Pandemic effect
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.

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.
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 and worked tirelessly to create remote learning. Our students, leaders at the Smilow Cancer Center, and many others worked together toward a common goal: to leverage our learnings to address the shortage, we reduced elective rotations; we gathered experts across the university and the community to collaborate and work across boundaries. One Saturday in March 2020, I was on call with Paul Vidich (chief executive officer, Yale Medicine), and I was told, “We need a Manhattan Project-style response.” The next day, we convened the first meeting of the COVID-19 Response Coordination Team; CoCiCT 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 go-live suite in a CT ZENV to get license plates one Saturday morning while on a conference call with all members of CoCiCT. 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 infrastructure, and the wide-spread 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 resource- ing and using ppe from across the country, and even from international partners. Because of the shortages, we reduced elective surgeries and routine patient clinic visits. To create capacity for patients, our leaders at the Smilow Cancer Center moved patients from the top three floors, as those floors had appropriate air handling for the treatment of COVID patients.

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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 work 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 Mary Horvath 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 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.”

Dixit’s lab maintains a colony of aging mice at Yale. Teamings with Andrew Wang, MD, PhD, assistant professor of internal medicine and immunobiology, the researchers tested 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. We are interested in the underpinnings of aging and 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 corona virus. But how that mouse dies of that coronavirus, now it’s telling us how people die of COVID. Isn’t that fascinating?” – Christina Prank

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

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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. “I saw that the criminal legal system is unique in the United States, and in not in good ways,” she told me.

Wang, an internist, is now the director of the SEICHE Center for Health and Justice at Yale School of Medicine (YSM), which is focused on health equity research. The center’s name (pronounced say-kee) comes from a Greek 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 by her experiences with prisons that 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 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

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 neighbors. 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. 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 wouldn’t 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 are 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 so we thought 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 alumni 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 could swap stories, and have a good time. “If one person hadn’t pulled their weight, it wouldn’t have worked,” said Shreve. “There were dozens of people behind the scenes.”

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chronicle

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 Nano Brown, MD, Yale College MBA. One member of her class was 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 hall way 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.

Akkio Braski, PhD, the Waldemar Von Zedtwitz Professor of Immunology, professor of molecular, cellular, and development 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,” Braski 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 caused by the pandemic and honing observation prowess to improve diagnostic skills and tight 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 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

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 epidermis to resist infection. Researchers from the lab of Valentina Greco, PhD, the Carolyn Walsh Skysman Professor of Genetics, including research associate Catherine Matte-Martone, found that these immune system soldiers are able to patrol themselves to protect vulnerable areas when necessary, while avoiding clustering in any single location.

ANSWER FOR SOME EPILEPTICS

With the help of robotic 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.

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. Archeological 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 sprouting bushland that exists today.

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 (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.
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.
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.
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 test 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 technicains 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 workspace that it needed to get started from other groups or labs. “Everyting was backordered. Borrowing was the only way,” Wang said. “Everytime 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 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—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.”

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Taking decisive action

By the first week in April 2020, the lab was running COVID-19 nasopharyngeal tests. To perform these, researchers use pipettes to add chemicals, and then spin the vials to separate the mucus and other nasal material from the cells they need to test. Another chemical causes 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 sequencing 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, 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 modified nucleotides),” said Sklar. “But without this, it wouldn’t be possible to scale up for COVID testing.”

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

Taking decisive action

By the first week in April 2020, the lab was running COVID-19 nasopharyngeal tests. To perform these, researchers use pipettes to add chemicals, and then spin the vials to separate the mucus and other nasal material from the cells they need to test. Another chemical causes 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 sequencing 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.

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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 New Haven Hospital 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 hard 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 we 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 disease. 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 Kryval, MD, ‘84, the Robert L. McNell, 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 social 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 it 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 public 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 YNH 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, 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 seeing 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 let 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 padding 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 sus- pended many of their 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 of faculty from the medical school, and hospital floors—often involving people from all three. In Internal Medicine, Desir cre- ated 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 massi- ve 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—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, clini- cians learned that the drug remdesivir and certain ster- roids 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 declara- tive 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.

