



**Pandemic effect**



**ON THE COVER** In October 2020, as we adjusted to masks being a part of daily life (outside the operating room, that is), crowds began to return to Cedar Street—much to the relief of food truck owners. As one doctor contemplates lunch options, the ebb and flow of passersby swirl past.

**THIS PAGE** Seven months earlier, in March 2020, just as COVID-19 was becoming reality, the same spot on Cedar Street was devoid of everything save for a few cars.

COVER AND THIS SPREAD: ROBERT A. LISAK PHOTOS

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Q&A DEAN NANCY BROWN



**A unified response**

The COVID-19 pandemic created many complex problems and posed powerful challenges to Yale School of Medicine (YSM). Dean Nancy Brown describes how the school crossed institutional boundaries to find solutions.

News of a deadly new virus spreading in China grabbed world headlines in January 2020, just as Nancy J. Brown, MD, the Jean and David W. Wallace Dean of Yale School of Medicine and the C.N.H. Long Professor of Internal Medicine, was moving to New Haven. When she officially began work on February 1, experts were already monitoring the spread of COVID-19 and planning for worst-case scenarios. A little more than a month later, Brown accepted the recommendation of the school's education leaders to pull students from their clinical clerkships and

halt in-person classes. YSM braced for impact as the virus swept over New York City and neighboring Connecticut, filling hospitals and straining clinics' capacity.

Dean Brown took time to reflect on the events of those first weeks and the months that followed, with challenges that included the long-term effects of closures on the educational and research missions; budget shortfalls; and institutional self-reflection in response to national events—and the ways YSM found opportunities to grow and improve in meeting those challenges.

**How did COVID start, from YSM's perspective? Looking back on the decisions you made, what drove some of the bigger moves?**

Leaders from the School of Public Health, the School of Medicine, the School of Nursing, and the School of Management began meeting at the end of February to consider scenarios and responses. I had not been here long. In fact, I remember standing in line outside a CT DMV to get license plates one Saturday morning while on a conference call with about 40 clinical leaders. After the first Connecticut COVID patient was hospitalized on March 7, 2020, the situation progressed rapidly. The Northeast was hit particularly hard by that first wave.

As a nation, we were not adequately prepared. We did not have the ability to conduct the widespread testing needed to evaluate the scope of the problem. Also, at the beginning of the pandemic, health care providers and hospitals lacked adequate personal protective equipment (PPE) required to treat patients safely. We were receiving and using pallets of PPE from all over the country, and even from international partners. Because of the shortage, we reduced elective surgeries and routine patient clinic visits. To create capacity for patients,

our leaders at the Smilow Cancer Hospital moved patients from the top three floors, as these floors had appropriate air handling for the treatment of COVID patients.

**Those swift and decisive responses certainly saved many lives. What other changes or innovations helped stem the tide?**

The most consequential response was our decision to gather experts across the university and health system to collaborate and work across boundaries. One Saturday in March 2020, I was on a call with Paul Taheri (chief executive officer, Yale Medicine), who said, "We need a Manhattan Project-style response."

The next day, we convened the first meeting of the COVID-19 Response Coordination Team, or CoReCT. Leadership and faculty from medicine, nursing, public health, engineering, social science, law, development, and the hospital met daily for several weeks. Our initial efforts focused on research and clinical responses. Our communications team established a web presence to facilitate collaboration and to make discoveries available in real time. We benefitted from a project manager who kept us on task. Bidirectional conversations with community leaders enabled us to respond to needs for testing and access to health care, and later to get word out about vaccination. At the same time, our colleagues in sociology and economics addressed the economic impact on the community.

CoReCT was an extraordinary group. It's rare to find so many leaders working together toward a common purpose. We changed the way we worked together, and we hope to leverage our learnings to address other challenges.

Other innovations emerged all over the school. Our education team worked tirelessly to create remote learning. Our students led creative initiatives such as the development of a course on the epidemiology of pandemics. Normally educational planning takes months to years; pivoting to socially distanced learning happened in a matter of days.

**After YSM settled into a rhythm and it had become somewhat routine to handle patients, what choices characterized the next phase?**

COVID started out as an infection that was poorly understood. Astute physician-scientists quickly defined the characteristics of patients who were most susceptible to severe infections and the role of the immune function and vascular injury in the illness. As the pandemic progressed from an acute problem to a chronic problem, other consequences emerged. Faculty, students, and staff faced emotional stress every day. Students and faculty had to respond to disruptions of their research programs, as social distancing limited the number of faculty and staff on campus and travel was limited. Nationally, women were disproportionately affected because child care was disrupted, and women often bear the primary responsibility for child care. Physicians and nurses were reassigned to new areas. Some who were unaccustomed to end-of-life care were abruptly faced with caring for patients who died.

We addressed these challenges in a number of ways. The university extended the tenure clock, and the School of Medicine made gap funding available to junior researchers. The only requirement to receive the funding was to meet with their mentorship committees; we used this [requirement] as a forcing function to make sure people were not becoming isolated. The Phyllis Bodel Childcare Center was able to obtain a PPP loan that allowed

them to stay open and extended the age of children eligible for care. Our Department of Psychiatry made a wide variety of resources available for people struggling with COVID-related trauma or anxiety. We offered coaching to teams of nurses and physicians we had disrupted when we moved wards to make room for COVID patients.

This work is ongoing. We're working with communities to stop the spread of misinformation about the vaccine or the virus, and encouraging people to vaccinate. There are also ongoing clinical trials to gauge the extent and nature of what's being referred to colloquially as Long COVID—the persistence of certain neurological and physiological symptoms long after the infection has subsided.

**How has YSM responded to some of the social and political events that occurred over the past year?**

The national protests that followed the deaths of George Floyd, Breonna Taylor, and others caused many Americans and institutions to look inward to consider racism in our own communities. We gathered in many town halls to listen. We accelerated the development of a strategic plan for diversity, equity, and inclusion. That goes back to the pandemic, too—COVID-19 disproportionately affected minority communities. It highlighted long-standing health disparities in chronic diseases such as hypertension and type 2 diabetes.

**Any final reflections?** Being part of the public health advising process for the larger university was meaningful to me as a Yale College alumna. On an even more personal note, my

father became gravely ill and passed away in May 2020. He did not have COVID, but I have no doubt that his care was affected by the pandemic. Paradoxically, because of work from home, I was able to be with him near the end when he came home to hospice care. That experience as a family member of a patient only serves to emphasize for me the importance of our work at Yale School of Medicine. Training future physicians and physician associates and assistants who will offer the highest quality of care and treat each patient with compassion and respect, making discoveries that will lead to new therapies and better health for all—this is what it is all about.

**From the editor**

The pandemic upended plans; paused the economy; and as of this writing has taken at least 600,000 lives in the United States while damaging millions more. This issue hopes to capture some of what happened for posterity.

When the staff started planning for this issue of *Yale Medicine Magazine* over a year ago, working in our office instead of fumbling with the unmute button on Zoom, we thought it might be useful to compare our efforts to check and then resolve the emerging COVID-19 pandemic to those of Yale School of Medicine (YSM) faculty and students struggling against the influenza pandemic of 1918. That, as it turned out, would not be possible.

For a number of reasons (chiefly the U.S.'s participation in World War I and the resultant wartime censorship), there was barely any reporting at Yale on the flu pandemic as a phenomenon. Stitching together an account of how the pandemic collided with early 20th-century New Haven is possible: that story can be found in data (for example, life expectancy in the U.S. dropped more

than 10 years among women and men from 1917 to 1918), photography, obituaries, and news stories.

But no single space exists in which people described an institutional response to the pandemic. Confronted with the absence of a single curated source of information about the day-to-day ways in which YSM had met 1918's pandemic, we realized the importance of documenting what was happening at YSM: The interruption of almost every facet of "normal" life in March 2020; the onset of critical illness and deaths; the scramble to coordinate a scientific and economic response; and the human toll—as well as the stories of people adapting to that adversity.

And so, this issue is dedicated not only to the scientists, physicians, students, and staff of the recent past and present, but to those of the future who, years or decades from now, will be able to draw inspiration from our failures and triumphs when they look back and discover this issue. These stories are a small—but we hope representative—sample of what happened here when the wave of infection first broke over our city and state in 2020.

*Adrian Bonenberger*  
Editor, Yale Medicine Magazine

**correspondence**  
Yale Medicine Magazine  
1 Church Street, Suite 300  
New Haven, CT 06510  
or email [ymm@yale.edu](mailto:ymm@yale.edu).  
Limit letters to 350 words and include a phone number.  
Letters may be edited for length.

**Editor**  
Adrian Bonenberger

**Contributing Editors**  
Robert Forman  
Jill Max

**Senior Writer**  
Cathy Shufro

**Contributors**  
Jenny Blair, MD '04  
Sonya Collins  
John Curtis  
Christina Frank  
Lori Freshwater  
Steve Hamm  
Christopher Hoffman  
Katherine L. Kraines  
Valerie Pavilonis  
Kathleen Raven  
Ilana Strauss  
Carleen Wild  
Benjamin Yeager

**Art Director**  
Jennifer Stockwell

**Copy Editor**  
Rebecca Frey, PhD

**Mailing List Inquiries**  
Rhonda Evans

**Printing**  
Lane Press

**Correspondence**  
Editor, *Yale Medicine Magazine*  
1 Church Street, Suite 300  
New Haven, CT 06510-3330  
Telephone: 203-785-5824  
Facsimile: 203-785-4327  
Email: [ymm@yale.edu](mailto:ymm@yale.edu)  
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**Yale School of Medicine**  
Nancy J. Brown, MD  
*The Jean and David W. Wallace Dean of Medicine and the C.N.H. Long Professor of Internal Medicine*  
Mary Hu  
*Associate Dean for Communications*  
Roopashree Narasimhaiah, PhD  
*Associate Vice President for Medical School Development*

Abbreviations used in *Yale Medicine Magazine* include HS to denote the final year of residency for house staff, FW for the final year of a fellowship, and YNH for Yale New Haven Hospital.

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## A coup for comparative medicine

AN OLD STRAIN OF MOUSE VIRUS becomes key for COVID-19 research in Yale School of Medicine’s Department of Comparative Medicine.

When the COVID-19 pandemic took hold of the United States in the spring of 2020, Yale’s Department of Comparative Medicine was uniquely positioned to adapt its research and pivot to studying SARS-CoV-2, the virus that causes the disease. Scientists in the department were already focusing on many of the chronic conditions and risk factors that predispose people to develop complications from COVID-19. When the labs were forced to shut down in March 2020, the department held a faculty meeting to discuss how to go forward.

“In the last 15 years the individual researchers who were recruited and excelled in their works represent aspects of COVID-19 that turned out to be the major vulnerabilities—aging research, research on obesity, research on diabetes,” said Tamas Horvath, DVM, PhD, the Jean and David W. Wallace Professor of Comparative Medicine and chair

of the department, and director of the Yale Program in Integrative Cell Signaling and Neurobiology of Metabolism. “It turned out that we have a full package. The researchers didn’t have to adjust their approach or conceptual framework, but they could ask questions about COVID.”

To hit the ground running, the department’s members had to have access to an appropriate animal model that would have translational value, and shed light not only on how the virus causes symptoms but also on why some patients fare worse than others. The answer was to use MHV-A59, a strain of mouse hepatitis coronavirus that naturally infects rodents and behaves similarly in mice as SARS-CoV-2 does in humans. (SARS-CoV-2 itself does not infect rodents.) Reserves of the murine virus were immediately available in the lab’s freezer.

Several MHV strains were discovered in comparative medicine several decades ago—a period in which there was robust research related to coronaviruses, lab protocols, and contagion—but,

according to Carlos Fernandez-Hernando, PhD, professor of comparative medicine and of pathology, these rodent coronaviruses didn’t get a lot of attention at the time. “People thought it’s only going to be relevant for ... mice and rats because they get sick from it and it spreads rapidly among laboratory rodent colonies—but these infection models that were available turned out to be what is needed today,” he said.

Fernandez-Hernando is studying how SARS-CoV-2 causes cardiovascular complications and the potentially chronic effects of COVID-19 as seen in so-called “long haulers”—those patients who recover from the acute phase of the infection but go on to have such lingering or permanent health problems as lung damage. The mouse model using a specific MHV virus strain (MHV-A59), he said, is ideal for studying these chronic issues, and fundamental for developing new therapeutic targets.

“Sometimes the way science works is very unexpected,” he said. “Nobody, at least most people, predicted that there would be a coronavirus that would cause such major havoc in the world. Suddenly, this expertise is deployed now to study that virus, and has become extremely relevant as a model for COVID-19—in fact, superior to current animal models, the transgenic or genetically manipulated models that exist today.”

Vishwa Deep Dixit, DVM, PhD, the Waldemar Von Zedtwitz

Professor of Comparative Medicine and of Immunobiology, is currently investigating the reasons that elderly people make up a disproportionate number of COVID-19 patients. “One of the biggest problems, as we all know now, is the risk of severe infections in the elderly,” he said. “Mortality is highest in the elderly. What we really do not understand is what are the mechanisms that are responsible for causing an increase in susceptibility to COVID infection in the elderly. For that, what we need are models that can be immediately deployed to study the underlying deficits in the immune system of aged individuals.”

Dixit’s lab maintains a colony of aging mice at Yale. Teaming with Andrew Wang, MD, PhD, assistant professor of internal medicine and immunobiology, the researchers infected the young and old mice with the MHV-A59 mouse coronavirus.

“We compare them to the young animals, study their responses, and how they are different in terms of their immune system. What are the underlying deficits in the metabolic systems? The idea behind this is that if we understand what are the basic problems and defects in the immune system of the aged, we can intercede at those particular steps to develop various interventions that could be deployed to do the preclinical research that could eventually go into clinical trials.”

“And that’s how this MHV-A59, I think, is something that is now



serendipitously important for studies of COVID-19,” Dixit said, echoing Fernandez-Hernando’s appreciation of the relevance of a strain discovered years ago.

Others in the department, including James Macy Jr., DVM, a professor of comparative medicine and director of Yale’s Animal Resources Center, are using a grant funded by the National Science Foundation (NSF) to investigate the host and viral factors that influence MHV disease. Another professor of comparative medicine, Caroline Zeiss, BVSc, PhD, is modeling a rat coronavirus infection to better understand the dynamics of infection in populations, including the emergence of herd immunity; she is also funded by the NSF. In addition, Zeiss is

developing a COVID-19 hamster model through an NIH grant, using SARS CoV-2 because hamsters can be naturally infected with the human virus.

“People thought that, oh, the mouse is getting sick off of coronavirus. But how that mouse dies of that coronavirus, now it’s telling us how people die of COVID. Isn’t that fascinating?”

