

JUNE 2022

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The Science
of Child Care

Mysterious Cosmic
Explosions

How the Brain
Builds Reality



AGE OF THE MAMMALS

After the dinosaurs died,
our ancestors thrived



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relationship
with our world



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ON THE COVER
Cimolestes, the size of a small rodent, lived alongside dinosaurs during the Cretaceous epoch. It belonged to a group of mammals known as the eutherians, which gave rise to the placentals. Placental mammals give birth to live, well-developed young. They constitute the largest group of mammals alive today and include creatures as disparate as bats, whales and humans.
Illustration by Beth Zaiken.

Steve Brusatte

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Laura Helmuth is editor in chief of *Scientific American*. Follow her on Twitter @laurahelmuth

Transition Times

Our ancestors' big break came 66 million years ago, on the worst day in Earth's history. An asteroid slammed into our planet, set off tsunamis and volcanoes and wildfires, and darkened the skies for years. The disaster was the end of the dinosaurs (aside from birds) but a new beginning for mammals—or at least the mammals that survived. In our cover article, starting on page 28, paleontologist Steve Brusatte fills out this origin story with fascinating new details about the mammals that thrived in the Before Times and a deeper understanding of how some survived into the After.

Childhood development is one of the richest and most productive fields of research today—there's just so much happening from birth through the first several years of life. The brain expands rapidly and builds a million connections per second, as children learn languages and social connections and how to explore the world. As childhood-learning researcher and physician Dana Suskind and writer and *Scientific American* contributing editor Lydia Denworth explain on page 48, research has identified two crucial factors that encourage healthy cognitive development: protection from stress and nurturing interactions with caregivers. The work they share has urgent implications for policies that help children thrive.

Going deeper into how the brain learns to understand the world, neuroscientist György Buzsáki on page 36 presents an “inside-out” theory of brain functioning. The classic “outside-in” conception holds that the brain starts as a blank slate and gets inscribed by perceptions and experience. But the brain has its own ideas about how to organize, generalize and respond to external stimulation. Studies in people and animals and AI research show how the brain's internal algorithms can be used to shape our experiences, plan ahead and learn efficiently.

Powerful flares called fast radio bursts erupt with as much energy in an instant as our sun emits in a month. Astronomers aren't sure what causes the flashes, but they made a lot of progress when an especially energetic fast radio burst in 2020 was traced back to a magnetar, an enormous remnant of a supernova. Not all fast radio bursts seem to come from magnetars, though, and some may be repeaters rather than single explosions. It's a hot area of astronomy, as science writer Adam Mann describes on page 44, and it's poised to get hotter—fast radio bursts might help reveal what matter they traveled through from their origins to our telescopes.

A fundamental injustice of modern times is that privileged people live longer, healthier lives than people who face discrimination, disempowerment and systemic bias. Our special package on health equity (*page SI*) explains what we know about disparities in our health systems and, more important, how to fix them. Heart disease, the leading killer worldwide, is even more deadly in disadvantaged groups. The world's oldest pandemic, tuberculosis, has been largely eliminated in the wealthy world but persists in poverty. Mental health care should be a right, not a privilege. And you will meet people who are finding solutions to health inequalities across the globe and who are drawing still relevant lessons from the HIV/AIDS epidemic.

All of us at *Scientific American* thank Curtis Brainard, our managing editor, for leading the health equity package in this issue and so many other innovations and projects. Curtis joined our publication in 2014 as the blogs editor and soon began overseeing all our online content. He became managing editor in 2017 and acting editor in chief in 2019 and got us through the beginning of the COVID pandemic. Curtis is leaving *Scientific American* (reluctantly, he says) for a sweet new job in Paris, and we all wish him well, but gosh, we're going to miss him! 📺

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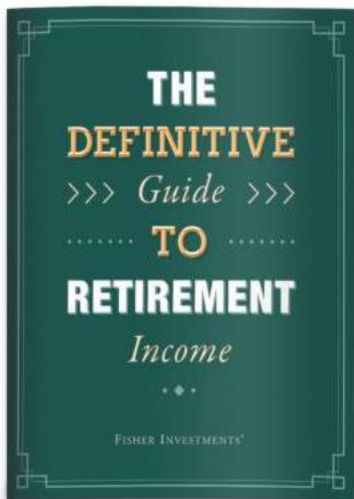
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February 2022