One of the key players in that command center, leaders at the hospi- tal 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 hospital staff members and staff 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 the faculty and staff members who were working nonstop would be encouraged to reach out to others for help. Leaders were effective in 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 cor- porate 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 develop- ment, including combining phases II and III of clini- cal trials. “This galvanized the community like never before,” Ogbuga 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. So the medical school 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 symp- toms, including severe headaches, seizures, and confu- sion. Farhadian and her colleagues established that the virus was indeed causing abnormal immune reactions in patients’ brains. They hope their 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 threat. Erol Fikrig, MD, the Waldemar Von Zedtwitz Professor of Medicine in Pathology and Laboratory Medicine, many were pressed into service on testing and diagnosis programs.

remdesivir and the Pfizer/BioNTech vaccine. 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 car- ing 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 pro- cess,” he said. “The message today is that this is the be- ginning 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—implying 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?

Steve Hamm is a frequent contributor to Yale Medicine Magazine.
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 mainstream,” 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 grooms the immune system to tailor antibody responses, 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 bio-informatics 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. "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. “Once the university had figured out what they wanted to do, we were prepared up to a certain point, but nobody expected [the pandemic] to last as long as it has,” said Charbonneau.

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 want 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 scientific research—all of what we’re seeing now is a result of that investment. And it’s specifically into immunology as well. It that hadn’t happened, we’d be nowhere.”

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

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 Grubbaugh, 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.

Trails 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.

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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-year students’ two-week course titled “Introduction to the Profession.” The course, co-directed by Nancy Angoff, MD ’90, MPH ’81, MEd, and David Rosenthal, MD, PhD, associate dean for curriculum, has 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, MS ’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 ventured on campus in 2023 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. 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.

“Right from the get-go, the physical exam was a manikin while interviewing their standardized patients via Zoom. Deigle 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 B. Angoff, MD ’90, MPH ’81, MEd, HS ’93, associate dean for student affairs. The med school has offered training for the internal medicine clerkships.

During the punches that the virus, the students have organized virtual activities like 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 or 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,” she said. “I think it’s hard.”

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 or other people to get to know people you might not feel comfortable reaching out to,” said first-year student Victoria Marks.

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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 candids capture their range of emotions. The photos have been minimally edited to maintain a documentary feel. Visit 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

Alaine 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

Riam Naiditch, MD, MPH
Ambulatory Chief Resident (NYUPC), Internal Medicine

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

Marceditas Villanueva, MD
Associate Professor of Medicine, Director, Yale UIC/IAIDS Program, Division of 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
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 Aulemni, MSII, 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 Degile 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.”
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 researchers 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, Professor of Medicine (Cardiology) and professor in the Department of Epidemiology, also emphasized the time it takes for contributions of many, including a dedicated staff at CSHL.

“Submitting an article for publication to most journals 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 slow 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 promote 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,” 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 paper 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.”

MedRxiv’s co-founder, 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 can be a very long time,” Krumholz 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.

Research, accelerated

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

BY VALERIE PAVILONIS

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, 1982–1996, 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 treating 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, 330 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 (HSMP) within Yale’s History Department who were responsible for curating the exhibit. The curatorial team also included Kristine Ericson, Meghan Liskai, Maya Sandler, and Beaux Veloci. Experts—along with the testimonials 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 Needle Exchange: an attempt to distribute clean needles to intravenous drug users in the community. It was a call to members of the local community to take a stand against this crisis.

The needle exchange program, now 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 combating 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, Clinical and Community Research, director, HIV in Prisons Program, and director, Community Health Care Van. “There were so many people who contributed to the efforts around understanding HIV/AIDS, laying the groundwork for where we are today,” said Reisman.

“We hope through this exhibit to show that ‘treatment’ in a broad definition, and [that] the response was driven by many individuals motivated by compassion and community. It was a group effort.”

Cover photo: Darin A. Latimore, MD, deputy dean of diversity and inclusion, associate professor of internal medicine, and co-director of PAPS.