—Christina Frank



### Prisoners of broken systems

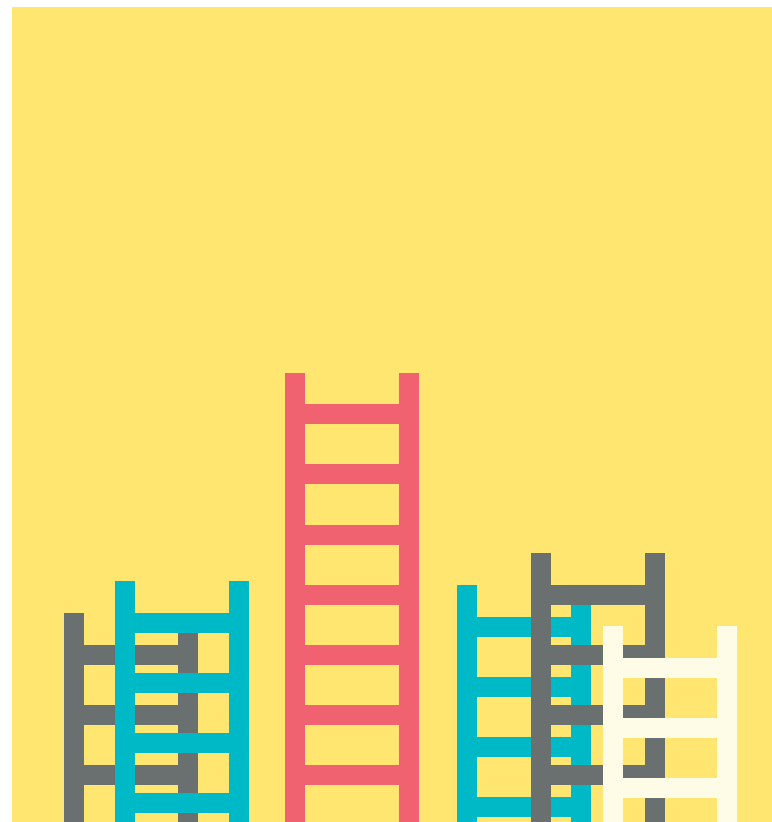
When Emily Wang, MD, professor of medicine (general medicine), was in medical school in the early 2000s, she started working in prisons and jails in the United States and abroad. Her time at a prison in Botswana surprised her and profoundly changed her worldview.

The Botswana prison was in the center of town and looked no

different from any home. While prisons in the United States are sealed off by layers of bars and gates, Wang walked through only one gate at the Botswana prison and found herself in the courtyard. There she saw prisoners moving around and laughing, and even one cutting hair. An American prison is a much grimmer place. “It’s meant for punishment,” she said. “You can feel it in your bones.”

The more Wang learned about prisons abroad, the more something became clear: “I saw that the criminal legal system is unique in the United States, and not in good ways,” she told me.

Wang, an internist, is now the director of SEICHE Center for Health and Justice at Yale School of Medicine (YSM), which is focused on health equity research. The center’s name (pronounced *saysish*) comes from a Swiss scientist’s term for a standing wave oscillating in an enclosed body of water; it reflects the center’s goal of bringing massive structural change to unjust closed systems. At the SEICHE Center, researchers work on issues like improving the prison system; studying the effects of COVID-19 on marginalized groups; and crafting public health policy. Wang is inspired to do this work because she knows different systems exist in other countries. In Finland, for instance, there is no death penalty, and the longest prison sentence is 14 years. “We have people serving double, triple life,” she said.



Her experiences with prisons inspired her to co-found the Transitions Clinic Network program, which hires formerly incarcerated people as community health workers. The program has reduced emergency department visits and future contacts with the criminal justice system.

“Those findings don’t surprise me,” she said. “What has surprised me is how little research there is on something of such profound importance.”

That’s because prison reform isn’t just about justice; it’s also about health. The prison system in the United States is a public health disaster. Health

systems within prisons are often understaffed and underfunded. Prisons were COVID-19 infection hotspots in 2020. Although taxpayer dollars pay for prisoners’ health care, the actual care provided is opaque to outside observers. “While health care is delivered behind bars, we have no way of knowing the quality or cost,” Wang said.

YSM has also looked at gun violence. There are plenty of government and police-led interventions to decrease gun violence, but few community-led ones. Yale decided to have a go at it. The team at Yale started by partnering with 20 community members from New Haven. The researchers learned that over 90% of the members had been exposed to gun violence; a significant minority had been present when someone was killed.

The team then used police data to do a social network analysis of gun violence in New Haven. Here’s where the Yale approach took a distinctive turn: lots of research teams trying to decrease gun violence focus on bad actors and dangerous neighborhoods. But the Yale team did the opposite: it focused on people who look like they should have been victimized but never were, and on areas that looked like they should have high levels of gun violence but didn’t. The team then tried to figure out what was so special about these areas.

“You’re looking at what works,” Wang said. That focus helped them figure out the relationship between factors like home ownership, green space, and closely connected communities to local crime levels. “The tighter your bonds are to your neighbors, and the more you’re acting in your collective benefits, the less your exposure to violence will be,” she added.

While many of these programs have been focused on New Haven, health equity research at Yale extends beyond Connecticut. Inequality has made it hard for marginalized communities to take preventive COVID-19 measures, and how existing health inequities have been worsened by the pandemic. On both the large and small scale, health isn’t just about individuals; it’s also about the societies in which they live. The COVID-19 crisis has laid those inequities bare.

—Ilana Strauss



### A reunion to remember

It’s one of the oldest traditions at Yale School of Medicine (YSM): Every year, on the weekend after Memorial Day, graduates gather for Reunion Weekend, when they catch up, reminisce, attend lectures, and have a good time.

That tradition fell by the wayside last year. Facing the raging COVID-19 pandemic, YSM cancelled the 2020 Reunion Weekend. The school resolved that that would not happen again, said Erin Shreve, YSM director of alumni affairs and giving. The only question was: would the reunions be in-person, virtual, or hybrid? The school settled on virtual.

Partnering with the larger Yale Alumni Association, Shreve and her team set to work moving everything from the Dean’s State of the School address to class get-togethers online. They worked closely with each class to set up virtual socials and other events. Numerous members of the medical school community pitched in to coordinate the weekend’s activities.

“If one person hadn’t pulled their weight, it wouldn’t have worked,” Shreve said. “There were dozens of people behind the scenes.”

The hard work paid off. The 2021 Reunion Weekend, held the weekend of June 5, attracted one of the highest participation rates in the event’s history. Preliminary figures show that of the just over 900 invitees—graduates—invited back every five years—over 350 registered to attend.

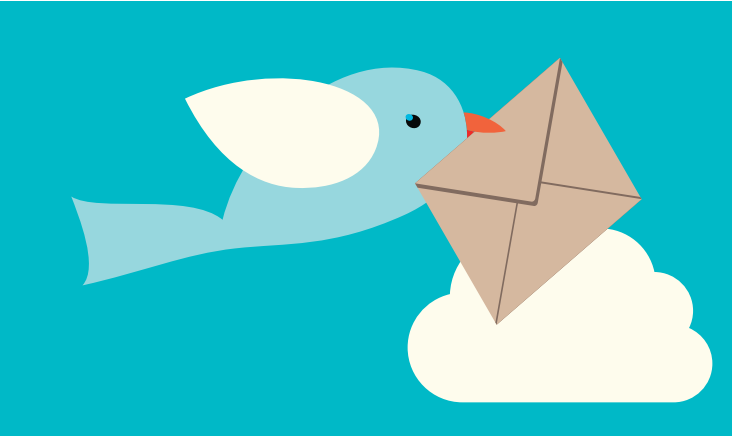
“The classes really took ownership,” Shreve said. “They did a great job getting the word out.”

Richard Moggio, MD, YSM ’71, who led the planning for his class’s 50th reunion, called the event a big success and credited Shreve and other Yale staffers. His class’s reunion attracted 40 alumni. The retired cardiac surgeon from Pound Ridge, N.Y., admitted to some trepidation beforehand, especially around the use of technology: “My personal nightmare was pushing the wrong button and accidentally cutting Dean Brown’s discussion with our class short,” he quipped. But his fears proved unfounded.

“The Yale planning team did a remarkable job,” Moggio said. “They created a great framework in which alums could swap impressions and catch up.”

Susan Ryu, MD, also said that she, Richard Kayne, MD, Alfredo Axtmayer, MD, and other members of the Class of 1976, were very happy with the weekend. Both Ryu and Moggio reported that the Zoom sessions led graduates to interact with a far wider group of fellow alumni than normal. Each leader held a session at which alumni were to provide brief synopses of their careers, only to see them give in-depth and in some cases deeply personal accounts of their lives. Both said that was one of the highlights of the online format.

“In person, what happens is you go back to the same group you hung out with,” said Ryu, a semi-retired ophthalmologist



from Palo Alto, Calif., who helped organize her year's reunion. "What happened in Zoom is [that] you are sharing your story with all these people. I think people were touched that they were hearing from classmates whom they might have barely said hello to in school."

Another upside to online reunions: people who live far from New Haven were able to attend, said Yin Ho, MD, YSM '96, MBA. One member of her class attended from Australia. "I have a feeling we ended up with more than we would have in person," said Ho, who organized her class's reunion.

The pandemic and 2020's national reckoning on race dominated weekend talks. In her State of the School address, YSM Dean Nancy Brown, MD, Yale College '81, told alumni that the medical school has increased commitment to diversity, equity, and inclusion in all areas—including recruitment, mentoring and retention of faculty, student enrollment, and patient care.

"This has been a year in which we, and all institutions, have turned inward to think about how we develop an inclusive environment and how we can continue to enhance the diversity of our faculty," Brown said. "We developed a strategic plan around diversity and equity. The features of that plan are designed to create an inclusive environment."

In what Brown described as "a hub-and-spoke model," each department now has a vice chair of diversity. This group meets monthly to share best practices. In another action, the school moved portraits of past deans that had been located outside the dean's office down the hallway to make room for recurring exhibits that "reflect some of our more modern history," she said.

Brown praised the response of students, faculty, and researchers to the COVID-19 pandemic. At the pandemic's peak, YSM doctors did "heroic" work in Yale New Haven Hospital, while students volunteered to help staff the vaccine program—which was so successful it inspired a visit from the Centers for Disease Control and Prevention. Members of the school community also conducted a trial of the Pfizer vaccine, developed a COVID test, and contributed cutting-edge research on the virus.

Akiko Iwasaki, PhD, the Waldemar Von Zedtwitz Professor of Immunobiology, professor of molecular, cellular, and developmental biology,

and Howard Hughes Medical Institute principal investigator, delivered a presentation on some of that research, focusing on Long COVID, a debilitating condition afflicting millions. "This is a major crisis going forward," Iwasaki said. "Even after we contain COVID with a vaccine, there will be millions of people suffering from the long-term consequences."

The weekend also featured lectures on coping with stress created by the pandemic and honing observation prowess to improve diagnostic skills and fight implicit bias.

Will virtual events become a permanent part of the event? Shreve thinks this year's event combined with experiences over the last year may create an expectation for online components in the future. "People have come to anticipate the ease of clicking in to a session or a panel at their convenience," she said. "So I do imagine we would have some sort of virtual component."

Alumni Ryu, Moggio, and Ho all thought that the school should consider adding some other online features to alumni affairs, such as virtual get-togethers between the five-year reunions. "I think it's something they should think about," Ryu said. With new remote technologies firmly entrenched in communications patterns across the globe, it's likely that how YSM alumni connect and stay in touch has changed for good.

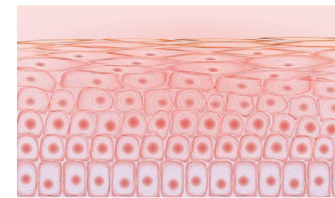
—Christopher Hoffman

# round up

a collection of recent scientific findings

## MESSENGER RNA INSTRUCTIONS

Advances in vaccine technologies over the last decade, along with unprecedented cooperation among governments, industries, nonprofits, and research institutes, accelerated the development of vaccines for SARS-CoV-2—the virus that causes COVID-19. Messenger RNA or mRNA vaccines—the platform adopted by both Pfizer-BioNTech and Moderna—recently matured sufficiently to be used against SARS-CoV-2. Unlike traditional viral vaccines (which may deliver an inactivated or weakened version of a virus or a piece of a virus like a specific protein to stimulate an immune response), mRNA vaccines deliver genetic instructions for making a portion of the target virus to an individual's cells. The SARS-CoV-2 vaccine is just the beginning of a revolutionary new phase in disease and infection prevention, with vaccines against rabies, Zika fever, HIV, influenza, and cancer on the horizon.



## AN ARMY OF IMMUNE CELLS

Skin is responsible for protecting the body against a wide range of possible infections. A new Yale study shows how this protection works: at a fundamental level, the epidermis—the outermost layer of skin—comprises an army of immune cells stationed at regular intervals across the skin's expanse to resist infection. Researchers from the lab of Valentina Greco, PhD, the Carolyn Walch Slayman Professor of Genetics, including research associate Catherine Matte-Martone, found that these immune system soldiers are able to reposition themselves to protect vulnerable areas when necessary, while avoiding clustering in any single location.



## ANSWER FOR SOME EPILEPTICS

With the help of robotics, experience, and advanced technology, surgeons in the Yale Department of Neurosurgery are one of only a few teams in the country that are regularly able to monitor activity in the insular cortex (a region of the brain's cortex invisible from the surface and traditionally inaccessible to surgeons); detect seizures that originate in this area; and perform precise surgical resections in the insular region. This combination of technology and technique has been a game-changer for many patients with drug-resistant epilepsy.



## AN END TO ANTIRETROVIRALS?

Scientists at Yale and the University of Montreal Hospital Research Centre published a study in the journal *Cell Host & Microbe* suggests that antiretroviral therapy, the most common treatment of HIV, may not be necessary in the future. Although antiretrovirals are effective, they are a lifelong necessity because patients continue to harbor latent HIV. In the absence of treatment, HIV can again replicate and rebound into AIDS. The study indicates that adding a single small molecule can rip away the shield that protects cells infected by HIV and expose them to the patient's own antibodies, which otherwise are not normally of much use against the disease.



## CONTROLLED FIRE

Ancient humans knew a bit more than we give them credit for, according to a report published in *Science Advances* in early May. Archaeological investigations led by Yale faculty on the shores of Lake Malawi in eastern Africa have uncovered evidence that humans used fire to reshape their environment over 90,000 years ago. Early humans used fire in a way that prevented regrowth of the region's forests, engineering their ecosystem to create favorable conditions for hunting and gathering food, and unintentionally contributing to the sprawling bushland that exists today.

DMITRII GUZHANIN ILLUSTRATION

CLOCKWISE FROM TOP: DR. AFTER 123 ILLUSTRATION, JOSE MORAES PHOTO, YAKUBOV ALIM PHOTO, BENJAMIN TOTH PHOTO, DENES FARKAS PHOTO



# Pandemic effect

MARCH 13, 2020, MARKED YALE NEW HAVEN HOSPITAL'S first admission of a patient confirmed to have COVID-19. What was by then a global pandemic was especially difficult for essential health care workers, who confronted more stringent safety precautions at work—and at home—to protect themselves, their patients, and their families. Doctors, nurses, EMTs, or emergency department personnel may come to mind immediately—but those working in a patient care site were and continue to be at risk.