DEDICATED READER

I have been reading *Scientific American* since I was in high school. I am now 90 years old and a longtime subscriber. The February 2022 issue is one of the richest ever. I just handed it to my daughter, the mother of a 13-year-old, to read the articles on teaching kids to spot disinformation in media [[“Schooled in Lies,”](#) by Melinda Wenner Moyer] and on how people often (wrongly) jump to conclusions [[“Leaps of Confusion,”](#) by Carmen Sanchez and David Dunning]. I read with enjoyment the articles on new research on the skills of Neandertals [[“Neandertals Like Us,”](#) by David W. Frayer and Davorka Radovčić] and how the promise of technological progress can conceal major costs and dangers [[“Breaking the Techno-Promise,”](#) by Naomi Oreskes; Observatory]. And I ordered two books you reviewed in *Recommended*.

MARION BUHAGIAR
White River Junction, Vt.

SOURCES OF CONFUSION

“[Schooled in Lies,](#)” Melinda Wenner Moyer’s article about teaching schoolkids to distinguish among different kinds of information to protect them from disinformation, covers a topic that is dear to my heart, although one for which I have little hope. As part of my high school chemistry class, I had students do a project on the safety of the artificial sweetener aspartame. I came to realize two things: The first is that assess-

“We need the political will to put a price on carbon and build smaller and safer nuclear reactors. Giving up is not an option.”

STEVE MUELLER *COLORADO SPRINGS, COLO.*

ing the validity of primary information on many topics is beyond most people’s capabilities. As a Ph.D. biochemist, I may be able to do so more than some others, but there are many topics that I am unqualified to analyze. The second is that we must therefore choose a source whose analysis we accept. Consequently, I added a part to the assignment asking why the students chose to accept, to trust, one source or another.

I observed that many of my stronger students chose to accept institutional sources, such as the American Cancer Society or the Food and Drug Administration, whereas many of my weaker students chose to accept more personal sources and stories. I wish I had more systematically collected the data, but these observations led me to hypothesize that those who prosper within a system tend to accept the system as trustworthy. Those who do not prosper so well tend to be more skeptical of the system, instead choosing to accept their own experiences or those of others known to them.

The article quotes journalism and media studies researcher Seth Ashley as noting “that the world is messy, and that’s okay,” but that is also what makes our choice of whose perspective to trust so challenging. There will always be reason to question one source or another. Maybe the best we can do is get to the point where students recognize the mess and, because of that, recognize that they could be wrong.

RUSSELL KOHNKEN *Skokie, Ill.*

NUCLEAR DEFENSE

Regarding Naomi Oreskes’s assertion that nuclear energy cannot help our climate crisis in “[Breaking the Techno-Promise](#)” [Observatory], I agree that nuclear plants have not lived up to their promise so far. As she notes, they take too long to build and bring online and are too expensive. And they result in high electricity costs. But I am surprised at the pessimism, given the urgent need to do something. New nuclear technologies are evolving, such as multiple

smaller modular plants that don’t take so long to build. Renewables are critical but will never be enough to replace fossil fuels. Nuclear fusion is too expensive and far away. We need the political will to put a price on carbon and build smaller and safer reactors. Giving up is not an option.

STEVE MUELLER *Colorado Springs, Colo.*

Even though it’s long term, nuclear energy development should be a high priority. As a retired engineer, I understand the extensive effort required for the completion of efficient, economical nuclear electricity stations. Technology improvements, development engineering and construction time must be *planned for* and *underway now*.

For the short term, we must use the sustainable technology of wind and photovoltaic farms and eliminate fossil-fuel subsidies. Also, let’s add a federal tax on gasoline and reduce the dependence on transportation via Eisenhower-era highways with more use of our mass-transit systems.

DON FINAN, SR. *Palos Park, Ill.*

SPACETIME EXPERIMENT

Reading Adam Becker’s riveting article on “[The Origins of Space and Time](#)” reminded me of when I was a high school student in Los Angeles in 1965 and read about two students at the University of California, Los Angeles, who were challenged by their science professor to devise a theory on time and space, complete with an example.

