epidemic of Inequality" on page 34.] By early May, the lab was running at near capacity.

"We've managed to not only keep ahead of the volume at UCSF but also help expand testing for the entire state," Thornborrow says. "I don't think that would have been possible without the work and support of so many people. It was definitely one of those 'it takes a village to test a village' kind of things." The speed and ingenuity with which the Biohub team brought this enterprise to pass is truly extraordinary, and its success has served as a model for other U.S. research institutions to create their own diagnostic labs. "We showed UC Berkeley how to do it; we showed UC Santa Cruz how to do it; we advised many, many people across the country," DeRisi says. Together, these academic-turned-service labs paved a path forward at a time when the country's inadequate testing capacity had tragically hampered its early pandemic response. "What we've learned is that universities and research centers like the Biohub have incredible, untapped potential to respond to emergencies in ways I don't think this country has seen before," DeRisi says.

In the meantime, the pandemic continues to spread, straining even the additional testing capacity the U.S. has managed to build piecemeal. Without a national strategy, local governments and health providers continue to make decisions about testing in isolation, competing with each other for workers and supplies. Many of the same bottlenecks that plagued this fragmented system at the start of the pandemic are beginning to reemerge, including shifting supply chains, backlogs at commercial labs, and long lines at testing centers.

Eventually, when the dust of the COVID storm settles, the Biohub team will return to its original mission, which includes hunting down pathogens in California, Cambodia, and other corners of the globe near and far. The student volunteers will resume their thesis projects, the borrowed robots will be marched back up 16th Street, and the clinical lab will be shuttered. For now, though, the team will continue churning out tests for as long as their service is needed – which, from the look of things, could be a very long time.

THESE DAYS, the Biohub's COVID testing lab hums from morning to night. Samples are barcoded, logged, and prepared for processing. Machines are loaded with test tubes and plates. Reagents are added. Data are checked and results reported.

#### **JULY**

7/7: The U.S. hits 3 million total cases; California breaks its daily record with more than 9,000 new cases

7/15: As UCSF Magazine goes to press, the pandemic continues to accelerate; testing bottlenecks still plague much of the U.S.



Alexander Merriman, another UCSF volunteer, prepares sample tubes to be loaded into a processing machine.





#### The COVID-19 pandemic has touched every corner of our lives, so it stands to reason that we wonder what is in store for us in the coming months – and years.

I am an infectious disease fellow at UC San Francisco, and my colleagues, friends, and family often seek my advice. The questions I'm asked most often are about when life might return to "normal" and what is needed to get us there. Of course, it's impossible to predict the future: the novel coronavirus - the agent that causes COVID-19 - is a pathogen humanity has never before dealt with.

And yet we are not entirely in the dark. After consulting several experts, I've come to see that the history of previous outbreaks is rich with lessons about what we might expect as we strive to bring the current one to an end - and how we can better prepare for the next one.

#### Adjusting to a new normal

The experts I spoke with anticipated at best a slow decline in COVID cases through the summer. Unfortunately, even that scenario may be optimistic, given the recent surge in cases in many hot spots around the country, combined with the fact that more businesses

are getting the go-ahead to reopen. And even if we do see a downward trend, it will likely be punctuated by small outbreaks in places where people dwell in close quarters, such as nursing homes, jails, homeless shelters, and ships. Experts further predict that during the fall and winter - as schools reopen and holiday get-togethers are held, in places where they're permitted - there will probably be an uptick in new cases.

Thus the challenge for scientists and policymakers alike will be to figure out the optimal timing and sequencing for reopening businesses and resuming our lives, while keeping cases from skyrocketing. "There are no scientific answers, so we have to look to history," says Brian Dolan, PhD, a UCSF professor of anthropology, history, and social medicine.

Previous outbreaks caused by respiratory viruses, for example, serve as reasonable models for understanding COVID's spread and predicting the impact of control measures such as social distancing and masking. These viruses, like the novel coronavirus, spread when an infected person coughs or sneezes, speaks, or sings. But they differ from one another in two important ways: how easily the disease can be passed from one person to another (its transmissibility) and the percentage of people infected with the disease that die (its fatality rate).

A century ago, an especially volatile combination of these two factors set off the 1918 flu pandemic, caused by an influenza virus, which sickened about one-third of the world's population and killed an estimated 50 million people; that made its fatality rate about 2%, or



A line of people on Montgomery Street in San Francisco waits to get masks during the 1918 flu pandemic. Failure to wear a mask was punishable by imprisonment or a fine.

20 times that of the seasonal flu. We are seeing similar patterns play out with COVID-19. As of mid-July, the disease had sickened at least 12.7 million people worldwide and killing at least 566,000.

In 1918, as today, officials in many places mandated masks and issued stay-at-home orders. In San Francisco, for example, as Dolan recounted in a recent article about the 1918 flu in Perspectives in Medical Humanities, the Board of Health closed all public gathering places, including bars, theaters, and schools, on October 18. Four days later, the city's mayor signed a bill requiring masks in public. The failure to wear a mask was punishable by imprisonment for up to 10 days or a fine of up to \$100. Ironically, mask-related arrests resulted in a "congested" city jail, turning it into a breeding ground for influenza. (The 1918 pandemic was also marked, like COVID-19, by anti-mask protests.)

Decisions to reopen society a century ago came in fits and starts. Only a month after enacting social-distancing ordinances, for example, San Francisco's public health officer cited the decline of new flu cases as evidence that the disease had "virtually disappeared," and on November 22, 1918, San Franciscans were allowed to ditch their masks. This decision unfortunately proved to be premature, as three weeks later, reports of new cases surged.

Protective measures were reinstated, then lifted anew in February 1919 as the city's mayor weighed concerns for public health against the interests of business owners and a restless populace. Although the

number of new flu cases increased between March and April 1919, that peak was not as high as the one the previous fall. By July 1919, the pandemic had abated, which experts attribute in part to the fact that, by then, it had been burning through the community for more than a year, conferring a degree of herd immunity.

In 2020, in hopes of avoiding the missteps of the past, California formulated a phased reopening. Spaces where the risk of disease transmission was considered lower, such as factories and outdoor museums, for example, got the go-ahead to reopen their doors first, as of May 8, to be followed by higher-risk spaces, such as movie theaters and gyms. Yet even that systematic approach wasn't sufficient to stave off a new surge. By early July, California was seeing record daily numbers of new cases, impelling Governor Gavin Newsom to reimpose some restrictions. George Rutherford, MD, the Salvatore Pablo Lucia Professor at UCSF and head of the Division of Infectious Disease and Global Epidemiology, points out that lifting restrictions too early is tempting but perilous. "Stay the course," he advises, "because otherwise we will see a big bump in the number of cases."

But regardless of how adherent to public health guidance a particular populace may be, the ease and ubiquity today of international travel may undermine any singular locale's efforts. "This is a virus that knows no borders," says infectious disease specialist Peter Chin-Hong, MD, a UCSF professor of medicine. And even if international travel is blocked, interstate travel can easily spread the virus. For this reason, many states have instituted 14-day quarantines for visitors from other states or screening of travelers for signs of infection, such as a fever.

For many people in California, life is already starting to seem more familiar. Many nonessential workers have begun resuming shifts, and residents are returning to places of entertainment, exercise, and worship. According to Rutherford, however, large public events, such as concerts and sports games, likely won't be permitted until 2021, when experts hope to have an effective vaccine.

#### Desperately seeking a vaccine

None of the experts I spoke with doubted that a vaccine against COVID-19 is inevitable. "There is a force of nature coming around this virus," says Monica Gandhi, MD, MPH, director of the UCSF Center for AIDS Research and medical director of the AIDS clinic at Zuckerberg San Francisco General Hospital. "Everyone in the clinical and research world has turned their attention to it."