On the following pages we examine ways in which the pandemic has affected the lives of Yale School of Medicine faculty, staff, students, researchers, clinicians, and administrators. We investigate the increased visibility of pathology labs, safety protocols, and vaccine development on campus; while off campus, where much of the work during the pandemic has been conducted, we take a closer look at the effects of working—and learning—from home.

Watching Yale's first livestreamed Commencement ceremonies just weeks ago led to the reflection that documenting an unprecedented public health crisis is more effective when it makes use of visual media. Two photo essays included in this issue demonstrate just that.

The first, *Metamorphosis*, is comprised of striking images captured over the course of the last 18 months. The blurred human figures direct the viewer's attention to the outside streets and interior spaces usually bustling with activity that have been nearly empty for over a year. In the second, a selection of images from an ongoing project titled *Faces of the Pandemic* focuses on portraits of essential workers.

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ROBERT A. LISAK PHOTO

# Metamorphosis

A series of four photoshoots—one dating to 2019; the remainder taken during the pandemic—show the contrast of life on campus.

PHOTOGRAPHS BY ROBERT A. LISAK

The Autumn 2019 issue of this magazine, which examined the relationship between diversity and better outcomes, necessitated an effort to visualize diversity across Yale School of Medicine's research capabilities, curriculum, student body, faculty, and staff.

Photographer Robert A. Lisak visited and captured images of many familiar spaces around the medical campus. Long camera exposures cause moving figures to blur and nearly detach from the very traits that usually enable us to identify and categorize people, allowing viewers to focus more on the work that happens across Yale School of Medicine (YSM). As those photos were being taken at the beginning of the 2019-2020 academic year, we were blissfully unaware that our lives—and the visual landscape of New Haven—would be changed forever within six months.

In the first weeks-to-months after the onset of the pandemic lockdown, Yale employees working from home requested permission, monitored their temperature, and made the necessary arrangements to visit campus. Charging cords, monitors, kids' artwork and family photos—left behind for what was assumed to be no longer than the length of a typical vacation—precipitated the visits, but the common element everyone noticed was how empty the med school campus—and New Haven as a whole—felt.

The black and white photos on this spread are a selection of images from the original 2019 photoshoot—done in part to show activity and community in spaces around YSM—as a marker of 'before.' Over the last 18 months Lisak visited campus three more times to document the impact of COVID-19, and throughout the feature stories in the pages to come, we share a selection from those shoots in full color.



**OPPOSITE PAGE** In 2019 people moved freely through the lobby of Yale Physician's Building, top.

The ambulance bay at Yale New Haven Hospital, bottom.

**THIS PAGE** Scenes around the medical school campus: a busy classroom, surgery in progress, the exterior of Sterling Hall of Medicine—inside, the rotunda—and a flurry of activity in a research lab.





Authorized Yale personnel and their guests only



**STAY HOME** if you have any of the following symptoms:  
Fever  
Cough  
Sore throat  
Shortness of breath  
Headache  
Muscle aches  
Loss of taste or smell  
Diarrhea  
Nausea or vomiting  
Stomach pain  
Unexplained fatigue  
New, worsening, or changing skin rash  
Red, swollen, or painful eyes  
New, worsening, or changing hair loss  
New, worsening, or changing hoarseness  
New, worsening, or changing voice  
New, worsening, or changing change in voice  
New, worsening, or changing change in voice

**Practice social distancing**  
Avoid close contact with others. Stay at least 6 feet (2 meters) away from others. Avoid crowded places and large gatherings.

**Clean and disinfect**  
Wash your hands frequently with soap and water for at least 20 seconds. Use hand sanitizer if soap and water are not available.

**Staying (6ft) apart keeps us together.**

Please swipe in individually, even if door is open.

**Wallet. Phone. Mask. Check.**

**New Year. Safe Haven.**

**Wash a mask in the morning in public settings.**

**Restricted access**



**It's ok to not be ok.**

**The future is in your hands. Please keep them clean.**

# Place of pride

Their expertise with procedures and tests has made YSM's Department of Pathology faculty some of the most popular people on campus.

BY SONYA COLLINS

Early in the COVID-19 pandemic, labs scrambled to meet demand for tests. The facilities that processed the specimens sometimes took up to a week to return results. Laboratories around the country started stepping up; they shifted focus from their day-to-day operations in order to stem the tide of coronavirus tests. Increasing testing capacity isn't just a matter of labs adding COVID-19 testing to their offerings; it is a major undertaking.

Scientists at Yale's Molecular Diagnostics Lab, part of the Department of Pathology, rose to this challenge. In March 2020, the pathologists had none of the equipment or space necessary and far too few technicians qualified to process COVID-19 tests. Over the course of the pandemic, the Molecular Diagnostics Lab evolved from manually processing nasopharyngeal swabs to playing a crucial role in the validation and execution of Yale's own FDA-approved SalivaDirect test. Here's how they did it.

## Building a COVID-19 lab through cooperation

On a typical day, the Molecular Diagnostics Lab performs tissue-based molecular testing related to cancer diagnoses. Extracting RNA from nasal swabs to detect the presence of an infectious pathogen was not a part of their routine. "Actually, we started from zero," said Jianhui Wang, PhD, a research scientist. Wang and his colleagues did not even have an appropriate place to run the tests. Their current facility was too small for the added operation; moreover, safe handling of the coronavirus required a separate stand-alone space.

In just two weeks, the lab had borrowed the space, the equipment, and even the workforce that it needed to get started from other groups or labs. "Everything was backordered. Borrowing was the only way," Wang said. "Every time I'd come into the lab," Susan Bell, interim manager of the Molecular Diagnostics Lab,

recalled, "different things were missing—pipettes, bio-safety cabinets—everything was disappearing as they moved it over to the other space."

As for the borrowed workforce, staff from other labs learned the safety protocols for handling the coronavirus—which included working in a hood, a mask, a face shield, and a hazmat suit. Then, in addition to continuing their own professional responsibilities, they volunteered for a few hours a week in the new COVID-19 lab.

At the same time, Pathology's in-house software engineering team moved quickly to create a platform for ordering tests, uploading results, and reporting positive results to the patient's home state according to that state's reporting regulations. Among its many functions, the platform allows clinics to print barcodes on a generic label printer and send specimens to the lab already labeled and ready to scan.

"It's pretty unique to have an engineering team as part of pathology," said Peter Gershkovich, MD, MHA, director of pathology informatics. "But without this, it wouldn't have been possible to scale up for COVID testing."

Like the lab, the engineers had their system up and running in two weeks.

## Taking decisive action

By the first week in April 2020, the lab was running COVID-19 nasopharyngeal tests. To perform this relatively complicated test, technicians must extract RNA from inside human cells and make copies of it to see whether it is viral. At first, the lab didn't have equipment that would automate this process. "You put the reagent in the tubes yourself, put the tubes in the machine, and turned them with your fingers," Wang said. "It was a very tedious job." The technicians continued to work this way until they acquired

polymerase chain reaction (PCR) machines that would do much of this work for them.

Meanwhile, Nathan Grubaugh, PhD, assistant professor of epidemiology, and Anne Wyllie, PhD, associate research scientist in epidemiology at Yale School of Public Health, had come up with a saliva-based COVID-19 test called SalivaDirect™ that would eliminate this tedious step. In June, the diagnostic test seemed ready for clinical use, but the researchers needed a lab to validate it. Just a few months earlier, the testing capacity required to validate this new diagnostic test might have seemed ambitious. By early summer, the Molecular Diagnostics Lab's COVID-19 operation was ready to help SalivaDirect make the final push into the clinic.

Over the next weeks, Wang and his team ran COVID-19 tests on 3,779 people—pulled from NBA players, staff members, and contractors. Their job was to confirm that SalivaDirect got the same results as the gold standard nasal swab test. The team confirmed the test results against the nasal swabs twice with equipment and supplies from different vendors to safeguard against potential supply chain shortages in the future. This crucial assist helped SalivaDirect obtain FDA-accelerated emergency use authorization (EUA) as a COVID-19 test.

## A closer look

Running COVID-19 tests can be grueling work. Manual RNA extraction, the method that Wang and his team used initially to process nasal swabs, takes about two hours, and technicians cannot stop during the process—a challenge given the required safety gear. "You look like an astronaut," Wang said. "But you can't stop until the manual extraction is done because it's very fragile and you have to move fast."

Researchers use pipettes to add chemicals, and then spin the vials to separate the mucus and other nasal matter from the human cells they need to test. Another chemical coaxes the cells open so the RNA can be extracted. Then a chemical reaction replicates the RNA multiple times so that there is enough of it to test for the presence of coronavirus.

After ushering the samples through these steps, the researchers would be soaked in sweat. They'd break, change clothes, and then start the next batch. Once the researchers acquired PCR machines that automated this process, the work moved faster and their testing capacity increased.

SalivaDirect makes things easier still. It's not necessary to extract viral RNA from the cells to perform the test. Technicians load vials containing saliva samples

into a 96-well plate—a tray with a hole for each tube. They use heat to inactivate the virus and then place the plate in the PCR machine, which copies the DNA and searches within it for the presence of coronavirus. A single "run" takes about an hour and 20 minutes.

The lab had fielded numerous PCR machines by winter 2020, each of which could perform seven or eight 96-sample runs per day. The lab receives hundreds of saliva and nasal samples daily.

## Peering into the future

A lot has happened since the Molecular Diagnostics Lab launched its COVID-19 testing lab in April 2020. Several COVID-19 vaccines gained official approval around the world; national vaccination campaigns have been undertaken in many countries; and new genetic variants of the virus, some of which may be more infectious or escape protection from vaccines, have emerged.

The lab of Jeffrey Sklar, MD '77, PhD '77, professor of pathology and of laboratory medicine, has taken up the next step in testing for SARS-CoV-2—the identification of viral variants. Mutations arise spontaneously as the virus replicates during infections. "Identification of variants requires analysis of the entire viral genome, which resembles a string of 30,000 beads (chemically termed nucleotides)," said Sklar of challenges facing surveillance for known and previously unknown variants. "Even a single change in one nucleotide among the 30,000 can potentially define a new viral variant."

Wang, too, knows there's still plenty of work ahead on the testing front, especially as schools and businesses look toward a full reopening that will depend on quick, effective diagnostics.

The lab continues to develop innovative ways to increase access and speed. The researchers recently applied for FDA approval of a point-of-care saliva-based test that they developed in their lab. A technician would administer the test on-site at a clinic and deliver the results in about an hour. "We've gained a lot of experience from SalivaDirect," Wang said. "If we ever need to scale up testing quickly for an epidemic or pandemic, we'll be ready." */yale medicine magazine*

*Sonya Collins is a frequent contributor to Yale Medicine Magazine.*



# Lessons learned

While the outbreak of COVID-19 fell heavily on the world in early 2020, researchers and clinicians at Yale School of Medicine acted swiftly to respond to the threat. Some of the school's leaders discussed lessons they learned from organizing and executing that response.

BY STEVE HAMM

On October 28, 2020, as infection rates of COVID-19 were surging for a second time, Yale School of Medicine and Yale New Haven Health conducted a virtual town hall aimed at convincing clinicians, faculty, staff, and trainees to seek help if they were feeling anxiety, depression, or other symptoms related to demands on them in the midst of the pandemic.

Five clinicians and administrators told of their own struggles with mental illness and occupational burnout. One of them, Michael Ivy, MD, the deputy chief medical officer of Yale New Haven Hospital (YNHH), had battled depression earlier in his career. After the town hall, he described why he was willing to speak out to colleagues. “In health care, there is a belief that if you ask for help with mental health struggles, your career is over,” he said. “I wanted to let people know that not only is it okay to ask for help if you need it, but you can thrive because you asked for help.”

The virtual town hall was one of multiple programs developed during the crisis to help workers cope with the severe stresses they faced—the long hours, the seriously ill and dying patients, and the risks to their own health and that of their family members.

This outcome was one of the significant takeaways from the COVID-19 disaster. No longer could the medical profession and health care system fail to ignore the toll of stress and mental illness on their own people. “We need to promote self-care as part of the professional lives of faculty, staff, and trainees,” said John Krystal, MD ’84, the Robert L. McNeil, Jr. Professor of Translational Research, professor of psychiatry and of neuroscience, and chair of the Department of Psychiatry at Yale School of Medicine and YNHH. “We need to address the stoic

culture of medicine. People are reluctant to identify themselves as needing help and hesitant to get help. We have to change that.”

Lessons from the outbreak of COVID-19 disease are profound and far-reaching for hospitals, clinicians, researchers, and medical schools. In department after department at Yale School of Medicine (YSM) and YNHH, which operate in parallel, leaders say the crisis marked a turning point in how they think about their jobs and how they get things done—and it should be a catalyst for more broadly transforming medicine.

Gary Desir, MD ’80, the Paul B. Beeson Professor of Medicine and chair of the Department of Internal Medicine at the school and hospital, said changes must take place at multiple levels. First, the public health system in the United States needs to be bolstered; it has been underfunded for years. Second, the medical profession has to widen its focus by not only studying and treating individual diseases but also seeking to improve population health outcomes. And last, the medical establishment must recognize and help correct health inequities. “Black and Brown communities have suffered more in both the number of COVID infections and complications,” he said. “If we needed confirmation that there’s a problem, this is it.”

In addition, leaders of health care and medical science recognized the need to address global issues that the crisis has brought into clearer focus. Because of population growth, environmental degradation, and climate change, it is likely that there will be larger and more frequent public health disasters in the coming years and decades. Disturbance of wildlife habitats leads to the spread of infectious diseases from animals to people. In a recently

published report, the British journal *The Lancet* draws direct connections between the COVID-19 crisis and climate change. “The window of opportunity is narrow, and, if the response to COVID-19 is not fully and directly aligned with national climate change strategies, the world will be unable to meet its commitments under the Paris Agreement, damaging health and health systems today and in the future.”

New Haven’s awakening to the COVID-19 crisis was a bit like the beginning of World War II had been for the mainland United States. The pandemic started in a far-off place, spread gradually at first, and suddenly it was in our backyard. On January 23, 2020, just two days after a World Health Organization (WHO) team arrived in Wuhan, China, to investigate the disease outbreak, Saad Omer, MBBS, MPH, PhD, director of the Yale Institute for Global Health, warned in a *New York Times* op-ed that the novel coronavirus could become a global pandemic if it were not handled correctly. He urged political and health care leaders to heed the lessons of earlier outbreaks, including severe acute respiratory syndrome (SARS) and Ebola. “Be ready for anything, and leave it to the experts,” he wrote.

The disease did spread worldwide in subsequent weeks. The outbreak in northern Italy in early March 2020 got the attention of health care leaders at Yale; they began to plan for the worst. On March 11, the WHO declared the outbreak a pandemic. The first patient with COVID-19 was admitted to YNHH on March 13. Within a few days, the emergency departments (EDs) on the two YNHH campuses were flooded with COVID-19 patients. Then the intensive care units (ICUs) were full, and many of the regular beds were converted to handle COVID-19 patients. At the peak of the crisis in April, there were 447 patients with COVID-19 on the New Haven campuses. “There will always be crises and disasters. We train and prepare for that,” said Gail D’Onofrio, MD, MS, the Albert E. Kent Professor of Emergency Medicine and chair of Emergency Medicine at the school and hospital. “But this was different. It wasn’t over quickly. It just kept going, and it wore our staff out.”