The two students took folding chairs to a street in nearby downtown Westwood, Calif., and sat in a vacant parking space for an hour after depositing the required coins in a parking meter. They subsequently wrote a report to their professor on what they had done, concluding, “In order to occupy space, you must first have time.”

DOUG WEISKOPF *Burbank, Calif.*

THE FIX IS IN

I was glad to read “[Freedom to Tinker](#)” [Forum], Kyle Wiens’s informative opinion

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piece on how Congress should uphold the right to repair electronic devices. Readers interested in getting involved with hands-on right to repair might be interested in checking out their local Fixit Clinic (<https://fixitclinic.blogspot.com>) or Repair Café (<https://repaircafe.org>). There are many such organizations around the world with dedicated volunteer repair coaches helping others learn how to fix their broken stuff. And over the past couple of years these clinics have been happening virtually, with global participants engaging in fun and informative repair activities. We try our best to work together to diagnose and repair appliances, electronics, and so on but are concerned about manufacturers making this more difficult, if not impossible or illegal.

WAYNE SELTZER

Boulder U-Fix-It Clinic, Boulder, Colo.

TRUTH IN LABELING

"Inside America's Militias," by Amy Cooter [January 2022], is chilling. The media and academics must stop calling these groups "militias." It gives them a legitimacy that they do not have and reinforces their irrational belief that they are the present-day equivalent of the militias that helped win the Revolutionary War. A more apt label would be "heavily armed political vigilante groups." Labels are important.

TERRENCE DUNN *Vancouver, Wash.*

BOREAL IMPORTANCE

In "Smartphone Patrol," by Annie Sneed [Advances; December 2021], much is made about the importance of the Amazon rain forest, which serves as a diminishing but necessary carbon sink and a provider of life-giving oxygen. Less attention, however, is paid to another forested region on our planet: the boreal forests in northern latitudes stretching across several regions of North America, Russia and Scandinavia.

In terms of sequestering carbon dioxide and contributing oxygen to our atmosphere, these boreal forests are as equally important as the tropical forests at lower latitudes. It should therefore be an equal priority to carefully monitor activities such as logging, clearing land for agriculture, road building and especially mining in these areas, which are often neglected in discussions about global warming.

BARRY MALETZKY *Portland, Ore.*

One World or None

Nuclear arms control is more urgent
now than ever

By the Editors

“It is either the end of nuclear weapons, or the end of us,” wrote 16 winners of the Nobel Peace Prize in an open letter in March that has since been signed by more than a million people. Decades after the end of the cold war and mere months after the U.S., Russia and other members of the United Nations Security Council agreed that “a nuclear war cannot be won and must never be fought,” the specter of nuclear apocalypse again looms over humankind.

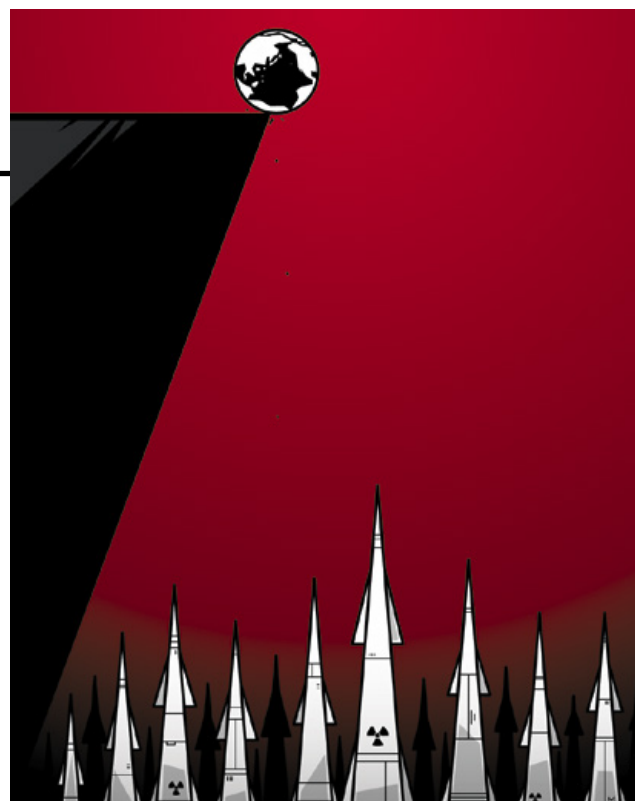
Western powers contemplating intervention in the war in Ukraine “must know that Russia will respond immediately, and the consequences will be such as you have never seen in your entire history,” President Vladimir Putin warned in a not so veiled threat of nuclear retaliation on February 24, the day Russia invaded Ukraine. Days later he raised the alert levels of Russian nuclear forces.