One factor aiding the vaccine search is that, so far at least, the novel coronavirus appears to be relatively resistant to mutation – meaning that once a vaccine is developed, it's likely to remain effective. This stability stands in marked contrast to the seasonal flu viruses, which mutate regularly. It is for this reason that the seasonal flu vaccine requires annual, rather than one-time, administration.

Yet the science of developing an effective vaccine is only the first in a series of challenges on the immunization front of the battle against COVID-19. The U.S. and many other countries lack sufficient infrastructure to manufacture and distribute a vaccine in the vast quantities that will be required. As Dolan says, "the ability to ramp up production and distribution to the scale needed is just not possible overnight."

"There is a force of nature coming around this virus. Everyone in the clinical and research world has turned their attention to it."

Monica Gandhi, MD, MPH



People hand out information about AIDS at an event in San Francisco in 1986. UCSF experts say communicating in a way that fosters public trust is an important lesson from the AIDS epidemic.

Figuring out the order of the distribution process is another challenge. It will be important to prioritize who gets the vaccine first, since there won't be enough doses available to immunize everyone right away. Those given preference may include older people; people with depressed immune systems; and people with chronic health conditions, such as diabetes or lung disease. "We will have to have a very clear and realistic sense of who is at the highest risk of exposure to and transmission of COVID-19," says Kirsten Bibbins-Domingo, PhD '94, MD '99, MAS '04, the Lee Goldman, MD, Professor and chair of the UCSF Department of Epidemiology and Biostatistics.

Finally, even if enough doses can be manufactured and distributed to those who need them, convincing people to get vaccinated may prove challenging. That reluctance has been fomented partly by misinformation spread by the anti-vaccination movement. But for peo-

ple who identify as Black, Indigenous, or of color, the reluctance to embrace a vaccine may also stem from mistrust of the medical system, which through a legacy of abuse, neglect, and unethical treatment of oppressed communities has sewn understandable fears.

Sadly, such communities are taking the biggest hit from COVID-19. [See "An Epidemic of Inequality" on page 34.] And disproportionately low vaccination rates would make this disparity even more pronounced. "In general, our adult vaccination rates are fairly abysmal, and we see big gaps by race and ethnicity," points out Bibbins-Domingo, who is also the UCSF School of Medicine's vice dean for population health and health equity. For example, Black people over age 65 are 10% less likely than non-Hispanic white people of the same age to have been vaccinated against influenza in the previous year, according to 2015 data from the U.S. Department of Health and Human Services' Office of Minority Health. "We need to have a plan to address that," she says.

Ensuring that people get vaccinated will require clear, unified communications from the federal to the community level - something that has been a major challenge in the past, including during the AIDS epidemic. "One of the most important things is that we communicate what we know in a way that fosters public trust," says Paul Volberding, MD, the Weiss Memorial Professor and director of the UCSF AIDS Research Institute. "That is probably the most important lesson from AIDS."

There are key differences between the human immunodeficiency virus (HIV), which causes AIDS, and the novel coronavirus. For instance, HIV spreads through blood and sexual contact, and once a person is infected, the virus remains in their body for the rest of their life. Yet like COVID-19, HIV takes a particularly heavy toll on people who historically have been oppressed.

"The conditions that continue to drive HIV cases, such as poverty and injustice, all remain and are playing out with the COVID-19 pandemic," observes Gandhi. That makes it all the more important that public policies and communication strategies address the structural inequities, such as overcrowded housing, and social determinants of health, such as lack of access to insurance coverage, that make vulnerable populations more likely to get sick and less likely to get vaccinated.

#### Insights from elsewhere

At the same time, even as the current pandemic is still raging, experts are giving thought to preventing – or at least mitigating – the next one. To this end, other countries' experiences with COVID-19 and other infectious disease outbreaks are instructive.

The 2014 outbreak of Ebola in West Africa, for example, prompted the Obama administration to establish a permanent National Security Council team tasked with keeping an eye on the United States' epidemic preparedness. This team, however, was eliminated in 2018. More recently, in late May of this year, President Trump announced that the U.S. would withdraw from the World Health Organization (WHO), which coordinates international health policy and alerts its 194 member nations about potential global infectious disease threats. Withdrawing from WHO has therefore left the country even less prepared to meet the challenge of future pandemics.

This lack of preparation stands in stark contrast to South Korea,



The 2014 outbreak of Ebola in West Africa prompted the Obama administration to establish a National Security Council team to manage U.S. epidemic preparedness, but the Trump administration eliminated the team in 2018.

a country in which lessons from a previous epidemic have bolstered its responses to subsequent outbreaks. In 2015, South Korea was hit hard by MERS, or Middle East Respiratory Syndrome, caused by another coronavirus. A major lesson South Korea drew from its experience with MERS was the importance of rapid and widespread testing. During that epidemic, all testing had to be sent to South Korea's national diseasecontrol agency. Consequently, the turnaround time for results slowed to 10 days. This backlog, in turn, led patients sick with MERS to hop from hospital to hospital seeking a diagnosis, says Seung-Youn Oh, PhD, an assistant professor of political science at Bryn Mawr College. Such diagnostic odysseys, she says, explain in large part why MERS spread extensively among hospitals.

So when COVID-19 arrived, South Korean officials were determined to make access to testing a priority. Early on, the country established numerous drive-through testing sites, as well as aggressive contacttracing of anyone who tested positive. This approach helped quickly identify people who were infected before they could spread the disease further.

Following MERS, South Korea also developed a crisis management infrastructure, including a system for communicating health information among officials and between the government and the public. This infrastructure, together with mandated mask-wearing, allowed the country to avoid a lockdown in response to COVID-19. "Centralized leadership and clear chain of command was very important," says Oh. Although South Korea was among the first countries to report a case of COVID-19, its death rate from the disease as of mid-July was only 5.6 per 1 million people. By comparison, Italy's was 579.1, and the United States' was 420.

New Zealand also has maintained a very low per capita death rate -

PHOTO: WONSFOK, JANG

only 4.5 per 1 million people as of mid-July. However, that nation took a different tack than South Korea, including a strict lockdown and very tight border controls. (One similarity with South Korea, however, was that New Zealand also ramped up its testing capabilities quickly.) In the United States, the response was closer to the one taken in New Zealand, focusing largely on stay-at-home orders.

But at least one UCSF expert, Dorothy Porter, PhD, a professor of anthropology, history, and social medicine, considers stay-at-home orders a "blunt, draconian, universal tool," that has been used to contain disease for centuries. She

recently wrote an article for *Perspectives in Medical Humanities* surveying the use of such orders from the time of the bubonic plague to the current crisis.

Because South Korea didn't require people to shelter in place during the COVID pandemic unless there was concern they were infected, Porter says, life went on as usual for most South Koreans, leaving that



Mask-wearing has become the norm in South Korea. The lessons the country drew from the MERS outbreak in 2015 allowed the country to effectively respond to COVID-19 without crippling its economy.

country's economy relatively unaffected. "They didn't have to close down their economy because they could just focus the quarantine on those already infected," she explains. On the other hand, although New Zealand's strict lockdown has had a significant economic impact, its restrictions have been so successful in tamping down the spread of the coronavirus that a recent poll showed 87% of residents approve of the way the government has handled the pandemic.

"Politicians have to give more authority to health professionals and support their work, rather than spinning the pandemic for their own gain."