The emergency departments adapted to the flood of patients. They quickly changed their protocols to deal with social distancing; using personal protective equipment (PPE); and frequent cleaning of surfaces and computer keyboards. Within days, clinicians set up a tent outside the emergency department on York Street so that they could do evaluations immediately when sufferers suspected of having COVID-19 arrived. Clinicians in the ED developed and validated a 12-point

COVID-19 severity index for guiding the treatment of sick individuals. This index helped the hospital manage a surge of patients that on occasion left 50 to 80 people waiting in hallways for admission. In early December, there were more than 180 COVID-19 patients on the New Haven campuses and the ICUs were nearing capacity. YNHH had learned from the first surge, however, and had stockpiled PPE and ventilators in advance of the second one while optimizing its treatment protocols and testing procedures. The EDs were ready for whatever might come.

In spite of the heavy patient workload, ED clinicians wrote more than a dozen articles for scholarly journals about dealing with COVID-19 and pandemics. One of the key lessons they learned was to avoid putting COVID-19 patients on ventilators too soon. The patients might not need them; and once somebody was on a ventilator, it could be difficult to wean them from it.

Because of the influx of COVID-19 patients in March and April 2020, the New Haven Hospital campuses suspended many of their more routine services. Surgeons, anesthesiologists, and other internists as well as specialists with the appropriate experience were pressed into service in the ICUs and on medical floors; they helped wherever they were needed. In the early days, daily coordination meetings were held at the university, medical school, and hospital floors—often involving people from all three. In Internal Medicine, Desir created a COVID response team that met every morning for three months. “The big lesson from the first wave was [that] we all had to come together as a team, and we had to make decisions and do things much more quickly,” he said. A key example was the fast and massive shift to using telemedicine in place of many in-person clinical appointments.

The greatest early challenge for clinicians was that so little was known about the disease—from how it spreads between people to how it affects the body. Initially, no medicines were known to be effective against it. Over time, through experimentation and rapid studies, clinicians learned that the drug remdesivir and certain steroids helped address symptoms in some cases, but that hydroxychloroquine was not effective—even though it was touted by politicians and some physicians. “There’s a lesson here that we know but often forget,” said Desir.

## Lessons learned

“When a new disease comes along, never make declarative statements about it because you just don’t know much. You can quickly lose the trust of your colleagues and of the public.”

In those early days and again in December 2020, staff members of all types in the hospitals and clinics were nearly overwhelmed. They typically worked extra hours or extra shifts—increasing the strain they faced in balancing the needs of their work and their families. The result was stress and fatigue; and in many cases, symptoms that included anxiety and depression. “One of the biggest challenges was that many people were so exhausted and emotionally depleted that they didn’t have one extra ounce of energy to deal with their own self-care,” said Krystal.

To deal with that conundrum, leaders at the hospital and medical school developed a number of new programs by redeploying staff resources and recruiting volunteers. These initiatives were designed to make it easier for clinicians and staff members to get help—a “mental health safety net,” according to Samuel A. Ball, PhD, professor of psychiatry and associate dean for faculty affairs at the medical school. Early on, the leaders sent out an anonymous self-assessment survey to monitor health-system-wide stress levels and direct people to the appropriate resources. By early December, the survey had been used more than 18,000 times. The new programs included a series of virtual town halls; hospital-based wellness check-ins; a discipline-oriented buddy system; and a counseling program. The idea was that different people would respond to different offerings based on their needs and willingness to engage. There are several key findings from the programs so far, according to Krystal: first, no single intervention works for everyone; second, it’s important to adapt quickly to changing needs; and third, leaders need education and outreach to raise awareness of mental health issues and to convey how easy it is to get help.

One of the initiatives connected employees who asked for help to psychiatrists, psychologists, and social workers who were willing to pitch in on a voluntary basis. This confidential one-on-one consultation program was developed jointly by the Psychiatry Department and the Yale Child Study Center. It was led by Ball and Claudia Moreno, MD, assistant professor of clinical child psychiatry and medical director of consultation-liaison services at Yale New Haven Children’s Hospital. More than 150 clinicians volunteered to provide one to four acute stress intervention sessions free of charge. They referred employees who needed ongoing mental health treatment

for further care. By mid-December, 70 employees had taken advantage of the program. Moreno said she hoped COVID-19 awakens the medical establishment to mental health issues among health care workers—including making some of the new programs permanent. “We have to take away the stigma and provide opportunities for relief and recouping,” she said.

While the departments of Emergency Medicine, Internal Medicine, and Psychiatry were on the front lines of COVID-19, people in nearly every department and function at the medical school and health system pivoted from what they were doing to focus on the crisis. It was an all-hands-on-deck situation.

In Pathology and Laboratory Medicine, many were pressed into service on testing and diagnosis programs. Early on, Marie-Louise Landry, MD, professor and vice chair of laboratory medicine, led a team that quickly developed a version of the Centers for Disease Control and Prevention’s diagnostic test. A consensus grew that the molecular (PCR) tests were superior because they were the most accurate although it took longer to get results—up to five days at first. “My regret is we were not totally automated,” said Chen Liu, MD, PhD, chair and the Anthony N. Brady Professor of Pathology. He’s now investing in new diagnostic equipment and techniques have potential for clinical diagnoses beyond COVID-19. CRISPR gene-editing technology is being developed for COVID-19 testing, for instance.

In the clinical trials programs, Onyema Ogbuagu, MBBCh, associate professor of medicine, switched from a focus on HIV/AIDS to COVID-19. He became a principal investigator on multiple trials, including those of remdesivir and the Pfizer/BioNTech vaccine. The Pfizer and Moderna vaccines were developed using a new approach to vaccine development—the mRNA platform. Rather than implanting weakened or inactivated virus cells in our bodies, these vaccines use single-stranded molecules of RNA to trigger immune responses. The platform is not only faster than traditional vaccine development techniques, but also less risky for patients. Virologists hope the mRNA techniques will be useful for other viruses, including HIV.

The biggest lesson from COVID-19 in the drug development sphere was the importance of information sharing and collaboration, said Ogbuagu. Two days after

China shared the genetic sequence of the virus, scientists around the world produced corresponding mRNA. BioNTech invented the vaccine but needed Pfizer’s corporate muscle to help develop and distribute it. Pfizer needed clinical trial programs like Yale’s, which are especially adept at recruiting people from the heavily affected Black and Latino populations. The U.S. Food and Drug Administration (FDA) helped accelerate development, including combining phases II and III of clinical trials. “This galvanized the community like never before,” Ogbuagu said. “You wish things worked like this always.”

Even while COVID-19 was raging, medical scientists were busy trying to figure out how it works and what could be learned that would benefit medical science more broadly. Researchers from Yale School of Medicine and Yale School of Public Health combined forces to create a shared repository for new information about the virus and the disease. They enrolled more than 300 COVID-19 patients at YNHH to provide information including tissue samples for a wide variety of studies.

One of the organizers of the initiative, Shelli Farhadian, MD, PhD, an assistant professor of medicine specializing in infectious diseases, used some of the data for her research into the coronavirus’s effects on the brain. Soon after the first surge began, it became clear that many patients exhibit neurological symptoms, including severe headaches, seizures, and confusion. Farhadian and her colleagues established that the virus was indeed causing abnormal immune reactions in patients’ brains. They hope these investigations may lead to new approaches to treatment that might modify the immune response in the central nervous system, including the possible use of immunosuppressants. There’s an important lesson here. “When thinking about symptoms and damage caused during a severe infection, we have to think about two sides: the damage caused by the pathogen and the damage caused by the body’s overreaction to the pathogen,” said Farhadian.

Some Yale researchers are already turning their attention to the next viral threats. Erol Fikrig, MD, the Waldemar Von Zedtwitz Professor of Medicine (Infectious Diseases) and section chief for Infectious Diseases, regrets that most of the medical community’s response to the coronavirus has been reactive. “Hopefully, for future pandemics, we’ll be proactive,” he said. That will require massive financial investments in identifying and studying emerging microbes. Fikrig believes we must develop tools for fighting viruses that are not pathogen-specific—for example, new

techniques for stimulating the body’s immune system that suppress viruses without causing overreactions.

Yale School of Public Health is also looking toward the future. The school’s dean, Sten Vermund, MD, PhD, the Dean and Anna Lauder Professor of Public Health, said government and health care leaders alike need to do a better job of heeding the lessons from each epidemic or pandemic and preparing for the next ones. “You need to keep working on medical problems even if they seem to go away,” he said. “I hope that policymakers have been disabused of the notion that prevention is a luxury rather than a necessity.”

For Omer, a key lesson from COVID-19 is that the medical community must speak out loud and clear, not just about the science of diseases but also about the appropriate social and governmental responses. He proposed a forceful communications plan for overcoming resistance to vaccines in an op-ed in the *Washington Post*, which was published on November 30, 2020. “I believe that universities bring substantial expertise to the table, which has been sorely missed,” he said. “We have to reach policymakers at different levels and the general public. We have to inform opinion on a mass scale.”

The COVID-19 crisis demanded a lot of health care professionals—and they responded admirably. It seemed like a symbolic turning point in the battle when Yale New Haven Health arranged for five employees to receive the Pfizer vaccine in front of television cameras on December 15, 2020. One of the five was Ogbuagu, who ran Yale’s clinical trial for Pfizer. He spoke from the heart. “As a researcher who worked on the vaccine; as an infectious disease specialist who has been on the front lines of caring for patients with COVID-19; as a dad of three kids who are never impressed by anything I do; as a person of color, it has been really gratifying to be part of this process,” he said. “The message today is that this is the beginning of the end of the pandemic. We all need to get this thing, to roll up our sleeves, and move on.”

His message was directed at the general public—imploping people to get the vaccine. But it could just as well have been aimed at the health care and medical establishment. The COVID-19 crisis was a wake-up call. Will it lead to long-needed changes? *yale medicine magazine*

*Steve Hamm is a frequent contributor to Yale Medicine Magazine.*



YaleNewHavenHealth  
**COVID-19 Vaccination Site**  
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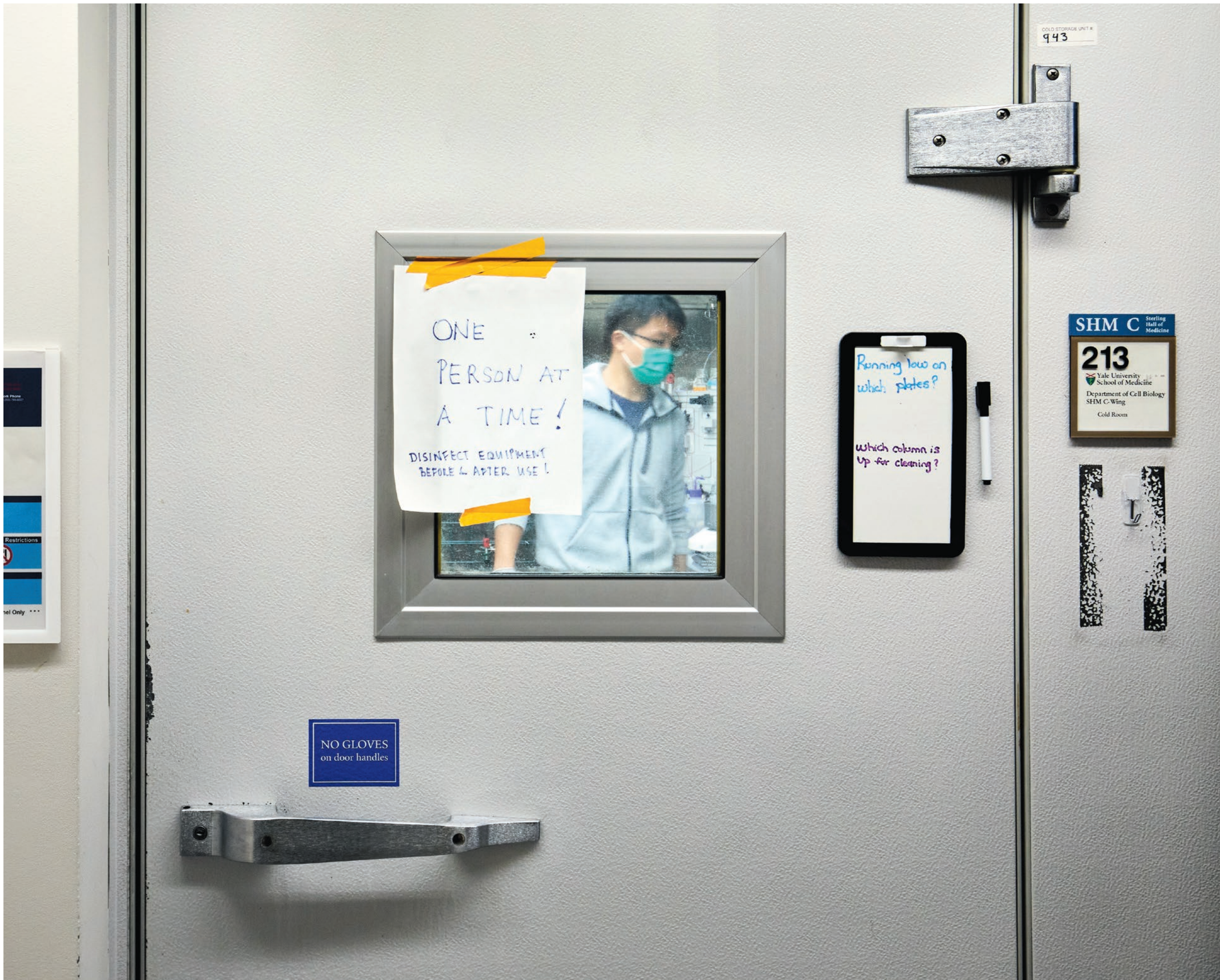
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# No shortcut

In developing a vaccine against COVID-19, a normally lengthy process was cut from years to months.

BY JENNY BLAIR, MD '04

On January 11, 2020, researchers around the world got their first look at the genetic sequence of the novel coronavirus SARS-CoV-2. By March 16, the first volunteer was injected with an experimental vaccine. The FDA authorized another vaccine on December 11, and the first Americans were dosed three days later, touching off a gigantic rollout. The stunning speed of this success has no precedent in vaccine science. It's the culmination of decades of investment and discovery, said Yale researchers.

"This is a watershed event in vaccinology and vaccine sciences," said Saad Omer, MBBS, MPH, PhD, associate dean (global health research) and professor of medicine (infectious diseases). "They sped it up by finding efficiencies, by using and taking advantage of platform technology, et cetera. But they haven't cut corners in the scientific process."

Normally, the pre-trial phase of vaccine development alone can last from three to nine years. Researchers discover and validate a target; study candidate vaccines in benchtop and animal research; develop a manufacturing process; and optimize an assay for testing the vaccine's efficacy. So how was the pre-trial process accomplished so quickly this time?

For one thing, researchers had a target in sight from early on: the coronavirus's spike protein or peplomer, with which it latches on to human cell surface receptors and begins the process of infection. From studies of other deadly coronaviruses, scientists know that an effective immune response includes antibodies capable of neutralizing the spike. That knowledge was invaluable when it came time to tackle SARS-CoV-2.