If the prospect of nuclear war does not terrify you, it should. If either Russia or NATO used shorter-range “tactical” nuclear weapons in a European conflict, researchers at Princeton University’s Program on Science and Global Security concluded in a 2019 analysis, it could rapidly escalate into a thermonuclear war that would kill or injure more than 90 million people within a few hours. Further, the one treaty constraining the nuclear arsenals of Russia and the U.S. will expire in 2026. The extreme level of distrust between the adversaries makes it hard for them to negotiate; nevertheless, they must urgently strive to reduce the nuclear threat.

The crisis in Ukraine could provide an impetus. In 1962 the U.S. and the Soviet Union narrowly averted nuclear war over the deployment of nuclear missiles in Cuba. The terrifyingly close call sparked an era of arms control. Ten years later the U.S. and the Soviet Union signed the Anti-Ballistic Missile (ABM) Treaty, constraining the development of defensive shields against incoming missiles, and also agreed to limit the numbers of intercontinental and other ballistic missiles. Another agreement in 1987 banned intermediate-range nuclear weapons, and the Strategic Arms Reduction Treaty (START) of 1991 forced significant reductions in U.S. and Soviet nuclear arsenals. These treaties created “guardrails,” says Daryl Kimball of the Arms Control Association, without which “one side or the other could go over the nuclear cliff.”

The doctrine of mutually assured destruction, or MAD, held that neither superpower could initiate an attack without itself facing annihilation. But in 2002 the U.S. withdrew from the ABM Treaty and began to build a missile defense system, destabilizing this uneasy balance and sparking a new arms race. In 2019 then president Donald Trump went further, abandoning the Intermediate-Range Nuclear Forces Treaty.

These eliminations leave the New Strategic Arms Reduction



Treaty, or New START, negotiated by former presidents Barack Obama and Dmitry Medvedev in 2010, as the only constraint on the numbers of strategic nuclear weapons. Negotiations for renewing and possibly expanding the agreement were scheduled to begin this year; these talks have now been suspended. But if New START is allowed to lapse, a new arms race will begin. If then unregulated nuclear warheads were combined with other unregulated technologies, such as hypersonic or autonomous weapons, the consequences would be unimaginable.

There is reason for hope: much of the rest of the world has been doggedly pursuing arms control. Almost all nations signed multilateral conventions that came into force in 1975 and 1997, banning biological and chemical weapons, respectively. These agreements may be hard to enforce, but they confirm that the global community deems the use of such weapons morally repugnant.

The U.N.’s Treaty on the Prohibition of Nuclear Weapons, advanced by civil society in partnership with nonnuclear states, came into force in January 2021. It aspires to “completely eliminate” nuclear weapons. None of the nuclear-weapons states signed on. But the U.S. and Russia are both signatories of the Nuclear Nonproliferation Treaty of 1970, in which nations without nuclear weapons agreed to never acquire them; in exchange, they got access to peaceful nuclear technology and, crucially, a promise from nuclear-armed nations to eventually eliminate nuclear weapons.

Elimination admittedly seems elusive. Still, the U.S. could immediately make the world a safer place by pledging to never be the first to use nuclear weapons. And as difficult as it may be, the U.S. must strive to resume negotiations with Russia to reduce the danger of nuclear warfare. We have lived long enough with this grotesque cold war relic. ■