Seung-Youn Oh, PhD

One of the most significant differences between the United States and those two countries – which both achieved very positive outcomes, albeit through divergent strategies – is the United States' lack of a coordinated, consistently applied strategy. Mask-wearing was mandated in some states, recommended in others, and mocked in a few. Stay-athome orders were strongly enforced in some states, loosely followed in others, and not even considered in a few. The availability of testing, as well as of sufficient personal protective equipment, was also patchy. Greater coordination and consistency likely would have resulted in fewer deaths as well as less economic turmoil, experts believe. In addition, Oh advises that whenever another pandemic arises, barriers to test development and deployment should be eliminated much earlier, as they were in South Korea and New Zealand.

Yet perhaps the biggest obstacle to developing an effective response to a pandemic lies in turning a scientific issue into a polarizing political one. "The degree of politicization of the COVID-19 pandemic is really a fundamental problem," Oh says. "Politicians have to give more authority to health professionals and support their work, rather than spinning the pandemic for their own gain."

#### Facing the future

Addressing COVID-19 in this country for however long the crisis remains – and preparing for the next outbreak – won't be easy. It will require developing strategies for infection containment, vaccine development and distribution, testing capability, contact-tracing infrastructure, and the production of personal protective equipment. It will also require careful consideration of which strategies to emphasize and then clear communication with government officials and the public.

A country's culture also comes into play when confronting a pandemic. The willingness of a group of people to prioritize the common good over individual liberty affects how readily a populace is likely to adhere to tactics intended to control the spread of disease. Ultimately, policymakers will need to consider what we should do and what we have the political will to do whenever "next time" rolls around; they must give scientists and public health authorities a seat at the table, allowing these experts to offer advice, and then make the best recommendations they can.

For as any infectious disease expert will tell you: The question isn't whether we'll suffer another pandemic. The question is when.



# AN EPIDEMIC OF INEQUALITY

Across the country, communities of color have been hit hardest by COVID-19. Meanwhile, hundreds of thousands of people have taken to the streets in an outcry against police killings of Black people. Both issues have roots in the same problem: inequality that started long before the COVID-19 crisis.

By Elizabeth Daube

When doctors at Zuckerberg
San Francisco General Hospital
first started to see patients with
COVID-19, they noticed a
curious pattern: Almost all
of them were Latinx.

Some of the physicians – also UCSF researchers – wanted to see if their observations in the hospital held up beyond its walls. In April, they launched a study of COVID-19 infections in San Francisco's Mission District. What they found in the neighborhood, which is about 58% Hispanic/Latinx, surprised them. The Mission's infection rate was 11 times higher than the city average, and 95% of the people who tested positive were Latinx.

In the Bay Area and in cities across the nation, people of color have faced more severe illness and higher death rates from COVID-19 than white people have. Experts initially cred-

ited this trend to increased levels of underlying health problems, like obesity and diabetes, among people of color. But those problems don't crop up out of nowhere, according to Alicia Fernandez, MD, director of UCSF's Latinx Center of Excellence (LCOE). They're diseases rooted in how people live – specifically, how they can afford to live.

Low-income people have long suffered from obesity and related health issues at higher rates than people who have more money and less chronic stress. Many of the COVID-19 patients Fernandez has seen are cashiers, delivery people, cooks, drivers, cleaners, or construction workers. They don't have the option to work remotely. They live paycheck to paycheck in crowded houses, sometimes with people they don't know well. If they get sick, there's no spare room in which to isolate. There's not enough money to stock up on groceries, let alone get a hotel room for a few weeks.

"Their biggest concern by far is the need to continue working," Fernandez says. "Are we crushing the curve, or is the curve crushing us? People really need to understand how desperate the economic times are."

Some physicians in the Bay Area have spoken publicly about how few patients in their hospitals have tested positive for the coronavirus. Fernandez says those statements, which are intended to uplift and reassure, also demonstrate the level of inequality in San Francisco, which has the widest income gap in California. She's seen plenty of COVID-19 patients – some needing intensive care – at Zuckerberg San Francisco General Hospital, because it serves all people, whether they can pay for care or not.

"The very definition of privilege is when you look out the window and you think that everyone has the same view, right?" Fernandez says. "That's really not the view we have working in the Mission."



Members of San Francisco's Latino Task Force for COVID-19 gather in the Mission District with UCSF infectious disease physician-scientist Diane Havlir (left). Working with city officials and other partners, they have provided free testing and services to help low-income residents in the Mission quarantine safely.

### Prioritizing patients without privilege

In the wake of the Mission findings, UCSF experts have launched more studies of COVID-19 in Bayview, Sunnydale, and Visitacion Valley – low-income neighborhoods that are home to many residents who are Black or Latinx or have Pacific Islander or Chinese heritage. The studies are part of a new project, the COVID-19 Community Public Health Initiative, that aims to better track and counter the spread of the virus in disproportionately affected groups.

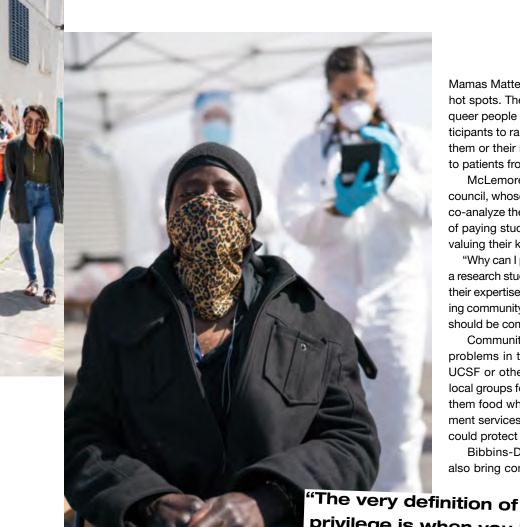
The initiative relies on the support of community organizations, according to Kirsten Bibbins-Domingo, PhD '94, MD '99, MAS '04, vice dean for population health and health equity in the UCSF School of Medicine. Residents tend to know these organizations already and have often received services from them over the years, like grocery or meal deliveries. The relationships that local staff have built can prove invaluable to researchers, who might be avoided otherwise.

"There is a legacy of mistrust because of bad actions we've taken as physicians and as scientists," says Bibbins-Domingo, who is also the Lee Goldman, MD, Professor of Medicine and chair of the Department of Epidemiology and Biostatistics, "but there's also mistrust because of government policies."

For example, the LCOE street outreach team – which distributes masks and fields questions in Spanish about COVID-19 at food bank lines around the Mission – has had to quell unfounded rumors about U.S. Immigration and Customs Enforcement showing up at testing sites. But undocumented people have reason to fear detainment and deportation right now. Since March, U.S. officials have turned away more than 20,000 people at the Mexican border, many of whom were seeking asylum.

Mistrust also stems from a long history of researchers using wildly unethical practices in their studies of people of color. One of the





UCSF recently partnered with community groups and public health officials to bring free COVID-19 testing to San Francisco's Bayview neighborhood.

better-known examples is the Tuskegee Study, a 40-year, federally funded experiment on Black men with syphilis.

The participants were not informed that they had syphilis, nor were they given readily available treatment. The researchers wanted to see what would happen over time. Not surprisingly, many of the men died. Some of their wives and children suffered with untreated syphilis too.

Community organizations offer researchers an entry point into diverse, low-income areas where people are understandably wary of outside experts. They can also offer important insights into how studies should be run in the first place.

That's one of the principles that Monica McLemore, RN, PhD '10, MPH, an associate professor in UCSF's Department of Family Health Care Nursing, brings to the nationwide PRIORITY study, which aims to answer urgent questions about how COVID-19 affects the health of pregnant women and infants. She co-leads the health equity component of the study, working with a national coalition called Black

Mamas Matter and partnering with community organizations in COVID hot spots. They aim to recruit more Black and Indigenous women and queer people of color into the study and to create opportunities for participants to raise their own questions about how the virus might impact them or their newborn babies, so the findings can ultimately be useful to patients from many backgrounds.