Another crucial piece of groundwork: a novel and powerful technology platform at the ready based on

nucleic acid vaccine technology. Researchers have known for decades that directly injecting mice—or humans—with DNA or RNA that encodes a pathogen’s protein can induce an effective immune response. Though no human vaccine on this nucleic acid platform had yet been fully developed, the technology has been around since the 1990s and has seen heavy investment since the mid-2000s.

“There was definite interest in the area, and many people were trying this out experimentally, but it hadn’t actually hit the mainstage,” said Richard Flavell, PhD, Sterling Professor of Immunobiology. “The pandemic accelerated this enormously; and luckily for the world, it looks to be working.”

“There has been an approach since 2005 or 2006 to invest in so-called platform technologies, such as mRNA technology, that would be useful irrespective of the pathogen that could lead to an outbreak,” Omer said. “Those things pay dividends.”

In the first approved coronavirus vaccine, synthetic messenger RNA stimulates human cells to create a simulacrum of the spike protein. That spike eventually gooses the immune system to tailor antibodies and immune cells that stand by in case the real thing happens along. “This approach is different from the initial trial-and-error approach,” Omer said. “Instead of looking at the pathogen, inactivating it, seeing [how] it works, tweaking the dose in an animal model, et cetera, now there’s more focus on exploiting the genetic information of the pathogen using bioinformatics to identify targets and using a fine-tuned precision-based approach.”

In this field, precision means speed. When nucleic acids are the basis of a vaccine, all that laboratories need to design a vaccine is the virus’ genetic sequence. Once scientists received the genetic code for the viral spike protein, they designed an mRNA vaccine within two days.

Trials came next. Ordinarily, these can last up to a decade. In 2020, enrollment in trials went faster because it took place at a high number of sites, so what would have been done in series was instead done in parallel, saving time. Moreover, the virus’ spread was so unchecked that researchers didn’t need to wait long for enough study participants to become infected.

Moreover, manufacturing vaccines based on nucleic-acid technology is easier than for such traditional vaccines as the ones that require recombinant proteins. For the coronavirus vaccine, federal funds from Operation Warp Speed allowed companies to gamble on their own unapproved vaccines by pre-manufacturing large numbers of doses, according to Flavell.

“That’s what they call at-risk manufacturing,” Flavell said. “Normally, a company would wait to see the results of clinical trials before manufacturing large numbers of doses of vaccine. In this case, that risk was assumed by the government, which enabled the entire process to be jump-started.”

The mRNA-based vaccines now being distributed around the world aren’t the last word. Dozens of others are in the pipeline, some of which will use other technologies and may prove to be easier to store or administer. But the first generation of SARS-CoV-2 vaccines carry the world’s hopes for holding the deadly pandemic at bay long enough to allow successive versions to emerge.

“It’s a wonderful example of immunology in action,” Flavell said. “The investment in research in general by the United States, which goes back to the end of World War II, when they created the NIH system of funding science—all of what we’re seeing now is a result of that investment. And it’s specifically into immunology as well. If that hadn’t happened, we’d be nowhere.” ***/yale medicine magazine***

*Jenny Blair is a frequent contributor to Yale Medicine Magazine.*

# COVID-free air

Sanitizing air and surfaces has always been a top priority for doctors and research laboratories. Environmental Health and Safety technicians had a significant if quiet role to play behind the scenes when COVID-19 struck.

BY ADRIAN BONENBERGER

Every occupation has a language particular to its needs: acronyms, vocabulary, and terms that capture its unique constraints and challenges. Yale’s Office of Environmental Health and Safety (EHS) is no different.

When the COVID-19 pandemic struck, the challenges and constraints of EHS were brought to the forefront of public consciousness for several months. Suddenly, the effectiveness ratings of masks became a matter of urgent importance. Supplies of disinfectant were emptied in a matter of days, with many people racing to stay up to speed with sanitation best practices. Home air purifiers flew off the shelves and the warehouses of online retailers as citizens tried to figure out the difference between biosafety level (BSL)-2 and BSL-3, and which rating would best protect against spreading the virus inside a home.

Meanwhile, Yale’s EHS was working overtime to accomplish three concurrent missions—ensuring that labs working on COVID were BSL-3 compliant; helping convert a wing of the hospital to treat COVID patients; and making sure other university facilities and housing were as safe as possible for students, faculty, and researchers.

“Our priority was to secure the university; to make the hospital as safe a place as we could make it for health care workers; and create spaces for researchers to understand the virus,” said Peter Reinhardt, director of EHS.

Another priority for Reinhardt was providing a context in which fellows, residents, and medical students could continue their education. EHS ensured that such fundamental elements of training as gross anatomy classes and examination rooms were properly ventilated and sanitized. “I thought, if we’re in the middle of a pandemic, we can’t stop training medical students,” Reinhardt said.

One innovation of which Reinhardt is particularly proud is a type of medical enclosure called a STUBBY.

EHS built custom-made enclosures in places where it was not possible to convert labs to BSL-3 compliance (the level required for safe handling and research of active COVID-19). One beneficiary of a STUBBY, according to Reinhardt, was Nathan Grubaugh, PhD, MS, assistant professor of epidemiology (microbial diseases) in Yale School of Public Health, whose work figured prominently in the development of an early saliva-based COVID test.

As if that were not enough, the group also evaluated and stored personal protective equipment (PPE) in the earliest days and weeks when supplies were short. “We were heavily involved with collecting donations for PPE,” added Kevin Charbonneau, EHS’s deputy director.

Furthermore, when the university established a field hospital in an empty Payne Whitney Gymnasium in April 2020, EHS was instrumental in bringing it online in accordance with regulations and best practice before pivoting over to student testing sites and other routine support.

“We’re safety professionals and we deal with ventilation all the time, so we were prepared up to a certain point, but nobody expected [the pandemic] to last as long as it has,” said Charbonneau.

Once more was known and understood about the virus, EHS swung back into action, helping reopen labs and sanitize public spaces for scientists, physicians, and researchers. This reopening meant the speedy continuation of paused clinical trials. It also permitted researchers to begin new trials and experiments.

“Once the university had figured out what they wanted to do, when, and where, we responded to make sure that leadership’s vision for education and safety were carried out,” said Reinhardt. ***/yale medicine magazine***

*Adrian Bonenberger is editor of Yale Medicine Magazine.*





# New learning methods

Students encountered a shifting curriculum and new ways of learning as the school made changes to blunt the impact of COVID-19.

BY JOHN CURTIS

When 100 first-year students arrived on Harkness Lawn for the White Coat Ceremony on August 28, 2020, they came in small groups. They wore masks and took socially distanced seats. And they donned their white coats without the symbolic assistance of faculty.

Before the ceremony, Yale health and safety staff had reviewed plans for the event. The open tent on the lawn posed more of a risk than open air, so the staff conducted smoke tests to map air flow.

The impact of COVID-19 was felt throughout the first-years' two-week course titled "Introduction to the Profession." The course, co-directed by Nancy Angoff, MD '90, MPH '81, MEd, and David Rosenthal, MD, assistant professor of medicine, with student directors Melanie Zheng '22, and Nensi Ruzgar '22, ordinarily takes first-year students into the hospital to glimpse their future roles in medicine. This year, the course was virtual. It focused on two public health crises: the coronavirus and structural racism exposed by the inequitably distributed effects of the virus among Blacks and Hispanics.

Since the spring of 2020, when faculty had just days to adjust the curriculum, the coronavirus has affected just about every aspect of the medical school. At that time, students had to abandon their clinical clerkships and attend lectures online, while many who lived in the dorms had to go home. Faculty began planning for the fall semester, finding ways to bring students back to New Haven.

"The biggest challenge was doing in-person activities in a way that was cognizant of and responsive to the restrictions that are in place," said Michael Schwartz, PhD, associate dean for curriculum. Students, he said, had been clamoring for such activities. Otherwise, they asked, what is the point of being in New Haven?

This balancing act remains a work in progress, and one expression keeps coming up. "It was very much building the plane as it was flying," said Dana

Dunne, MD, HS '90, FW '92, MHS '20, associate professor of medicine (infectious diseases), and director of the internal medicine clerkships.

To keep students safe, lectures were kept online and activities outside of class had become virtual. Libraries across Yale were closed. Labs were open in staggered shifts. Students living in dormitories were tested for COVID-19 twice a week. Students living off campus had the option to be tested once a week. Any students who venture on campus in 2021 must fill out an online survey to ensure they have no symptoms associated with COVID-19.

How students are affected by the restrictions depends in large part on where they are in their training. Students in their clinical years had to make up for time lost when they were pulled out of their clerkships. There wasn't enough personal protective equipment (PPE) to go around, and health care providers in the early days of the pandemic were stretched thin. "The preceptors that were going to be responsible for mentoring, teaching, and training our students were being overwhelmed themselves," said David Hersh, MD/PhD, assistant professor of pediatrics and director of all clerkships.

Clerkship blocks were shortened from 12 weeks to 10 by moving didactic sessions online. To avoid crowding in break rooms at lunch time, when masks would come off, unused auditoriums where people can maintain social distancing have become lunchrooms. On rounds, teams try to limit how many people can enter a patient's room.

The experience, Hersh said, will likely stay with students throughout their careers. "It's pretty rare that you get to live through a pandemic and see the impact on patients, on families, on providers, and see what it's like for clinicians to go through this," he said.

Lectures in the pre-clerkship semesters, said Peter Takizawa, PhD, assistant professor of cell biology and co-director of the pre-clerkship curriculum, are offered

in three formats: podcasts; live online lectures; or hybrid classes that allow up to 35 students chosen by lottery into a lecture hall while others attend via Zoom. Teaching on Zoom is a very different experience, he said.

"When I'm giving a lecture on Zoom, all I see are my slides, so it's hard to judge how what you're saying is landing with the students. If you're in the room, you can see if the students look confused," he said. Takizawa stays on Zoom after the lecture in case students have questions; he is also available during office hours.

Second-year student Degife noted that even before the pandemic, many students chose to watch lectures online rather than attend in person. Workshops also went online, she said, adding, "I do miss that small-group learning in person."

Her classmate Nobles said that she resists the urge to mute herself to avoid creating background noise. "At the same time, it stifles the natural reactions you might have like agreeing with someone or chiming in with an opinion," she said.

Some classes, like anatomy and physical examination skills, require students to be present, and precautions are in place. In the anatomy lab, students study in two shifts so that only half the class is present at any one time. Students wear extra levels of PPE, including face shields, and the rate of air exchange in the lab has been increased. Instead of roaming the room to work with students, faculty teach via Zoom from a dissection table.

Classes in physical examination remain in person, but interviews with standardized patients are remote. Students perform the physical exam on a manikin while interviewing their standardized patients via Zoom. Degife said this arrangement presented an unforeseen problem, however. "The manikin was heavy, so it was falling off the table. It was difficult to keep it in place while you're listening," she said.

Graduating students are the first ever to have their residency interviews online. Virtual visits eliminate the cost of travel, but they make it harder to get a sense of a program. "They'll have resident meetings virtually, but it's not the same as having a dinner the night before and getting a feel for their personalities," said Nancy R. Angoff, MD '90, MPH '81, MEd, HS '93, associate dean for student affairs. The med school has offered training in how to interview online, she said.

Another change is the National Board of Medical Examiners' cancellation of Step 2 CS, an exam that requires graduating students to travel to one of five centers to assess their physical examination and history-taking skills with standardized patients.

On campus, students have organized virtual social activities, like online pumpkin carving for Halloween and a virtual Day of the Dead in November. At Thanksgiving, students gathered online in small groups over meals from DoorDash with vouchers provided by the university. "Some students set up random events where they meet three other people to get to know people you might not feel comfortable reaching out to," said first-year student Victoria Marks.

"Socially, the part I struggle the most with is the more peripheral friendships," said one of her roommates, Jacqueline Ihnat. "Every time I hang out with people it has to be so intentional, so you only hang out with people you have shared interests with."

Despite precautions, some students tested positive for COVID-19 in 2021—not from hospital exposures but from small social events. Angoff and Schwartz, the medical school's designated health and safety officers, said that another dozen have had to quarantine because of exposures to others who tested positive, mostly domestic partners or roommates. Those who do test positive get regular phone check-ins from Angoff. "That way they just don't feel as alone," she said.

While the fall semester neared its end, faculty were planning for the spring of 2021. They know that things can change quickly during the pandemic. They anticipated a surge in infections, illness, and hospitalizations even as the nation embarked on a vaccination program. Lessons learned from the spring of 2020, which required a quick reaction with so much unknown about the virus, have informed the school's plans.

"As opposed to then, when things happened in a matter of days and weeks, there have been a lot of planning meetings in recent months, to think about if things get worse, what precautions do we need to take and how to best reorganize what we are doing?" said Schwartz. "We are also in continuous and active conversations with the health system, to make sure that the experience of our learners in the clinical environment is being considered and addressed." ***yale medicine magazine***

*John Curtis is a frequent contributor to Yale Medicine Magazine.*



Medical Library Book Pickup

Medical Library Book Pickup  
YALE UNIVERSITY LIBRARY





*FACES OF THE PANDEMIC* is an ongoing portrait photography project documenting the experiences of essential health care workers throughout the pandemic—an unprecedented time for Yale’s medical community, the nation, and the world. It is meant to show appreciation for these individuals and provide a platform for them to share their stories.