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Whether we're talking about socks or stocks, I like
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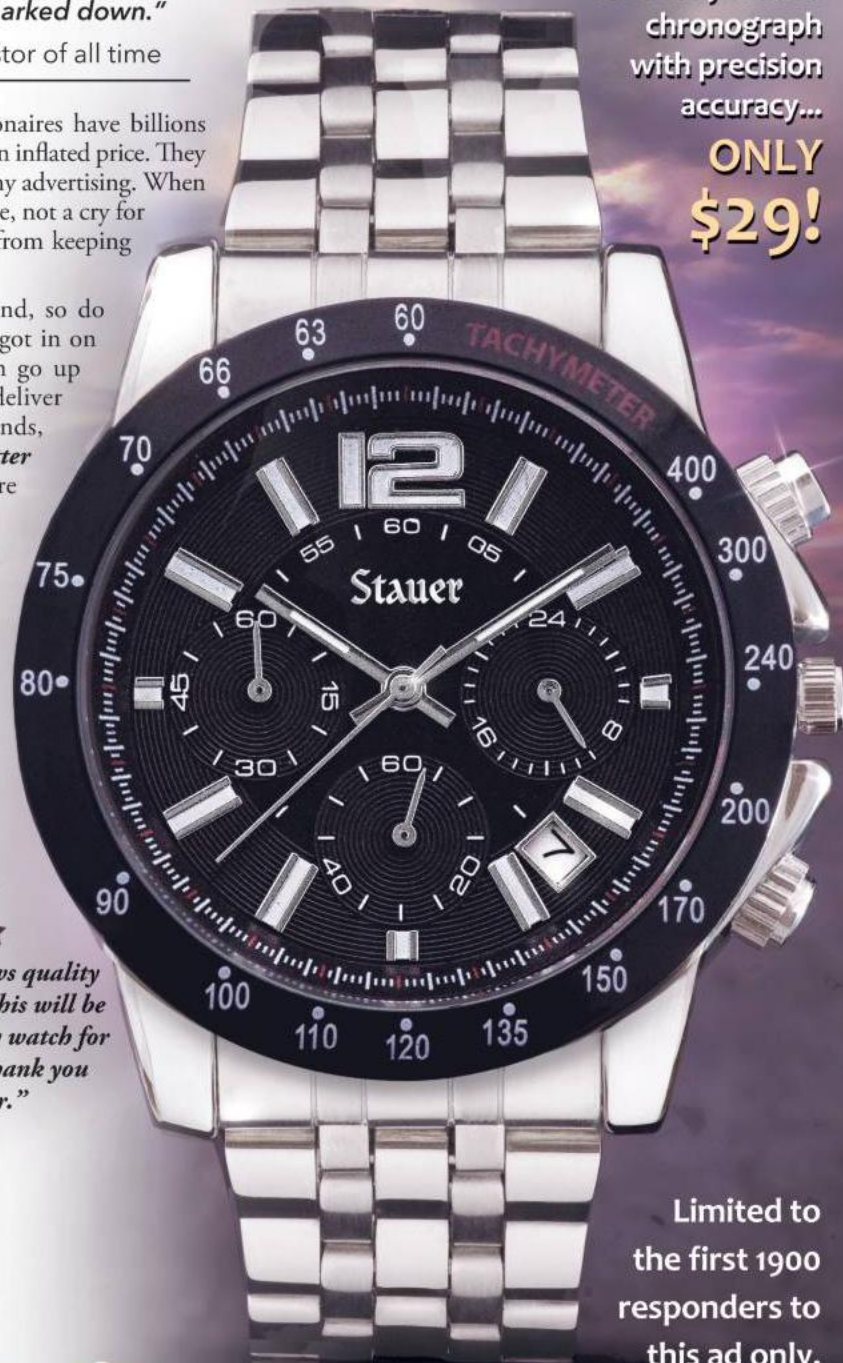
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One Million Dead from COVID Is Not Normal

News media and policy makers are normalizing a staggering death toll

By Steven W. Thrasher

Despite being the wealthiest nation on the planet, the U.S. has continued to have by far the most COVID infections and deaths per country: one million dead, with no end in sight. This is an unfathomable number, yet in contrast to the beginning of the pandemic, the news media has often downplayed the one-million mark. In May 2020 the *New York Times* ran a sympathetic headline reading “U.S. Deaths Near 100,000, an Incalculable Loss,” using its entire front page to print names of some of the deceased. But when the death toll reached nine times that number, the *Times* callously wrote, “900,000 Dead, but Many Americans Move On.”