McLemore and her team have also set up a community advisory council, whose participants will be paid to advise the research team and co-analyze the findings. While some researchers worry about the ethics of paying study participants, McLemore believes payment is crucial to valuing their knowledge and their time.

"Why can I put a percentage of effort in my budget to be able to design a research study, but then we can't compensate community members for their expertise?" she says. "I can get paid for mine. When you are extracting community wisdom, and that is the innovation of your work, then they should be compensated for that expertise."

Community organizations also do the hard work of trying to resolve problems in their neighborhoods, whether they're coordinating with UCSF or other partners. After the study in the Mission, for example, local groups followed up with participants who tested positive, bringing them food while they were quarantined or connecting them to government services. Some patients were able to get free hotel stays so they could protect their roommates or family members from infection.

Bibbins-Domingo notes that UCSF's local studies of COVID-19 also bring communities and city officials together to discuss findings,

with the hope that the data might lead to more or better resources for lowincome people. She says this kind of collaboration has already led to new government initiatives, like temporary wage protection for workers who get COVID-19 and need to stay home.

"What we need to do is mobilize for a health crisis, but also mobilize the social services," says Bibbins-Domingo, who also co-founded UCSF's Center for Vulnerable Populations. "More people are realizing that we can't solve this with just one of our sectors at the table."

privilege is when you look out the window and you think that everyone has the same view, right? That's really not the view we have working in the Mission."

Alicia Fernandez, MD

### The health crisis that goes back generations

One in 1,500 Black Americans have died from COVID-19 in the last few months, but the pandemic is far from the only problem that has an outsized impact on people of color. Public health experts estimate that one in every 1,000 Black men and boys in the U.S. will be killed by police.

"COVID and Black Lives Matter are coming together in the same time and space," Bibbins-Domingo says. "The communities affected by COVID are also affected by violence, oppression, and systemic racism. They come from the same thing – the same set of structural issues."

The Black Lives Matter movement emerged in 2013. Since 2015, the American Public Health Association has increasingly highlighted how racism and related inequalities – from housing discrimination to the poor quality of public schools in many Black and brown neighborhoods –

# MATTERS BLACK HEALT!

"If you're more likely to be shot by the police, the calculus that you use to weigh whether or not you would be out in a pandemic is different than, say, if you have no perceived risk."

Monica McLemore, RN, PhD, MPH



this banner atop Bernal Heights Park in San Francisco.

shape people's opportunities in life and lead to disproportionate illness, suffering, and early death among low-income communities of color. In other words, the root cause of racial health disparities is racism, not race.

Police killings of Black people haven't stopped. But attention to those deaths has surged in recent months, as people have organized ongoing protests in dozens of cities to rail against racism and police brutality. While some have raised concern about the potential spread of COVID-19 at the protests, public health officials haven't seen a significant rise in infection rates attributable to the demonstrations, likely because they're held outdoors and most participants wear face coverings. Experts have described the protests themselves as a kind of public health intervention.

"Some of the ways we make change to structural issues is through demonstration and protest," says Bibbins-Domingo. "You can't use public health as a way to mute people's rights to protest."

McLemore urges people worried about the health implications of protests to also consider the perspectives of the demonstrators.

"If you're more likely to be shot by the police, the calculus that you use to weigh whether or not you would be out in a pandemic is different than, say, if you have no perceived risk," McLemore says. "If you are already overexposed because of your occupation, it may not be that big of a deal for you to be re-exposed. That's different than me at home for 10 weeks in my house, where I can shelter in place and get all my work done. Risk is not equitably shared."

#### White Coats for Black Lives

Many doctors, nurses, and medical students across the U.S. have gathered to protest police brutality and the racism that fuels it. Though they've showed up in rising numbers recently, the White Coats for Black Lives movement started more than five years ago – and UCSF medical students helped found it.

This spring, Fatuma-Ayaan Rinderknecht and Aminta Kouyate, secondyear medical students at UCSF and co-founders of the UC Berkeley-UCSF

Joint Medical Program's chapter of White Coats for Black Lives, helped organize a June 6 rally that drew hundreds of health care workers. They called for the political, criminal justice, education, and health care systems to launch and enforce anti-racist policies. Rinderknecht and other students at the UCSF School of Medicine have also been asking the school to expand and improve the anti-racism components of the curriculum.

"I'm Black and I'm the child of immigrants, and I came to medicine with a social justice focus, hoping to relieve health inequities that I had seen firsthand," Rinderknecht says. "We [at White Coats for Black Lives] are really interested in dismantling the systemic racism that exists, especially in medicine."

Health disparities aside, Rinderknecht says racism in medicine manifests itself in many ways. Issues range from physicians who don't believe patients of color when they report pain symptoms to barriers that lowincome students face when they apply to medical school – an endeavor that can cost as much as \$10,000 for fees and interview travel.

Rinderknecht notes that racism and inequality - and public demonstrations in response to these problems – have been going on for many years, but several factors have converged in this summer's protests.

"These killings have continued to happen," she says. "People are in quarantine. People have been losing their jobs. People have been sick and dying. There's a lot of want for change. That's why maybe this has gotten so much momentum this time - because we're at a bit of a boiling point right now. It feels like we don't have a choice. It won't stop unless we go out and try and make a change."

Since May, more than 1,200 public health and infectious disease experts - including about a dozen UCSF faculty members - have signed an open letter urging police to stop using tear gas against protesters because it causes coughing and other symptoms that can spread COVID-19. The Do No Harm Coalition, a Bay Area-based group seeking structural changes to address health disparities, also educates medical professionals who want to support street medicine at demonstrations. Rupa Marya, MD, an associate professor of medicine at UCSF and the faculty



First-year neuroscience student Ellery Jones speaks during a rally at UCSF Mission Bay.

director of Do No Harm, says the group's last online training drew more than 4,000 people from across the country.

Eric Smith, a fourth-year medical student at UCSF, volunt

medical student at UCSF, volunteered as a street medic during an Oakland protest in late May, when police used tear gas on demonstrators. Some people started to cough and panic, as tears and mucus streamed down their faces. Smith and his roommate – shielded by goggles and bandannas – ran up to them to help wash off the chemicals and ease the pain.

People have been losing their jobs.

People have been sick and dying.

There's a lot of want for change....

We're at a bit of a boiling point

right now." Fatuma-Ayaan Rinderknecht

"A lot of it is just connecting with somebody and saying, 'I know what's happening. I'm here,'" Smith says. "It's the least I could do."

For Smith, showing up for the recent Black Lives Matter protests didn't feel optional. His great-great-grandmother was a slave. Growing up, he saw how systemic inequality threatened the health and well-being of his friends and family.

"Black people are just so sick and tired of being considered secondclass citizens," Smith says. "Black and brown folks are suffering the brunt of the pandemic. Despite the theoretical risks of exposing themselves to COVID at these protests, they're still out there.

"Because when you're out there, you feel the love. You feel the community. There's pain. There's anger. There's also love, and there's hope in it."

### **Turning point**

While UCSF and countless other organizations have made public statements in support of dismantling racism and inequality, it's been difficult for many people in the health field to predict exactly what will change moving forward.

Renee Navarro, MD '86, PharmD, UCSF's vice chancellor of diversity and outreach, has called attention to some of UCSF's ongoing efforts to challenge racism and inequality, which include training thousands of people on unconscious bias, microaggressions, and how to support anti-racist efforts. In early June, UCSF Chancellor Sam Hawgood, MBBS, announced that his cabinet would work on a campus-level response to structural racism affecting the UCSF community and launch a new task force to review UCSF's practices and policies around campus safety.