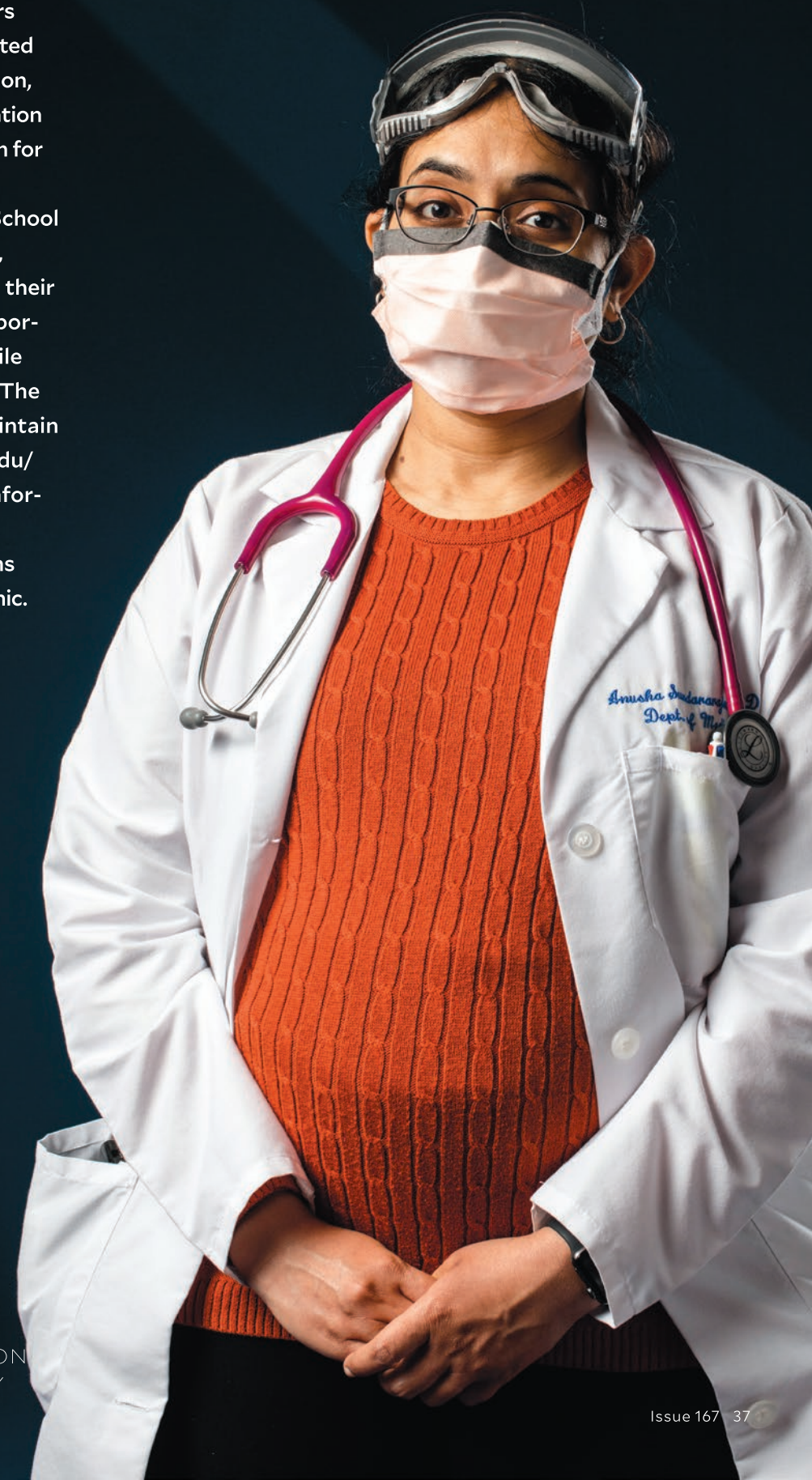
Representing a variety of roles at Yale School of Medicine and Yale New Haven Hospital, each participant is photographed wearing their typical work attire, including PPE. Formal portraits display respect for the subjects while candid captures their range of emotions. The photos have been minimally edited to maintain a documentary feel. Visit [medicine.yale.edu/communications/photo/faces](http://medicine.yale.edu/communications/photo/faces) for more information and project updates.

Each participant answered five questions to catalogue their experience of the pandemic. For *Yale Medicine Magazine* we’ve chosen to highlight a common thread:

## The pandemic has...

taught me more about the value of family, friends, and colleagues

**Anusha Sundararajan, MD**  
Clinical Fellow, Nephrology



ALLAIRE BARTEL CREATIVE DIRECTION  
ANTHONY DECARLO PHOTOGRAPHY



shown me that I'm  
instrumental  
and essential in  
patients' recovery

Cesar Vazquez  
Environmental Services Associate



made me appreciate  
life and brought  
my family closer

Sandra Johnson, PCA  
Patient Care Associate,  
Gynecologic Oncology



prompted me  
to pursue the role of  
community  
physician

**Hiam Naiditch, MD, MHS**  
Ambulatory Chief Resident (NHPCC),  
Internal Medicine

solidified that we  
need to stick  
to the medical and  
scientific facts

**Merceditas Villanueva, MD**  
Associate Professor of Medicine;  
Director, Yale HIV/AIDS  
Program; Donaldson Firm  
Chief, Infectious Diseases





reminded me  
that caring for  
critically ill patients  
is a privilege

**Felipe Lopez, MD**  
Assistant Professor of Medicine,  
Pulmonary, Critical Care, and  
Sleep Medicine

applied enormous  
pressure to find  
answers where  
we had none

**Alice Lu-Culligan**  
MD-PhD Student, Immunobiology



sharpened my  
awareness  
of our vulnerability  
and mortality

Rabbi Leah Tenenbaum, DMin  
Rabbi, Spiritual Care



## Yearlong home-work

The pandemic changed many aspects of people's lives, including working at home. Students, faculty, and staff acknowledged some benefits from the change, while lamenting what had been lost.

BY JOHN CURTIS

In the months since the coronavirus pandemic shut down YSM offices and classrooms, people quickly noticed the little things they'd lost—bumping into someone in the hallway, popping into a colleague's office with a quick question, going for coffee after a lecture.

"I miss the grapevine. I miss saying hello to people walking down Cedar Street. I miss people walking up to my door and saying, 'Can we talk?'" said Nancy R. Angoff, MD '90, MPH '81, MEd, HS '93, associate dean for student affairs. She began working from home in March 2020.

Ever since, faculty and staff have kept things running at a distance. To be sure, moving just about every interaction to Zoom, email, or the phone saves time. And working at home can be a boon for parents of small children. But most agreed that something important had been lost.

"The atmosphere of a community is based on the ability to have and be part of conversations beyond the work you do together," said Michael Schwartz, PhD, associate dean for curriculum. "If you're talking about things in the office or getting together in the conference room, everybody hears the conversation and may hear something important to them. Working virtually sometimes makes it feel like you're left out of conversations that might impact what you're doing."

"We all feel like we get more done when we're in the office," said Susan Larkin, MBA, associate director of the Office of Education, which at one point had staggered its schedule so that no more than two people were in the office on any day (as a resource for students and faculty). "Connecting on a personal and professional level is so stilted on Zoom."

Email also comes with glitches, Larkin said. "Trying to have a conversation over an email trail often times leads to miscommunication or confusion. In our

office we say that if it's going back two or three emails, just pick up the phone."

Jill Aulenti, MEd, director of student programs in the Office of Student Affairs, saw working at home as a mixed bag. "I miss the camaraderie of sitting around the lunch table and having a cup of coffee," she said. "We have a great group in our office, we consider ourselves family." But she liked being at home with her two school-age sons. "I'm able to drive them to school and pick them up. That eliminates the risk of them being on the school bus."

Students also missed casual encounters. First-year students say they have yet to meet all their classmates, but they have formed small bubbles based on where they live. Four women who share an apartment a few blocks from the medical campus live directly below and above classmates. "It's easier to see people who are in our building," said Victoria Marks, one of the four roommates.

Marks has also found that classes on Zoom create a sort of barrier. "At the end of the lecture, Zoom ends and I don't get to meet the person sitting next to me and find out what lab they're in," she said. The same holds for small workshops. "Instead of walking out of the room and chatting with the people you did it with, and going out and getting lunch, you're alone in your room."

Second-year student Ellelan Degife said that her class spent a semester together before the coronavirus separated them. "We were on the precipice of getting to know our classmates—and I haven't seen the vast majority of them in person for the last 10 months," she said. "I think that that is something difficult, and hopefully there is time to recuperate those relationships later on." */yale medicine magazine*

*John Curtis is a frequent contributor to Yale Medicine Magazine.*





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EMERGENCY

# Research, accelerated

As the COVID-19 pandemic continues, Yale affiliates' preprint service dramatically speeds the availability of medical research.

BY VALERIE PAVILONIS

When scientists submit a paper to a journal for publication, their next step is to wait for the reviewers' comments and the journal's final verdict. The clock ticks; and in the meantime, the results remain locked from the public eye for months. Many researchers complain that the process delays the opportunity to obtain feedback from others and foster collaboration.

The website medRxiv (pronounced med-archive) was created to address this delay. Launched in July 2019, the website is a preprint server where medical researchers can upload their studies before peer review, which can take years, and involves back-and-forth between researcher and reviewer. According to two of its founders, Harlan Krumholz, MD, SM, the Harold H. Hines, Jr. Professor of Medicine (Cardiology) and professor in the Institute for Social and Policy Studies; and Joseph Ross, MD, MHS '06, professor of medicine (general medicine) and of public health, medRxiv accelerates this process.

"There's a lot of research where it's imperfect, but we can learn from it," Ross said. "And the long road from finalizing the paper to getting it published prevents us from learning from one another. And so that's part of what we're trying to address here."

Krumholz's deep interest in open science began with the recognition that scientific progress had been impeded by a culture of academic competition that sequestered data and blocked full transparency of methods. Together, he and Ross involved themselves in several open-science efforts, most notably founding the Yale Open Data Access (YODA) project, which facilitates access to clinical trial data. And according to Ross, medRxiv was the next step in their quest to foster transparency in medical research.

Preprint servers exist for many disciplines, ranging from economics to mathematics to data science, and provide platforms for scientists to share work that is

not yet peer reviewed. They offer an opportunity to share findings before they appear in journals; medRxiv is a clinical research preprint service.

medRxiv's partnerships grew out of the 2017 Peer Review Congress in Chicago, where Krumholz gave a talk announcing a preprint service for the medical sciences. Krumholz and Ross had planned the announcement and were working out the details of how it would take place. After the presentation, Krumholz and Ross met with attendees from both Cold Spring Harbor Laboratory (CSHL) and *The BMJ*, a medical journal published by the British Medical Association. The groups soon decided to join forces after talking.

"If it can help people, then time matters," said Krumholz, "because you're trying to create progress. If our work is languishing within the peer-review process, which can take years, then it's by definition slowing down scientific effort."

Krumholz's speech at the congress sparked several questions. Some medical editors expressed concerns that posting research before peer review might harm patients and spread misinformation. Krumholz and Ross said they could answer most of the questions but recognized that medRxiv required more guardrails than other preprint services.

These safeguards are important during the screening process. The research cannot identify participants, use unregistered clinical trials, or be submitted by an anonymous author. The final check is a question: could any harm result from the research? Usually, the answer is no; but if the study draws particularly strong conclusions—Krumholz gave the hypothetical example of someone's claiming that cigarettes increase life expectancy—the team at medRxiv would reach out to the author and suggest the study go through standard peer review instead. Ross added that during weekly

meetings, questionable submissions are one item on the agenda along with general medRxiv policies that might require alteration.

One safeguard of medRxiv stands out on the homepage of its website: a disclaimer in red type that cautions readers against using the studies posted for "clinical practice or health-related behavior."

As significant amounts of research ultimately end up unpublished, preprints allow for registered trials and their results to appear online. Preprints also protect the provenance of an idea: two people could be working on the same project at the same time, but first publication might be based simply on luck. "In terms of actually making progress, you want to see today what people did yesterday, so tomorrow you can learn from it and maybe build on it," Krumholz said.

The medRxiv site, which is owned by CSHL, works with volunteers from the scientific community who sign up to read papers. These readers examine the ethics of the papers and make note of any concerns. Krumholz and Ross emphasize that medRxiv is a resource to the scientific community and that it benefits from the contributions of many, including a dedicated staff at CSHL.

Rachel Dreyer, PhD, assistant professor of emergency medicine, has worked with medRxiv since mid-2019 and reviews papers. She first reads the abstract to check for offensive material or disturbing claims or conclusions; then ensures that the ethics of the research, particularly regarding human subjects, have been correctly addressed. Dreyer estimates that she passes about 95% of the papers she reviews. The service has been particularly important in the pandemic: medRxiv has seen an influx of COVID-19-related papers—which would typically take months to be published.

"I'm interested in and passionate about open science, and just the idea of preprints," Dreyer said. "Submitting an article for publication to most journals is such a lengthy process, and I think there's a lot of value in submitting unpublished research that you're working on that can get out there in the scientific literature to share with others in the field."

Joshua Wallach, PhD, MS, assistant professor of epidemiology, also emphasized the time it takes for medical research to make it through the peer-review process. When he reviews research for peer-reviewed journals, he typically dedicates one to four hours to reading, making comments, and fleshing out those comments into a structured document. Scanning pieces for medRxiv does not require as much time—though Wallach also emphasized that despite medRxiv's

expedited posting process, researchers are still expected to submit their work to journals.

After receiving a submission, editors at peer-reviewed journals screen papers and identify peer reviewers with proper expertise. But there's never any guarantee that the journal will ultimately accept the research—and if a study is rejected, the process begins anew. As a researcher who has waited for review, Wallach added, the long time frame can be frustrating.

"If you're working in a rapidly changing field, six to 12 months is a very long time to wait to get that information out there, especially if other people are working in that field and are hoping to be able to read your paper, build upon what's been done, maybe learn from the techniques and methodology," Wallach said.

But medRxiv has alleviated some of that frustration. As the COVID-19 pandemic has progressed, Wallach added, medRxiv and other preprint servers have allowed for mass dissemination of research among scientists. Krumholz also noted that in June, the website posted a study by British researchers on the effects of dexamethasone in COVID-19 patients almost a full month before the *New England Journal of Medicine* published it. As of spring 2021, dexamethasone is widely used to treat severe cases of COVID-19, according to the World Health Organization (WHO). Nevertheless, Krumholz emphasized that the preprint server provides a service that is complementary to peer review.

Since its inception, medRxiv has boomed. According to Ross, while it's impossible to quantify the exact impact of COVID-19 on the site's growth, the number of submissions exploded from 7.2 papers a day in January 2020 to 77.1 in May. Now, Ross says, the number has settled around 50 papers per day in November and December 2020.

Wallach added that while he expects the bulk of research to continue to revolve around COVID-19, he's also looking forward to seeing what's submitted once the pandemic wanes. But no matter what the topic, Wallach emphasized that medRxiv is a worthy enterprise. "It is something that is just done out of interest and belief in medRxiv as a preprint service and as a service to the scientific community," Wallach said.

*/yale medicine magazine*

*Valerie Pavilonis is a first time contributor to Yale Medicine Magazine.*

# Shedding new light on an underacknowledged epidemic

HIV/AIDS took years to reach the public’s consciousness. A new exhibit highlights Yale’s role in raising awareness of the disease.

By Adrian Bonenberger

It took only weeks to appreciate the threat of COVID-19 as it raced around the world in early 2020. But nearly 40 years ago, before the arrival of social media and the smartphone, people had considerably greater difficulty coming to grips with the HIV/AIDS epidemic. Its resolution was a process that stretched from years into decades.

*Community in a Time of Crisis: Yale, New Haven, and HIV/AIDS, 1981–1996*, an exhibit sponsored by the Yale School of Medicine’s Program for Art in Public Spaces (PAPS), examines the early years of discovery, defining the newly emerging disease, and treatment of HIV/AIDS. With both online and in-person components, the Yale exhibit uses videos, photographs, historical documents, and articles to tell the story

of how HIV/AIDS arrived on the national and New Haven scenes. The exhibit is on view at Sterling Hall of Medicine, 333 Cedar Street.

Much like COVID-19, HIV/AIDS was poorly understood at first—a characteristic that led to stigmatizing the illness. “In the early years, HIV/AIDS became associated with what were thought of at the time as marginal communities: the gay community, impoverished communities affected by drug use, communities of color,” said Sarah Pickman, a member of a team of PhD students in the History of Science and Medicine Program (HSHM) within Yale’s History Department who were responsible for curating the exhibit. The curatorial team also included Kristine Ericson, Megann Liciskai, Maya Sandler, and Beans Velocci.