The *Times* wasn't alone; several large mainstream publications, as well as politicians of both major political parties, have been beating a drum to get “back to normal” for months. The effect has been the manufactured consent to normalize mass death and suffering—to subtly suggest to Americans that they want to move on.

The media has helped to shape public opinion so business can return to the very circumstances that created this ongoing crisis. A return to normal would allow companies to reap profits, while some people work in relative safety from their homes (the target audience of many news organizations' advertisers) at the expense of more vulnerable people who must work or study in person.

This past winter David Leonhardt, the writer of the *Times*'s newsletter “The Morning,” asked Michael Barbaro, the host of the company's podcast “The Daily”: “If COVID is starting to look like a regular respiratory virus, is it rational for us to treat it like something completely different and to disrupt our lives in all these big and consequential ways[?]”

About 200,000 children in the U.S. have lost one or both parents because of COVID—roughly one in every 375 children. This is a big and consequential loss, and those children are probably not among the many who are ready to “move on.” So is it rational? To be calling for the end of lifesaving mitigation efforts and saying they harm children when so many have been orphaned here and worldwide?

Is it rational for Democrats, Republicans and much of the news media to press on toward what writer Tom Scocca calls a policy of “unlimited” COVID?

Is it rational, when as many people have died of COVID in a month as died of AIDS in its worst year (near 50,000 in 1995), to think of the novel coronavirus as a “regular respiratory virus”—and to think that the big and consequential disruptions to worry about are mask wearing and ventilation and not death and debilitation?



Steven W. Thrasher is a professor at Northwestern University in the Medill School of Journalism and the Institute for Sexual and Gender Minority Health and Wellbeing. He is author of the forthcoming book *The Viral Underclass: The Human Toll When Inequality and Disease Collide*.

Is it rational to ignore high community viral loads in American society and to not do more to lower them so that fewer people are exposed, become sick, transmit onward and possibly die?

Well, it depends on what it is you are trying to rationalize.

If you're trying to get people to accept that what the nation has been doing is okay and that 50,000 deaths in a month should be normalized, then it's rational.

If you don't want people to wonder why in just two years the U.S. death toll for COVID was about 130 percent of the death toll of four decades of HIV—while global COVID deaths amount to less than 20 percent of the world's AIDS deaths—then it's rational.

If you want to manufacture consent for looser pandemic measures in the U.S. rather than more comprehensive ones as communal viral rates demand, then making these claims is rational.

Is it rational to ignore high community viral loads and to not do more to lower them so that fewer people are exposed, become sick, transmit onward and possibly die?

But it's not ethical to manufacture what I call a viral underclass, and it's incorrect to pretend the news media have no role in creating it or in persuading the public that so many deaths are inevitable.

It's a shame that major news outlets are hyping up moving on and returning to normal and not running more pieces calling for an increase in government-funded mitigation efforts (more free high-quality masks and tests, upgraded ventilation in work sites and schools) to stem the tide of death. American norms (rampant incarceration, eviction, homelessness, lack of health care, poor ventilation, and economic inequality) are fairly deadly as is.

Acceding to the “urgency of normal” is “wishful thinking,” epidemiologist Gregg Gonsalves wrote in the *Nation*. Intentionally or unintentionally, “the urgency of normal”—a phrase cropping up a lot lately—is evocative of a phrase Martin Luther King, Jr., used in his 1967 speech “Beyond Vietnam” at Riverside Church in New York City, where he preached about “the fierce urgency of now”: “We are now faced with the fact that tomorrow is today. We are confronted with the fierce urgency of now. In this unfolding conundrum of life and history there is such a thing as being too late. Procrastination is still the thief of time.”

If he were still alive, do you think King would have fought for the fierce urgency of the very normal that produced all this death? **✉**

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ADVANCES



Scientists propose sending a message to space using California's Allen Telescope Array (seen here) or China's Five-Hundred-Meter Aperture Spherical Radio Telescope.