Rinderknecht is optimistic about the changes that she's seen corporations, governments, and universities announce. The Joint Medical Program chapter of White Coats for Black Lives recently received a \$60,000 grant to create a new initiative that will help premed students from underrepresented backgrounds get into medical school. The initiative will feature a mix

of mentors to help students navigate the application process and stipends to cover related expenses.

Smith had more mixed feelings about what to expect in the coming months and years.

"This is the biggest thing I've ever seen in my generation, but I'm 28. I was born when they beat Rodney King," he says. "It seems to me that more people are paying attention. But the truth is the status quo is working for some people."

To truly address inequality in

communities, McLemore believes the nation needs to elect politicians with a commitment to overhauling unjust policies and supporting the least advantaged people.

"We don't have policies that support the removal or the reduction of health disparities," she says. "Until we have that, I don't see things changing."

For many people who work on racial health disparities, the COVID-19 crisis – and all the inequalities it has laid bare – seems like it might be a turning point. But which way will we turn?

While the pandemic has drawn attention to long-standing problems, Bibbins-Domingo says, that attention doesn't necessarily translate to lasting change. She worries that the country's current momentum around confronting racism and structural inequality might fade over time.

But she also sees potential in how COVID-19 has impacted everyone, regardless of their wealth or privilege. While those effects are in no way equal, the threat of a rapidly spreading virus has helped people understand how we are all connected.

"In some ways, the pandemic itself makes me hopeful that things will change," Bibbins-Domingo says. "The way I survived in the pandemic is probably the way a lot of people did. I had my food delivered.

"But if we can't figure out how those people who are producing our food, delivering our groceries – how they're safe? Then we cannot actually be safe anymore."





### You've called this pandemic your worst nightmare. Why?

I have heard people say "viruses are the great equalizer." That's a total fantasy.

People who are homeless are disproportionately older and sicker. Many have underlying conditions, such as lung disease and diabetes, that set them up for disastrous outcomes. Add a highly communicable disease that spreads through a respiratory mode to a population living in crowded conditions with poor access to basic hygiene, and you have a nightmare scenario.

#### How are people who are homeless faring?

The situation is heartbreaking. People are terrified. They are wondering, "Am I going to catch this? Am I going to die out here?" We have a study cohort of older, homeless adults in Oakland who we've been following for years, and we're worried about them. We don't know how some of them are doing because we're not allowed to do study visits in person during the COVID-19 outbreak, per UCSF policy.

### The COVID-19 pandemic is laying bare some ugly societal problems. Can you talk about that?

Two things are strikingly obvious. One is that many of the people who need to keep working are the very same people who are at risk for homelessness; are living in overcrowded houses; or, in many cases, are experiencing homelessness. They can't just Zoom into their jobs; they perform essential work: restaurant work, cleaning, and transit. They can't afford to get sick, and yet they are some of the

least protected and lowest-paid workers.

Another is the insidious effect that racism has on health. COVID-19 is exacting a devastating toll on Black Americans, on Indigenous Americans, and on Latinx populations. These are the same people who are exquisitely vulnerable to becoming homeless, nearly homeless, or living in severely overcrowded housing.

#### Can you elaborate?

Say you live in a house you were able to buy in a suburb because two generations ago, your family was allowed to live in the suburbs because they are white. You've had access to high-quality education your whole life, and as a result, you have a job you can Zoom into during the pandemic so you can continue to get paid. Or you have money so you can shelter in place.

You're going to be infinitely more protected from a pandemic than someone working a low-paid, frontline job while living four to a bedroom and sharing a bathroom with 10 people. Or someone who's living outside or in a homeless shelter.

Viruses are not racist, but viruses operate within societal conditions. We have built structures based on inequities, racism, and injustices. This has left communities of color exposed to acquiring and getting sick from this virus.

# What did you do when you heard about the shelter-in-place order?

You can't shelter at home if you don't have a home. That's why I and others pushed really early for an aggressive response that included resources like hotel rooms to provide sanctuary and the ability to self-isolate. I wrote the initial guidance for the state of California that informed Project Roomkey – an effort to house people at highest risk of serious complications from COVID-19 in hotels, with state and federal support.

# Housing people in hotels sounds complicated. What are some of the challenges? It's challenging from the standpoint of logistics, costs, and, for some, philosophical differences.

Logistically, coordination is needed between multiple government agencies and community-based organizations to rent the hotels, provide medical services and staffing, and to do cleaning and laundry. It's complicated, and how the model is implemented differs across the state.

The costs to lease hotels are negotiated by counties or by the state and are paid for with federal, state, and city funds. This may include Federal Emergency Management Agency reimbursements and federal stimulus funds, as well as payments from city funds.

Moving people into housing quickly requires that we dig deep into the principles that we know are effective for getting and keeping people housed. This "housing-first" philosophy means recognizing that many people who are homeless have experienced immense trauma. We need to treat them with dignity and respect and make arrangements to meet their needs, whether those are medical or related to substance use or mental health problems.

### What happens if we keep the status quo?

Look, our humanity has always been wrapped up in other people's humanity. That has always been true. It is just more evident now. Something like a pandemic makes it clear that for a society to be healthy, we need to attend to the health needs of everyone.

But the story of San Francisco has been the tale of two cities. Overall, San Francisco has done remarkably well due to the incredible efforts of our public health officers and of our mayor, London Breed. The decision to shut down the Bay Area early in the pandemic is going to be heralded as one of the great public health triumphs of our lifetime.

However, we can't ignore the fact that despite a low overall number of COVID-19 cases, some members of our city have suffered disproportionately, such as the Latinx community and people experiencing homelessness. In order to safely open up our cities and get people back to work, we must attend to the needs of those most vulnerable to becoming infected by and sick from this virus. These are the same populations experiencing the most stress, poverty, and racism. They are part of our communities.

# In what ways is UCSF making a difference in this crisis-on-top-of-a-crisis?

Many UCSF people are doing heroic work on the front lines, such as Elizabeth Imbert, a physician at Zuckerberg San Francisco General who is working directly with the Department of Public Health to keep people who are homeless safe during the pandemic. I've provided advice to those in the San Francisco Department of Public Health and other city agencies on best practices. I worked with the State Emergency Operations Center pretty early in the pandemic on a strategy for California. The policies we created were then pushed out across the country through agencies such as the U.S. Department of Housing and Urban Development. There has been an incredible spirit of sharing and learning.

# What lasting results do you hope for at the end of the pandemic?

Recognition that the solutions to homelessness will require massive commitment from our government, starting with our federal government. All levels of government need to acknowledge homelessness as an existential threat to health. As important as health care, at this point, is ensuring that people have a good place to live.

We actually know what it will take to solve homelessness for most people: living wages and affordable housing. For people with complex, behavioral needs, it will take subsidized housing partnered with services for mental health, substance abuse, and other issues offered on a voluntary basis. But these solutions require a lot of funding, so we're going to have to make monetary sacrifices.

I am hopeful that we can take this opportunity to reevaluate our priorities and create a more equitable, and therefore more healthy, society.

### What role can health professionals play?

Educate the public, hold our elected officials' feet to the fire, and lean into evidence-based practices to explain that housing is the best medicine.

As we launch the Benioff Homelessness and Housing Initiative, the need for expertise on the overlap between homelessness, housing, and health has never been more obvious. Having a centralized place where we can both develop and translate evidence into recommendations and policies is crucial. We aim to create a healthier world by doing our best to end the homelessness crisis once and for all.

Margot Kushel is also a resident alumna, a professor of medicine, and the director of the UCSF Center for Vulnerable Populations.

# Sheltering in Place Is Nothing New for These Families

When your child has a serious medical condition, social distancing is all too familiar. Five families have some advice for the rest of us.