Clockwise from far left: examples from Five topics that comprise the exhibit: Community and Caring/YES: AIDS Prevention Week, 1991. The collection of 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 Needle Exchange: an attempt to distribute clean needles to intravenous drug users in the community. It was a call to members of the local community to take a stand against this crisis. Peter’s Retreat, was chosen from an open call to members of the YSPH and community artists who submitted work related to the theme of HIV/AIDS. Co-cammell: In commemoration of the 25th anniversary of APNH in 1991. The project was commissioned by HAND and sponsored by Yale and the William N. and Marie A. Beach Foundation. Photographer: Chris Brewer, Dominick Malardede, George Ed-ward, and others.jpg (in text) in the Hartford Courant, 1992. Lurie: Community Health Care Van, 2020. AIDS in the Clinic: Gerald Feibestd, MD, Director of the AIDS Program, Yale School of Medicine; Peter Salovey, PhD; Gregg Gonsalves, PhD, assistant professor of epidemiology (microbial diseases) and co-director, Clinical and Community Research, and director, HIV in Prisons Program, and director, Community Health Care Van. "There were so many people 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’ in a broad definition, and [that] the response was driven by many individuals motivated by compassion and community. It was a group effort."
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, 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 has strong ties to Yale’s immunology clinic there. “We call it an immune wellness clinic,” she said. Price also said she hasn’t been back recently, but her mother told her that much of her grandmother’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 tested 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 tocilizumab (Actemra) and mechanical ventilator outcomes, patients at Yale seemed 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 tocilizumab (Actemra) and mechanical ventilator outcomes, patients at Yale seemed to be doing better.” Since the publication of the Yale study, randomized controlled trials have shown that tocilizumab, when given to very sick patients and in addition to corticosteroids as dexamethasone, has significantly improved survival. “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 grandmother 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 grandmother. 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 grandmother’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 grandmother in her 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 photo, 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 grandmother’s medical equipment ended up in a museum in Chinatown.

“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 immunototoxicities 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 reaching 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 his 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 Yale, his investigative medical 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 (organ on a chip) technology, which uses microchips lined with living human vascular and 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 win on both ends,” 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, preclinical 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 occupationary 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 swirl around my childhood, which I somewhat absorbed.”

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

“Among the most important innovations is a little vector called ‘vaccine,’” she says. “It’s this nexus that I’ve only made sense of after a career in the history of science and medicine.”

—from the archives

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

ANTHONY DECARLO PHOTO

Joanna Radin, professor of the history of medicine, has written about how people in the past imagined the life-changing potential of medicine.
The history of frozen blood also reveals insights into our present crisis. A focus on the cutting edge, she said, considers not 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 curricula 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 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 Veueger

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 the Black Lives Matter movement and calls for the unknown future. “You can see my 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 procession 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 every thing from nutrition to personal finance.

Windham-Herman said, “Going from being aphasic, paralyzed on the table from a stroke, to being completely normal five minutes later because their phys ician 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 groundbreaking pharmaceutical to treat addiction.

Malpani, the child of two doctors in Kolkata (Calcutta), India, remembers waking up in the morning and seeing his father in a suit and tie leaving for the hospital to treat addiction patients. The result is a focus on technology: “I think 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 curricula to address issues of racism in the training and practice of medicine. “Looking at mundane objects, the kind of colonialism, the way technology was unusually accessible to people who choose what to do with it.”

Then came the covid-19 revolution, 23andMe, and our obsession with Who We Are, all in a patriarchal culture where women in a patriarchal culture who take a holistic approach to people’s lives being saved.”

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Radin 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 entre- preneurship 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 co- creators 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 and the US, a groundbreaking pharmaceutical to treat addiction.

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 Veueger
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 reigned 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, 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.

To nominate a subject for Q&A, contact
Yale Medicine Magazine, 1 Church Street, Suite 300, New Haven, CT 06510, or email ymm@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 frac- tured 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 cur- riculum. She calls her book “a revitalized arials,” modeled on the handbooks for dying published in 15th-century Europe following the Black Death. Dugdale explains how to proceed to 21st-century morals: to routinely acknowled- ge our mortality; to lean on a community for solidarity; to explore whether spiritual- ity and rituals might provide comfort; and to consider avoiding hospitals once the body becomes frail.

Dugdale suspects that ironi- cally, doctors may be among the least capable guides when approaching death. The knowledge they acquire dur- ing 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 mov- ing.” 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 cranked and claustro- phobic in their small apart- ment, 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 mortal- ity. When her kitten har- nessed during a run or she needs glasses to read small print, she thinks, “Wow, I’m only in my 40s, but things all apart. These are the kinds of things that add up to my death.”

When one of her daughters was just 3, she and Dugdale 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 pre- tend it’s not there. Or you can just sit with it.”


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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