Experts—along with the testimonies of celebrities affected by HIV—were able to change the public’s

understanding over time. Meanwhile, researchers at Yale and elsewhere were working hard to develop effective treatment protocols along with the prospect of a vaccine or cure. To date, there is no preventive or therapeutic vaccine for AIDS, though antiretroviral therapy (ART)—personalized combinations of drugs from six different classes—can arrest the disease’s advance, effectively turning it into a serious but manageable chronic condition.

It is easy to forget how damaging it was socially and professionally to receive an HIV/AIDS diagnosis, which was seen in the early 1980s as a public death sentence. This fact scared off many physicians and scientists, but a few leaders at the School of Medicine and in New Haven saw opportunities

to make a difference. “We wanted to capture and commemorate the outstanding work done by the Yale and New Haven communities in the early years of the AIDS/HIV epidemic as the country came to grips with this crisis,” said Darin A. Latimore, MD, deputy dean of diversity and inclusion, associate professor of internal medicine, and co-director of PAPS, along with Anna Reisman, MD, director of the Program for Humanities in Medicine and professor of internal medicine.

One conspicuous innovation focused on prevention of bloodborne diseases. The New Haven Needle Exchange—an attempt to distribute clean needles to intravenous drug users in the community—was started by a Yale School of Public Health (YSPH) student, Jon Parker, in violation of the law and protocol. Parker clandestinely collected used needles and exchanged them for new



ones. The program was run out of a storefront and a van that evolved into a mobile clinic. Staffed by faculty and students, the Community Health Care Van still offers a broad range of services to New Haven’s vulnerable populations and is now being used to help fight COVID-19.

The needle exchange program grew, and was sponsored by the city’s government from 1991 to 2017. The New Haven program was so successful in

its early years that it was ultimately adopted by the City of New York, and has since gone on to justify the prevention efforts of many communities in and outside the United States.

Other prominent Yale faculty played roles in combatting the epidemic on a variety of fronts or worked to raise awareness, including Yale President Peter Salovey, PhD; Gregg Gonsalves, PhD, assistant professor of epidemiology (microbial diseases), and co-director, global health justice partnership; Edward Kaplan, PhD, the William N. and Marie A. Beach Professor of Operations Research,

professor of public health, and professor of engineering; and Rick Altice, MD, professor of medicine (infectious diseases) and of epidemiology (microbial diseases), and director, Clinical and Community Research, director, HIV in Prisons Program, and director, Community Health Care Van. “There were so many who contributed to the efforts around understanding HIV/AIDS, laying the groundwork for where we are today,” said Reisman.

Over time, Yale and New Haven were able to bring HIV/AIDS under relative control. This success, more than anything else, is what *Community in a Time of Crisis* hopes to explain.

“There tends to be a narrative when we look at epidemics of the past; there’s a sense that only bold medical treatment options got rid of the disease,” said Pickman. “We hope through this exhibit to show that ‘treatment’ has a broad definition, and [that] the response was driven by many individuals motivated by compassion and community. It was a group effort.”

Clockwise from far left, examples from five topics that comprise the exhibit:

**COMMUNITY AND CAREGIVING**  
A 1986 AIDS Project New Haven (APNH) newsletter. APNH, established in 1983, was a hub for AIDS care and advocacy.

**NEEDLE EXCHANGE**  
Program director Elaine O’Keefe, foreground, with outreach workers (l-r) Michael White, Chris Brewer, Dominick Maldonado, George Edwards, and Sonia Lugo (in van) in the *Hartford Courant*, 1992.

**LEGACIES** Community Health Care Van, 2020.

**AIDS IN THE CLINIC**  
Gerald Friedland, MD, Director of the AIDS Program at Yale from 1991–2010, on the cover of *Newsweek*, 1986.

**STUDENT ACTIVISM**  
AIDS Prevention Week at Yale poster, 1986.

Original art from two community members is also included:

**KELLY JO CARLSON**  
Carlson’s collage, *Peter’s Retreat*, was chosen from an open call to members of the YSM community for artwork related to the theme of HIV/AIDS.

**CO CAMPBELL**  
In commemoration of the 25th anniversary of APNH in 2008, Campbell was commissioned to handcraft a quilt honoring local community members lost to AIDS.



## Generations of medical expertise

CHRISTINA CHIA PRICE'S ANCESTORS and extended family members work in health care. That network has helped her excel in her chosen field—immunology.



Christina Chia Price's ancestors and extended family members work in health care—a network that's helped her excel.

Christina Chia Price, MD, assistant professor of medicine and of pediatrics, and clinical chief of allergy and immunology, is at the forefront of her field. She conducts critical research on aspects of clinical immunology including COVID-19, yet at cocktail parties everyone seems to think she is the person to ask about their allergy to cats. “I’m an allergy immunologist. But most people, when they think of allergies, they’re thinking of allergy shots. But immunology is a very robust field,” she said.

In addition to her duties at Yale School of Medicine, Price, a board-certified allergist and clinical immunologist, is also chief of allergy and immunology at the VA Connecticut Healthcare System in West Haven. She has a particular expertise in patients with immunodeficiencies and immune dysregulation. Price explained that she is unusual in that she sees adult patients with immune deficiencies, as most allergy immunologists specializing in immunodeficient patients are pediatricians. Price said, “There is actually a significant portion of adults with immune deficiencies—some that are subtle and some that are not as

subtle. I have an expertise in patients with immune deficiency and immune dysregulation, and how to immunosuppress the immunodeficient.”

Price has long been drawn to the complexities, challenges, and promises of the human immune system. “I remember when I was a student, I thought—if these patients have a hard time generating the protective antibodies to fight infections, then they would have less chance of having autoimmune disease, but it’s actually the opposite. It’s that the ability to generate functional good antibodies to fight infection is so distorted that they also often generate auto-antibodies.”

It is not a surprise that Price was thinking about these complexities at a young age. Her father and brother are doctors; her aunts are nurses; and some cousins are doctors. When Price’s grandfather, Yee Yu Chia, was a young boy, his family sent him away for safety during a period of civil war in China. Her grandfather went on to become a practitioner of Chinese herbal medicine in Chinatown in Kuching, the capital of the state of Sarawak in Malaysia. “My father, grandfather, and great-grandfather—all went into medicine.”

When Price was growing up in St. Louis, Missouri, she didn’t see a lot of her grandfather in Malaysia. “I remember it took a whole day and we had to take three planes and it was a journey to get over there.” When her 11-year-old son Jacob was working on a family tree

for a school project, Price shared a fascinating family photo of her grandfather. She said, “My son was so cute. He was like, wow, how far does this go?” They had discovered that the Chia family (Price’s maiden name) had been in medicine for generations.

Several years ago, Chia felt a little homesick and searched the Internet to see whether anything came up for her grandfather’s medicine shop in Chinatown. Price was hoping for a picture of a storefront or even just a picture of Kuching’s Chinatown to ease her homesickness. When she searched for Chinese medicine shop in Kuching, Malaysia, to her surprise the first image that came up was a picture of her grandfather in his shop.

He’d passed away a few years before, but a Lonely Planet photographer had taken photos of him and posted them online. Price contacted the photographer and bought a few photos, one of which is now framed and hanging in her living room. “Those old-fashioned Chinese medicine shops look so antique. They had canisters full of medical ingredients and a grinder—a wheel guided by your feet,” she said. Price also said she hasn’t been back recently, but her mother told her that much of her grandfather’s medical equipment ended up in a museum in Chinatown.

Now, instead of fielding questions about food and pet allergies, Price finds herself living through history as the COVID-19 pandemic has fostered a new

awareness of her immunological work. “Because of COVID, everybody knows about antibodies and neutralizing antibodies and how important it is to have antibodies that work and do what they’re supposed to do. And importantly, not do what they’re not supposed to do.” Price’s research was recently featured in the national conversation about COVID-19 treatments. In the October 2020 issue of the journal *Chest*, Price was the lead author of a study on the drug tocilizumab (Actemra). She and her fellow clinician-researchers reported their results on the drug.

“Because this was not a randomized control trial, we couldn’t say at that time patients who were treated with tocilizumab had a survival advantage, but compared to other published data on survival and mechanical ventilator outcomes, patients at Yale seemed to be doing better.” Since the publication of the Yale study, randomized control trials have shown that tocilizumab, when given to very sick patients and in addition to such corticosteroids as dexamethasone, had significantly improved survival, saving one in 12 lives and cutting the time spent in hospital by a week to 10 days.

Price was also asked by the magazine *Rolling Stone* to weigh in on the drug dexamethasone (Dextenza), used to treat rheumatoid arthritis. The magazine reported that Price was paying close attention to the results of a dexamethasone trial because

she was a co-author of the peer-reviewed paper on tocilizumab. Both are anti-inflammatory drugs and were thought to be a possible effective treatment for hospitalized COVID-19 patients. Price told *Rolling Stone*, “The hyperinflammation that happens in some cancer patients as a result of T-cell immunotherapy resembles the cytokine storm in COVID-19 ... During the cytokine storm ... the body’s immune system overreacts, and immune cells and fluid flood into the lungs. ... This condition leads to respiratory failure and death in the most severely ill patients.”

A leading researcher on immunotherapy to treat cancer, Price said, “The really groundbreaking and revolutionary treatment in cancer therapy has been immunotherapy, which is turning on the immune system to fight cancer right through these checkpoint inhibitors.” She explained how it is like working on the brakes of the immune system, easing up on them a little bit so that they can fight your cancer. “But you could imagine that in return, letting up the brakes a little bit might cause you to fight your own cells, resulting in immunotoxicity, and this would be related to immune dysregulation.”

Price has strong ties to Yale’s Cancer Center, having initiated an immunology clinic there. “We call it an immune wellness clinic because we didn’t want to call it an immune toxicity clinic,” she said. Owing to scientific advances, rather than using the medical

equivalent of a sledgehammer, clinicians can now use precision medicine to treat immunotoxicities and inflammatory events, whether they are connected to COVID-19 or to cancer. “Science and medicine won’t be the same after this,” Price said.

—Lori Freshwater



**Yale’s Senior Advisor to the FDA Commissioner**

David Gortler, PharmD, was four years into teaching pharmacology at Yale School of Medicine (YSM) when he was first approached by the U.S. Food and Drug Administration (FDA) to present his research in Washington, D.C. It wasn’t long before he was on the FDA’s staff as a medical officer evaluating new drugs for approval.

Gortler recently completed a second tour on the FDA’s executive leadership team as the first and only pharmacist/pharmacologist appointed senior advisor to the FDA commissioner. He served as an expert in drug safety, FDA regulatory affairs, and science policy. “It was a dynamic and high-pressure role, especially as we helped see through the emergency authorization of two novel mRNA vaccines to treat COVID-19,” Gortler said.

Gortler was also part of the leadership team at the FDA that identified essential medicines, medical countermeasures, and critical inputs to serve patient needs in the event of another

public health emergency. He was valued there chiefly for his expertise and advocacy concerning the return of medication production to U.S. soil from overseas; and a strong commitment to rigorous quality assurance and quality control (QA/QC) of the international medical equipment and pharmaceutical supply chain.

“QA/QC is a very serious concern,” said Gortler. “We spend billions of dollars and years evaluating clinical data to make sure drugs are safe to take. In the end, third-party insurance companies called PBMs (pharmacy benefit managers) require patients to take tablets from the cheapest manufacturer possible. Unfortunately, many of these tablets are of questionable quality. In the U.S. and Europe, the FDA can walk in at any time to a drug manufacturing facility to inspect them. In China and several other countries, you can’t. Frequent and unannounced inspections are a vital part of the FDA’s mission.”

Passionate about the issue and concerned for the overall health of Americans, Gortler personally conceptualized and helped found Valisure, the world’s first analytical pharmacy, in 2015. The goal is to ensure that any drug produced globally is labeled accurately with regard to milligram strength and without toxic adulteration. That analytical pharmacy was instrumental in having the drugs ranitidine (Zantac) and valsartan (Diovan) pulled from shelves around the world.

“There’s no way for consumers, pharmacists, or physicians to know whether what is stated on every bottle at your pharmacy or hospital is accurate. Unlike the U.S., if an inspector goes to China or India and an inspection is refused, the FDA just issues an obscure note on its Import Alerts website because it has no Congressional recall authority. Import alerts don’t affect the pills already in the U.S.,” said Gortler.

After Gortler’s residency at Columbia, his investigational medicine research and drug safety career continued at Pfizer, where he designed, composed, and supervised a team of scientists covering the first in-human and early-phase investigational medicine clinical trials. It was during that time that he was offered the chance to return to Yale as an assistant professor before being recruited later for his first position with the FDA.

While at the FDA, Gortler also advocated for reducing or eliminating the FDA’s requirements for animal testing in favor of brand-new state-of-the-art OOC (human organ-on-a-chip technology, which uses microchips lined with living human cells to model human disease states). “In addition to reducing harm to animals—a regrettable longtime necessity for scientific progress—this device stands to greatly speed up drug development and approval. It’s a win on both sides,” he said.

Gortler recently accepted a position as senior scholar with the Ethics and Public Policy

Center (EPPC) think tank in Washington, D.C. He believes that there is a lot more work needed to modernize FDA policy in regard to speeding up drug discovery, approval, quality control, pre-clinical testing, drug safety, and adverse event reporting.

—Carleen Wild



**A historian of medical futures looks back**

Professor Joanna Radin, PhD, was 17 when the Kings Park Psychiatric Center closed in her Long Island hometown. Since its founding in 1885 to alleviate overcrowded city asylums, the massive hospital grew with and came to define the town. Eventually it too was overcrowded, its occupational therapies replaced with lobotomies and shock treatments. Radin remembers growing up playing on the asylum’s grounds, seeing the derelict buildings through the trees from her bedroom window. Friends’ parents worked there; certain patients were well known around town. “It was normal, almost. The idea of mental illness wasn’t a fiction,” she said. “It was a reality for the town. Kings Park was a company town. Instead of a mill we had an asylum.”

From her upbringing on the boundary of this now-empty monument to our country’s biomedical secrets to what most would conceive of as a classic haunted asylum fantasy, grew an insatiable curiosity about

the wisdom of science fiction in relation to biomedical infrastructure; the violence of the past and conceptions of the future; the forms of communications central to good science; and the nature of innovation.

Radin is an associate professor of the history of medicine and teaches across disciplines. She is the author of *Life on Ice* (University of Chicago Press, 2017), a book about American scientists’ efforts to collect and stockpile frozen blood samples from indigenous communities around the world; and co-editor with Emma Kowal, MBBS, PhD, an Australian medical anthropologist, of *Cryopolitics: Frozen Life in a Melting World* (MIT Press, 2017). Radin has a new project forthcoming—a look at the history of American science through the work of physician-turned-author Michael Crichton, MD.

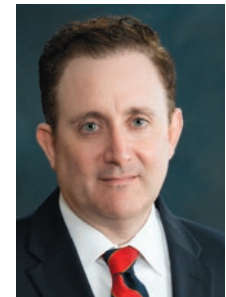
From Kings Park at the tail end of the Cold War, Radin devoured books and films about unwieldy scientific leaps like Crichton’s *Jurassic Park* and *Westworld*, which conveyed the message that science will produce monsters. She attended a summer camp at Cold Spring Harbor Laboratory, where at 10 years old, she was encouraged to think about the futures latent in DNA. Later in life she learned that the lab had been the epicenter of the American eugenics movement, and many of the patients at the Kings Park asylum had been subjects of experimentation by its scientists.