By Beth Tagawa



In his hospital bed, Kaysan gets ready to celebrate his brother Zyan's first birthday.



In 2016, Lily finished her last round of chemo at age 15. She's now a college student at UC Davis.

Most of us are now living an unfamiliar existence: home-bound, our world seized by uncertainty. But there are some people for whom the shelterin-place lifestyle is second nature, who habitually reach for hand sanitizer, whose heads instinctively snap at the sound of a cough.

They have, in a sense, been through this before - spending months, even years, with their lives spiraling out of control, their days bleeding into each other, unable to venture outside for fear of germs beyond their walls.

These families have, in fact, endured much worse than a pandemic: the diagnosis of a child with a severe illness.

Kids who've been really sick - immunocompromised or otherwise extra-susceptible to infection – also know the drill. They've been pulled out of school, separated from friends, stuck at home. It's an irreversible element of their childhood, one that the current pandemic has either resurrected or extended.

Here, five families who've survived this sort of journey - thanks to the experts at UCSF Benioff Children's Hospitals - offer advice for those of us navigating such circumstances for the first time.



Mother Brittany cuddles with Kaysan during his treatment.

Aleera's mother, Monica, stayed by her side while she was hospitalized.

### Practice gratitude.

On April 13, Kaysan turned 7. He splashed in a new inflatable pool and teetered around on his first bike – a friend's hand-me-down, thoroughly sanitized.

It was a low-key event, just like nearly all of the family's celebrations since Kaysan was diagnosed with leukemia four years ago.

"I'm sure a lot of kids are missing their birthday parties and having a hard time with that," says his mother, Brittany Azam. "In that sense, I'm grateful for our experience. Eating cake at home is a normal birthday for Kaysan."

The family is finding lots to celebrate lately, largely because they've been through much greater hardships than a pandemic. Following Kaysan's diagnosis, he was put in isolation at UCSF Benioff Children's Hospital San Francisco to protect his fragile immune system. His brother, Zyan, only 8 months old at the time, could join him in the hospital. But if Zyan was taken outside, he wouldn't be able to re-enter his brother's room due to the risk of infection.

His parents were faced with a tough choice: Gather everyone in one hospital room, or break up the family.

"How could I choose between my sick son and my nursing baby?" Brittany says.

It took three bone marrow transplants to jump-start the production of healthy blood

cells in Kaysan's dangerously fragile body. The family ultimately lived together in his hospital room for seven months. In that room, Zyan celebrated his first birthday, took his first steps, and said his first words.

Brittany was, at times, consumed by jealousy. "I could barely look at Facebook and see people going on playdates, to the beach, even pictures of people shopping at Target," she recalls. "You want all that for your own family so badly."

But now, in COVID quarantine, gratitude is a constant. They've weathered their share of challenges this time around: Attending school for the first time, Kaysan was bitterly disappointed to be taken out. His father, who worked in retail, was laid off, a major financial setback. Brittany gave birth to a third son in January and misses the support of friends and extended family.

But, at the same time, isolation has given the Azams a chance to spend time together in strained but far less personally trying circumstances. Plus, at home in Sacramento, they have what feels like infinite space compared to a single hospital room: their own kitchen, a shower with a curtain, familiar beds.

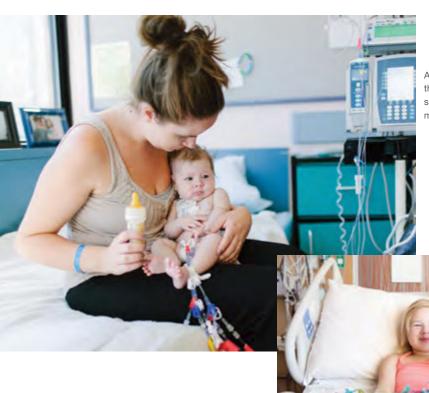
"If you are home and you are safe, that's what matters," Brittany says. "I hope people can be grateful for every moment with their family and think of this as a chance to focus on what's important."

### Feel your feelings.

In the fall of 2016, 11-year-old Aleera's face faded to pale – "ghost white," says her mother, Monica Valdovinos – and massive bruises surfaced all over her body, seemingly at random. When the vomiting began, Monica rushed her daughter to the emergency room.

At UCSF Benioff Children's Hospital San Francisco, Aleera was treated for severe aplastic anemia, a life-threatening condition that occurs when the body stops producing enough blood cells. After a year of chemotherapy, Aleera underwent a bone marrow transplant, then suffered a significant complication that destroyed her kidneys. She has





Alissa holds Riley at the hospital, where she spent the first few months of her life.

> Riley enjoys a chocolate donut during a more recent hospitalization.

since relied on dialysis, every day for nearly three years.

While Aleera remained resilient throughout months of grueling treatment and isolation, Monica was overwhelmed. A single mother, she had quit both her jobs to be at Aleera's side, causing her to fall behind on her bills, and had sent her other two children to live with a friend in Nevada. Monica stopped eating and couldn't sleep.

"Around my daughter I was a rock, but when I was alone I had moments of complete devastation," Monica says. "It was hell on earth."

She attributes that, in part, to keeping her feelings bottled up. "It emotionally destroys you when you don't know how to tell people, 'Hey, I'm struggling today,'" Monica says. "I didn't know how to voice that."

But in the age of COVID-19, Monica is vocal: quick to remind the guy breathing down her neck at the grocery store why social distancing is essential or to pour her emotions into a Facebook post.

"I tell everyone, 'I'm here if you want to talk. FaceTime me, message me. I will help you because I have already dealt with this," she says.

Essential to overcoming hardships, she says, is first acknowledging that they're hard.

"You need to allow yourself to feel what you're feeling. If you're angry or depressed, you need to know that it's okay to cry. If you

need to go outside and scream, do it," Monica says. "Don't deny yourself your emotions."

Of course, for some, that advice might be moot. Aleera, now 15, seems pretty unfazed by the pandemic. She does her schoolwork, hangs out on her back porch making TikTok videos with her siblings, and sends quarantine memes to friends. After all, being isolated is nothing new for her. "I'm kind of used to it," she says. "Plus, I'm a teenager, so I like to sleep a lot anyway."

### Prioritize joy.

Imagine finding yourself in Alissa McDonald's living room during a moment of maternal frustration. Maybe Presley, 9, is whining about her homework, or Riley, 6, is demanding her 10th snack of the day. So Alissa erupts in annoyance.

What you hear next might surprise you. One of her girls will likely respond not with an exasperated sigh or ear-splitting shriek but with a cheerful non sequitur: "Hospital mayonnaise." "Yogurtland spoons." "Chickens in unexpected places."

Then they all dissolve into giggles.

Alissa and the girls keep an ongoing list of things that bring them joy. When one gets upset, the others' job is to randomly blurt out something from the list.

"It's hard to continue being irritated when someone is reminding you of things that make you happy," Alissa explains.

Strategies like these help the family control their own happiness, Alissa says. They learned the necessity of positive thinking the hard way: Riley was diagnosed with severe combined immunodeficiency (SCID), often called "bubble boy disease" when she was 3 weeks old.

At risk of being killed by even a common cold, Riley spent months at UCSF

Benioff Children's Hospital San Francisco, followed by isolation at home and a string of additional hospitalizations - totaling about one-third of her life so far. After a bone marrow transplant, stem cells donated by her mother did the job; since then, Riley has had a functional immune system. She was finally enjoying the life of a typical first-grader – until COVID hit. But they're taking the current situation in stride.

"I'm used to having zero control over what happens. The only thing I can control is my attitude," Alissa says. "Right now, my girls and I are having fun. I know we're in the midst of a global pandemic, but we just are."

Alissa has framed social distancing to her daughters as their opportunity keep others safe, a welcome change from having to protect Riley. And getting to enjoy time together with Riley in good health is, in her mother's eyes, nothing less than a gift.

"I hope that people embrace the fact that this is happening whether we want it to or not," Alissa says. "You can choose to see this as a beautiful thing. And we do."



Linda, Joseph's mother, donated a kidney to him in January 2020 after his first transplant failed.

Lily was diagnosed with cancer in high school. At the end of her freshman year of college, she went skydiving.

### Stay productive.

When sheltering in place began, Joseph's life didn't change much. The 19-year-old had already been practicing social distancing in preparation for a kidney transplant early this year.

In fact, much of the new normal – diligent handwashing, avoiding sick people, staying on high alert for symptoms – has been the status quo for Joseph for as long as he can remember.

At age 6, he was diagnosed with a rare kidney disease that triggered high fevers, infections, anemia, cataracts, and other complications. By age 11, he desperately needed a new kidney and, incredibly, his stepfather was a match. But his body ultimately rejected the organ, forcing him to put his life on hold – a few months ahead of the rest of us – to prepare for his second transplant.

These experiences have inspired him: He's studying to become a pediatric nurse. "Some people might be scared of hospitals," he says. "But when I'm in a hospital, I feel safe, because I know I'm going to be taken care of."

At first, Joseph's mother, Linda Gutierrez, was skeptical. Was it really safe for him to be around sick people after all these years of avoiding them? Thanks to the enthusiastic blessing of his medical team at UCSF Benioff Children's Hospital Oakland, she's now proud of his choice.

"I think it's coming full circle," she says. "Maybe all this was supposed to happen to him so he could help others. If he helps even one child, it's worth it."

Joseph credits his medical challenges with shaping him into a responsible and goal-oriented young adult. He's been managing multiple daily medications for years and has maintained honor-roll grades with many of his teachers not even knowing he was sick.

During his recovery, Joseph is taking time off from college. He's also been unable to go to his job as an after-school program leader

since before his surgery – too many little-kid germs. But, true to his nature, he maintains a routine, and he recommends establishing daily habits as a way to prevent anxiety and depression.

On a typical day, he'll take his dog out for walks, play ball with his 5-year-old brother, and help his 12-year-old sister with her homework. He's also using this time to study Spanish, which many members of his family speak but he somehow never picked up.

"If you have something you've been putting off, do it," he advises. "You don't have an excuse now. That's the way to make the best of the situation."

### Focus on what's possible.

It sounds counterintuitive: Lily is grateful for her experience with cancer.

But hear her out. "I have met some of the most amazing people who will be in my life forever because of cancer," she says. "And it taught me to always focus on the pros – that focusing on the cons will do no good."

After experiencing hormonal symptoms, Lily was diagnosed with cervical cancer at age 15. With the support of the experts at UCSF Benioff Children's Hospital San Francisco, she beat it. But two years later, she began having chest pains. The cancer had spread.

This time around, a novel immunotherapy treatment saved her life but caused her to develop an autoimmune disease. She lost 40 pounds and became so weak that it was difficult to leave the house.

Just like all high school students around the world now, Lily missed many senior-year milestones, including a much-anticipated class trip to Mexico. While she grieved that loss, she eventually found that alongside her sadness bubbled an even more powerful feeling of anticipation of joyful moments to come. She urges anyone mourning a loss to seek out and home in on those flickers of forward-thinking.

"Maybe you'll find yourself crying about missing out on something, like your graduation, and that is completely okay. Hold space for that. But then you'll wake up the next day and feel excited about something else in the future. Both feelings can exist at the same time," she says. "The world will find ways not to replace the memories that were lost but to fill that void with new experiences."

# Tweeting a Pandemic

How I learned to use social media to advance the public's understanding of COVID-19.

By Robert Wachter, MD

On March 18, 2020, feeling useless and fearing that I might fall ill from the coronavirus, I decided to start tweeting.

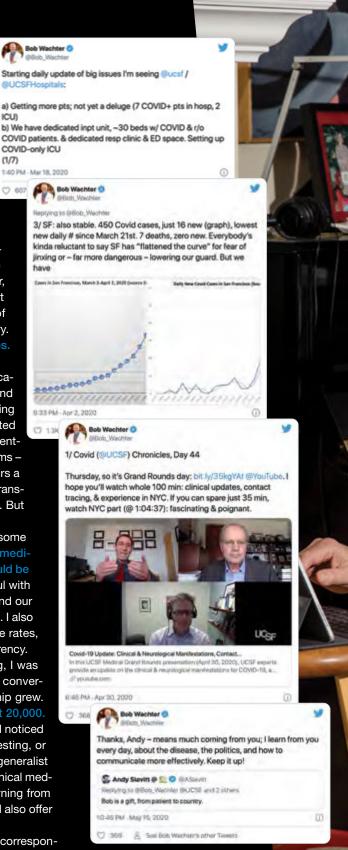
By mid-March, we'd already seen massive outbreaks of COVID-19 in China and Italy. Cases were emerging in the U.S., too, many in a nursing home outside Seattle. And in early March, the Grand Princess cruise ship, with more than 100 passengers and crew stricken by the SARS-CoV-2 virus, had sailed under the Golden Gate Bridge; I could see it from my window at UCSF's Parnassus campus. Taken together, these incidents made it seem inevitable that San Francisco - the second densest city in the U.S., and one that relies on tourists - would get hit by the full force of the pandemic. As a 62-year-old man, it was clear that I was in a high-risk category. My mind did what anxious minds do: spool out a series of worst-case scenarios. Is my will up to date? Does my wife know my passwords?

My feeling of uselessness was a bit more surprising. I'm chair of one of the top academic departments in the nation, with 800 faculty; a yearly budget of \$600 million; and world-renowned clinical, research, and educational programs. My life consists of making decisions, some of them important ones. Yet UCSF's response to COVID-19 amounted to a health care version of martial law, with all key decisions made by a small incidentcommand task force. This was crucial - there was no time for committees and fiefdoms but it left me without many decisions to make. I found myself spending about 12 hours a day on Zoom updates, drinking in a fire hose of information about disease curves, transmission rates, the ins and outs of PPE, the ethics of rationing ventilators, and more. But there wasn't much I could do with the information.

And so, on the night of March 18, I got on Twitter and wrote a thread describing some of the key issues we were facing. I had a sense that people - both laypeople and medical professionals - were hungry for information, and that without it the vacuum would be filled with rumor, fiction, and existential dread. And I wanted to do something useful with all the new information I was taking in. I talked about PPE; testing; our workforce; and our new dedicated COVID units in the hospital, the emergency department, and the clinic. I also shared some of our data regarding our early experience with COVID, including case rates, hospitalizations, and fatalities, taking advantage of UCSF's long tradition of transparency.

That first tweet generated a lot of interest, so I decided to do more. Before long, I was spending a couple of hours each day on my tweets, pulling in compelling articles, conversations with experts, anything that seemed interesting and important. My readership grew. I had been on Twitter since 2011 and had generated a healthy following of about 20,000. Now, my followers grew by about 5,000 each week, reaching 90,000 by mid-June. I noticed that some experts were tweeting in their particular niches, be it epidemiology, or testing, or policy. I decided that my tweets would take advantage of my broad interests as a generalist and my position as a leader, talking about COVID-related issues as they applied to clinical medicine, policy, ethics, technology, and epidemiology, while layering in what I was learning from my front row seat to the inner workings of a world-class academic medical center. I'd also offer a special focus on San Francisco and California.