“It’s this nexus that I’ve only made sense of after a career in the history of science and medicine,” she said, “that helped me realize there were all of these potent, very real, terrifying, but also powerfully optimistic forms of horror and hope and hype swirling around my childhood, which I osmotically absorbed.”

A question central to science’s tug of war with power, she tells her students, is the identity of those who make the future. How do we inherit ideas about innovation? “If you look into history, some of the most powerful and important innovations are not always the most expensive or sexy.”

Joanna Radin, professor of the history of medicine, has written about how people in the past imagined the life-changing potential of medicine.



Former YSM assistant professor of pharmacology David Gortler takes the mission of ensuring drug safety very seriously.

PHOTO COURTESY OF THE U.S. FOOD AND DRUG ADMINISTRATION

ANTHONY DECARLO PHOTO

Mold, for example, disrupted the world of biomedicine when a mold called *Penicillium rubens* proved to be the source of the first major antibiotic.

But Radin is particularly preoccupied by freezers.

She was attracted to freezing because unlike gene sequencing, for example, freezing is rather ordinary. “Looking at mundane technologies allows us to see different ways of understanding innovation,” she said. Cattle breeders, she found, were working with freezer technology to preserve sperm in order to standardize variation. But the human biologists and epidemiologists Radin was paying attention to wrote to the cattle breeders to learn how they might adapt cold storage to preserve variation across human groups.

“This was such an object lesson in the history of technology,” she said. “It’s not that technology tells us what to do; technology is developed by people who decide what to do with it.”

Then came the cheek swab revolution, 23andMe, and our obsession with Who We Are, all made possible by freezers full of genetic material from indigenous people across the world—ephemeral material considered a resource for the unknown future. “I just got so fascinated by the kind of perversion of that thinking, the kind of colonialism, the hubris, and the lack of consideration for the lives and ideas of the people whose bodies were being collected for science.”

The history of frozen blood also reveals insights into our present crisis. A focus on the cutting edge, she said, considers only having a safe and effective vaccine, but not how that efficacy is achieved; upon whose bodies it is tested; and who is shut out from access. “It’s not a coincidence that the pandemic has come along with the Black Lives Matter movement and calls for efforts to rethink our institutions and the place of expertise within them.” To that end, she has been working with colleagues in the Infectious Diseases Section and the Department of Genetics at Yale Medical School, which invited her to collaborate on curriculum to address issues of racism in the training and practice of medicine.

It’s easy to see this crisis as emblematic of the one facing science writ large: how—and particularly *whether*—science is communicated or trusted. Radin has watched with dismay as the Trump administration eroded faith in the CDC and disregarded the knowledge and needs of clinicians. Faith in science—and simple technology, for that matter, PPE, mundane paper technology—beyond the shiny solution of a vaccine, could have profoundly mitigated this crisis.

For Radin, lately everything comes back to Crichton, whose fiction shaped the way many think about the promises and perils of technology. It matters what stories we tell about science and technology. Crichton’s tales of science

gone amok influenced a generation ... but how can we learn to love our monsters, to better care for our creations and each other?

Radin’s inquiries have returned to Kings Park—those huge and now-empty buildings. Through writing about it, she hopes to understand the relationship between eugenics and ideas about what it means to be free in a way that can help us navigate the present. “I grew up looking at these buildings and not knowing the secrets they contained.” she said.

—Benjamin Yeager



### The next wave of physician-entrepreneurs

Fourth-year medical students Rohil Malpani and Marley Windham-Herman reflect a growing trend at Yale School of Medicine (YSM): they bridge gaps among medicine, business, and technology.

Both Malpani and Windham-Herman came of age during a moment in which emergent technology was unusually accessible, making business opportunities plentiful. Studying at YSM helped guide them toward designing devices with an eye toward patient care.

Windham-Herman’s inspiration came from his father’s interventional radiology (IR) practice as a kid. “You can see people’s lives being saved,” Windham-Herman said. “Going from being aphasic, paralyzed

on the table from a stroke, to being completely normal five minutes later because their physician was able to reach inside the artery and grab the clot out with a small wire.” His mother works in family practice with addiction patients. The result is a composite interest: Windham-Herman is focusing on device design in IR as well as on a groundbreaking pharmaceutical to treat addiction.

Malpani, the child of two doctors in Kolkata (Calcutta), India, remembers waking up to use the bathroom at three in the morning and seeing his father in a suit and tie leaving for the hospital to treat a patient’s heart attack. “He worked relentlessly but with purpose and joy,” Malpani said. “He was very happy with what he does; and I thought, if such a job, such a life was possible, I wanted it too.”

In a blog post, Malpani wrote about another influence on his career: “It was through my mother that I came to understand the all-encompassing profession of medicine.” A family physician and Ob/Gyn in India who takes a holistic approach to her patients’ well-being, Malpani’s mother empowers women in a patriarchal culture and helps them with everything from nutrition to personal finance. Malpani matched to the

University of California, San Francisco, for radiology, and plans to complete a fellowship in IR.

Windham-Herman elected to pursue an MBA along with his MD, as he wants to understand those areas of medicine that overlap with business, economics, and administration. Like his father, he has chosen to practice IR, with a focus on technology: “I think being involved, being capable and competent of engaging in entrepreneurship or in industry in a collaborative way is going to be a huge driver of clinical change in the field,” he said. Windham-Herman anticipates changes as radiologists increasingly become coordinators and communicators within the health care system, going beyond diagnostics and moving further into treatment. In March 2021, he learned that he’d matched at University of California, San Diego for its integrated IR program.

During medical school Windham-Herman started a medical device company called ReCore that features an image-guided procedural tool for biopsies. ReCore is working to deploy in lower middle-income countries to deliver effective procedures rapidly and with a minimal amount of equipment. Windham-Herman designed them to be affordable and accessible with a systems-wide approach. He is also building on his mother’s work with addiction by investing in a plant-derived substance called ibogaine, a naturally occurring psychoactive compound that has psychedelic and anti-addictive properties. Ibogaine is a drug that targets some underlying neural correlates of addiction and mental illness.



Malpani too is interested in device design; he was the leader of the medical innovations group while at YSM, and also served on the Society of Interventional Radiology’s Biodesign and Innovations committee. He is a prolific organizer of contests and hackathons. Ultimately, he’d like “to be able to help a lot of people through device design,” he said, “but also work directly with the people I’m helping through my research and medicine in general.” The first stage he calls the back end, involving research; and the latter the front end, the actual delivery of care, working with patients one on one. “In general, I’m trying to make a difference in people’s lives.”

—Benjamin Yeager

Rohil Malpani and Marley Windham-Herman are two YSM alumni looking for opportunities to improve medical devices while practicing medicine at the bench.

## You have to have empathy

SINCE THE START OF THE PANDEMIC, physical isolation has been a strategy to help slow the virus' spread and save lives. The Black Lives Matter protests that reignited in the summer of 2020 after the killings of George Floyd and Breonna Taylor by police officers laid bare how unaware many white people were of systemic racism in the country. In medicine, bias and stereotypes can change the quality of health care a patient receives. Four years ago, Darin Latimore, MD, deputy dean and chief diversity officer and associate professor of internal medicine (general medicine), was recruited to the medical school to direct the newly formed Office of Diversity, Equity & Inclusion. He coordinates efforts across many groups, including Minority Organization for Retention and Expansion, Committee on Diversity, Inclusion, and Social Justice, and the Dean's Advisory Council on LGBTQ+ Affairs, to support issues of diversity and inclusion on campus. *Yale Medicine Magazine* conducted a video interview with Latimore to discuss how Black Lives Matter protests have impacted the medical school community.

**How have the protests affected dialogue between people of color and people of privilege in our community?** There's been a lot more dialogue. People of color do not need to explain or prove they face racism every day. This has allowed conversations to start from a healthier place. The questions are more likely to be "How is this impacting you?" or "What can I do?" versus "Prove that to me" or "I don't believe you." What has also been significantly different is that a much larger group of privileged people want to be part of the solution and not be quiet allies on the sideline. They are recognizing that the vast inequities relative to how Black and Brown people are treated in this country are real. Doing nothing is no longer an acceptable option.

**Is your office doing anything differently to keep this momentum going?** The interest from students, staff, and faculty in workshops and training around these issues has exponentially increased. We have doubled our efforts to try to meet this demand. We are offering more training—all of it is voluntary. Since the beginning of the semester, I've led dozens of town halls, webinars, and workshops on topics ranging from implicit

bias to microaggressions to crucial conversations about anti-racism. Some departments and sections have independently organized meetings just to provide space for people to share their experiences or listen in silence.

**What changes are planned within the curriculum to help address racism?** We've hired Beverly Sheares, MD, MS, associate professor of pediatrics (pulmonology), to take a deep

dive into our curriculum. Unfortunately, in medical education, we still act as if race is a biological and not a social construct. We confuse gender and sex quite often. There are a lot of other identities and we act as though they don't exist at all. So she will help modify the curriculum so it's more reflective of reality. We're hoping it will help students get rid of bias and increase the chances of giving high-quality health care to all patients moving forward.

**How can everyone contribute to anti-racism efforts?** We can pause to think

about what we're doing and why we're doing it. After that, we can more easily see where our assumptions are coming from. I think we've already started to move forward by better understanding language around racism and what is truly being said. We need to have empathy. There are many reasons people are where they are and we're all starting from different places. Some people may want to read about racism

and better understand the issues. Others may benefit more by being a part of the dialogue. The journey will be different for each of us. What is most important is to never forget that where you are now does not in any way predict where you will end up. This is not a sprint. It's a marathon with ups and downs. America has been this way for centuries. We're not fixing it in one year. Hopefully all of us will realize that we all benefit from an equitable and just society. We're not there yet, obviously, but hopefully one day we will be.

One characteristic of the experience with COVID in 2020 was the spontaneous outpouring of anger and outrage over systemic injustice in the U.S. At YSM, Darin Latimore has been coordinating efforts to achieve equity for all students, staff, faculty, and patients at the institutional level.

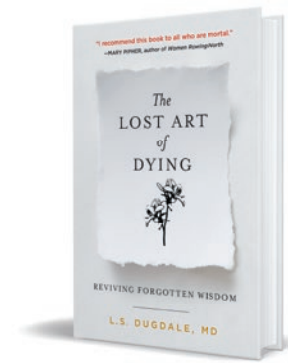


ANTHONY DECARLO PHOTO

To nominate a subject for Q&A, contact [Yale Medicine Magazine](mailto:yymm@yale.edu), 1 Church Street, Suite 300, New Haven, CT 06510, or email [yymm@yale.edu](mailto:yymm@yale.edu).

# The Lost Art of Dying: Reviving Forgotten Wisdom

By Cathy Shufro



The first time internist Lydia Dugdale met Mr. Turner, he was dead. She'd heard a code on the loudspeaker at Yale New Haven Hospital, run to the man's bedside, and helped restart his heart. Some of his ribs were fractured in the attempt to revive him. Dugdale, MD, FW '09, MAR '18, sought out Mr. Turner's family and suggested that they allow the 88-year-old man to die. The family said no, hoping Jesus might spare him. A few hours later, Dugdale helped revive Mr. Turner again. The third time, his heart stopped for good.

"It was excruciating to resuscitate this skeletal, aged, cancer-riddled man three times in one night," said Dugdale, who was a School of Medicine faculty member for a decade before moving to New York in 2019. An associate professor of medicine, she now directs the Center for Clinical Medical Ethics at Columbia University and continues to see patients.

Even as a medical student, Dugdale wondered how to

prevent the "horrible deaths" she sometimes witnessed. That became her central question when she studied for a master's degree in ethics at Yale Divinity School. The key, she decided, is that both doctors and patients must acknowledge on a visceral level that death is real. But how can we weave that awareness into everyday life?

In *The Lost Art of Dying: Reviving Forgotten Wisdom*, Dugdale provides a curriculum. She calls her book "a revitalized *ars moriendi*," modeled on the handbooks for dying published in 15th-century Europe following the Black Death. Dugdale explains how to proceed to 21st-century mortals: to routinely acknowledge our finitude; to lean on a community for solidarity; to explore whether spirituality and rituals might provide comfort; and to consider avoiding hospitals once the body becomes frail.

Dugdale suspects that ironically, doctors may be among the least capable guides when approaching death. The knowledge they acquire during training can give doctors the illusion that they don't

fear death. Suggesting another last-ditch treatment serves as a distraction. "If no one presses 'pause,'" Dugdale warns, "the medical machine keeps moving." As the body slows, so should medicine.

Dugdale recommends that doctors practice talking about death with patients. They can also direct patients to such websites as Five Wishes that address issues surrounding death and provide end-of-life planning documents.

Preparing for death doesn't mean embracing it, Dugdale says, but rather learning "how to live well with a view to the endgame." Last spring, reminders of that endgame pervaded life in New York City. "During COVID, there were sirens, sirens, sirens—everywhere, all the time," said Dugdale. "One day I saw a neighbor from across the street being taken out [through] the window. I guess the person was dead, and they [the ambulance crew] couldn't get in through the door."

Dugdale thought, "That could have been one of us,"

and she told the story to her husband and their two school-age daughters. All four felt cranky and claustrophobic in their small apartment, but she told them, "We need to treasure these days together, because we don't know how long we will be together as a family. There is no guarantee that we will get through this pandemic with all four of us alive."

More ordinary events also remind Dugdale of her mortality. When her knee hurts during a run or she needs glasses to read small print, she thinks, "Wow, I'm only in my 40s, but things fall apart. These are the kinds of things that all add up to my death."

When one of her daughters was just 3, the two of them stumbled upon a dead mouse while walking across a field in Vermont. Her daughter was shaken. "We sat there for a while and talked about death," Dugdale recalls. "You can walk past it and cover it up with some leaves and pretend it's not there. Or you can just sit with it."

More information about the author and the book is at [lydiadugdale.com](http://lydiadugdale.com).



## After more than two decades, an icon steps down

WHEN NANCY ANGOFF, MD '90, MPH '81, MED, HS '93, finally decided to become a doctor, she'd had two children, helped put her husband through medical school while she was a junior high school English teacher, and was in her late 30s. When asked what she would do if she could pursue any career, Angoff's first response was always "I'd be a doctor." She'd found medicine fascinating, but for many reasons did not believe that door was open.

The biggest opportunity Angoff encountered—one that would define her career—was the position of associate dean for student affairs under the administration of David Kessler, MD. "It's a hard but fulfilling job. You're on all the time," said Angoff of the role. Her background as a teacher and caregiver filled her with a sense of purpose and duty that carried her through nearly 23 years of service. "You share the lows of students and their families, and the highs. It may be difficult, but it's also been enormously rewarding."

—Adrian Bonenberger

full interview available at [ymm.yale.edu](http://ymm.yale.edu)

OPPOSITE: ROBERT A. LISAK PHOTO

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