Each day, I began my tweets with a local update. Each model was that of a war correspondent embedded in an army unit, my tweets serving as a kind of "news from the front." While



(1/7)



I thought I'd be chronicling a tsunami, as the days passed it became clear that, due to strong and early actions by political and corporate leaders and impressive cooperation from citizens, San Francisco and the Bay Area had, in fact, "flattened the curve."

At the time I launched my tweets, I also decided to repurpose another forum to disseminate information: our Medical Grand Rounds. Until mid-March, these rounds were a relatively sleepy and traditional forum in which experts presented updates on the latest clinical findings or research advances. The audience might have hit 100 for a particularly newsworthy topic or speaker.

We quickly converted them into COVID Grand Rounds, highlighting the most interesting topic each week: the disease curve, new treatments, insights into the workings of the virus, our evolving understanding of testing, COVID and health disparities, and more. Our live Zoom audiences for Grand Rounds often topped 2,500, and our first 10 conferences were viewed on YouTube more than 300,000 times.

It's remarkable to consider that all of these methods of communicating – Twitter, Zoom, and YouTube – did not exist 15 years ago. Their popularity, and the fact that they are now seen as go-to sites for up-to-date and trusted information about COVID, creates an extraordinary opportunity to communicate with professional and lay audiences around the world. Of course, they also create opportunities to spread misinformation. The Wall Street Journal profiled me in mid-May, and the title of the article – "Doctors are Tweeting About Coronavirus to Make Facts Go Viral" – cleverly made this point.

I decided early on that part of my goal was to be authentic, which meant that if real life influenced my worldview, I'd post that, too. So people got to see my dog, Newman, and his terrible pandemic haircut. And on April 1, they got to see my lunch of SpaghettiOs and Double Stuf Oreos.

And they got to see the poignancy of the pandemic, too, such as when I posted my interviews with UCSF physicians who had volunteered to care for patients in the hardest-hit areas of the country: Queens, New York; and the Navajo Nation. Or the story of the Kansas farmer who selflessly donated his mask to the state of New York.

Perhaps most interesting and gratifying was feeling the appreciation of the public as I did my best to explain the science and the medicine of COVID. There's never been a time that I can recall in which everyone wanted – needed – to know things that physicians and scientists spend years learning: how viruses spread, how to interpret test results, how clinical trials are designed, and what abbreviations ranging from PCR to PPE mean. While scientists had the advantage of knowing a lot of foundational information and concepts, COVID-19 was a great leveler: on January 1, 2020, no one knew anything about this particular virus.

And so we have all learned about it together.

Robert Wachter is chair of the UCSF Department of Medicine, the Lynne and Marc Benioff Professor of Hospital Medicine, and the Holly Smith Distinguished Professor of Science and Medicine.

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# 5 lessons from the pandemic



When future historians look back on this moment, they will draw many conclusions from our response to this crisis. Here are five big lessons that UCSF experts already see taking shape:

# 1. Science doesn't always move slowly

"It's been fantastic to see how fast science can move when people collaborate. We've been breaking down silos between scientists, laboratories, and institutions worldwide, as well as between universities and pharmaceutical companies. Structural biologists are talking to virologists who are talking to clinicians. It is the way we should do all science in the future. It's not just connections between, for example, work on genes and work on proteins; it's about building connections between people."

- Nevan Krogan, PhD, professor of cellular and molecular pharmacology; director, UCSF Quantitative Biosciences Institute

# 2. We are failing the most vulnerable

"This pandemic exposed deep, preexisting inequities. Although COVID-19 can affect everyone, the impact of this epidemic is not felt equally, and managing the pandemic will require us to focus on the most marginalized among us. We've learned that we have to pay attention not just to the conditions that lead to increased transmission but also to the things that make it hard for people to isolate, to quarantine, to get tested."

- Kirsten Bibbins-Domingo, PhD '94, MD '99, MAS '04, Lee Goldman, MD, Professor of Medicine; chair, Department of Epidemiology and Biostatistics

# **3.** Supply chains are a weak link

"We've learned that the supply chain is an extraordinarily complex organism. And it is fragile in the sense that, if you take out a few key sources, it's difficult to ramp up as quickly as we've needed to. The vast majority of supplies we needed - PPE and swabs came from the two countries that were the most devastated early on, Italy and China, and U.S.-based suppliers didn't have the capability to scale up quickly."

- Joshua Adler, MD, chief medical officer and executive vice president for physician services, UCSF Health



# **4.** Video visits are here to stay

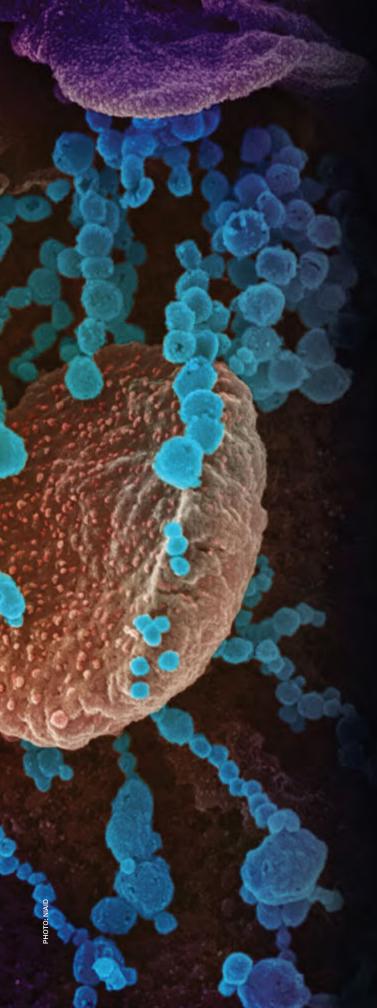
"Before the pandemic, about 2% of our visits were conducted as video visits. Currently, we're at about 60%, with some clinics at 90% to 100%. We'd been working on increasing those numbers for several years, and there had been a lot of resistance. And then all of a sudden, we changed. We've learned that we can conduct a fairly complete evaluation, including - more so than you would guess - parts of the physical exam. There's no question in the early data that patients really appreciate this, particularly patients who come from quite a distance to be seen."

- Susan Smith, MD, chief faculty practices officer and senior vice president, UCSF Health

## 5. Delayed consequences enable bad behavior

"Today, we know a lot about the virus, including how it spreads and how to prevent it. Today's risks are mostly about behavior, particularly masking and social distancing. And the surges we have seen have predictably occurred in places with the most at-risk behavior. A friend recently said to me, 'The virus is a great teacher.' No, not really. Fire is a great teacher: Touch it and it hurts like hell. For SARS-CoV-2, a person or a state can act badly and do fine for a while, confirming their belief that precautions are for wimps. By the time they feel the fire, it's too late."

- Robert Wachter, MD, Lynne and Marc Benioff Professor of Hospital Medicine; Holly Smith Distinguished Professor of Science and Medicine; chair, Department of Medicine



# There's no sugar-coating it: This has been hard.

And there's so much more to do.

But we were made to meet this moment.

To the thousands of donors who have buoyed UCSF's once-in-a-generation response to the COVID-19 pandemic, **THANK YOU**.

Here is just some of what you have made possible:

- Creating what Bloomberg "Opinion" called the "lab that could save America" – in just eight days
- Setting up new testing facilities, clinics, and quarantine spaces across San Francisco and dispatching UCSF heroes to New York and the Navajo Nation
- Providing childcare and hotel accommodations for critical frontline health workers
- Expanding outreach, education, and testing for vulnerable communities in the Bay Area while also strengthening the pandemic response in low-income countries
- Procuring PPE enough not just for UCSF's staff but also to share with other health care centers in need
- And so much more ...

Looking for ways you can help? **Visit coronavirus.ucsf.edu/help** 