- Slimy orbs trap marine microbe prey
- Amino acids form vibrant microscopic landscapes
- Scientists map drug contaminants in the world's rivers
- Tough, flexible “ionogels” hold promise for new technology

SPACE

Long-Distance Call

An updated proposal for beaming a message to the stars

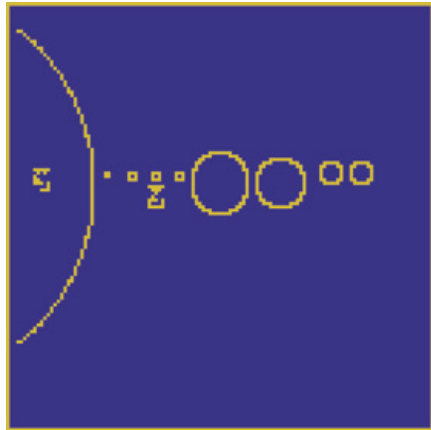
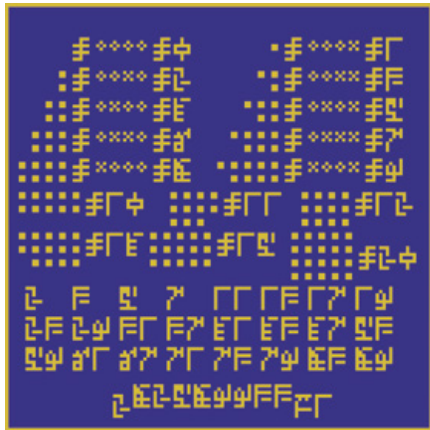
If we ever encounter intelligent life beyond Earth, a key first question will be: “How can we communicate?” An international team of researchers, led by Jonathan H. Jiang of the NASA Jet Propulsion Laboratory, recently detailed a new mission intended for reaching out to extraterrestrial recipients. The 13-part “Beacon in the Galaxy” updates the 1974 [Arecibo message](#)—humanity’s first attempt to send a communication that extraterrestrial intelligence might understand.

Jiang and his colleagues propose aiming the message toward a dense ring of stars near the Milky Way’s center that are likely to host promising planets. The transmission also features a freshly designed return address that will help any alien listeners pinpoint our location so they can—the researchers hope—kick off an interstellar conversation. “The motivation for the design was to deliver the maximum amount of information about our society and the human species in the minimal amount of message,” Jiang says. “With improvements in digital technology, we can do much better than 1974.”

Nearly all the messages humans have broadcast into space so far start with an attempt to establish common ground using basic science and mathematics, which are presumably familiar to both ourselves and any extraterrestrials advanced enough to receive a radio signal. But scientists must



Seth Shostak/SETI Institute



choose how to encode these concepts. Rather than using arbitrary human languages or numeral systems, many attempts (including the new “Beacon in the Galaxy”) opt to design their messages as a bitmap, a method of creating a pixelated image using binary code.

A bitmap is a logical approach; the on/off, present/absent nature of a binary system seems like it would be recognized by any intelligent species. But this strategy is not without shortcomings. When Frank Drake, a pioneer in the search for extraterrestrial intelligence (SETI), created a prototype of the Arecibo transmission, he mailed the binary message to several colleagues—including some Nobel laureates. None understood its contents, and only one realized it was a bitmap.

And even if space aliens manage to decode the message, they might not be able to see any images within. “One of the key ideas is that because vision has evolved independently many times on Earth, that means aliens will have it, too,” says Douglas Vakoch, president of METI (Messaging Extraterrestrial Intelligence) International, a nonprofit organization that studies how to communicate with other life-forms. “But that’s a big ‘if,’ and even if they can see, there is so much culture embedded in the way we represent objects.”

Jiang and his colleagues based much of their design, published in the journal *Galaxies*, on the 2003 “Cosmic Call” message broadcast from the Yevpatoriya RT-70 radio telescope in the region of Crimea. This featured a custom bitmap “alphabet” designed to be robust against transmission errors. After an initial transmission of a prime number to mark the broadcast as artificial, Jiang’s message uses this alien alphabet to

Pages from “Beacon in the Galaxy” codifying numbers, illustrating the solar system and inviting the receiver to reply at a specific frequency. Researchers propose transmitting the message’s 13 parts using binary code for the recipient to assemble into images.

introduce our base-10 numeral system and basic mathematics. The missive then uses a universal phenomenon—the radio wave a hydrogen atom releases when switching energy states—to explain the idea of time and to mark when the transmission was sent from Earth. The message also introduces common elements from the periodic table and depicts DNA’s structure and chemistry.

The final pages are potentially the most interesting to extraterrestrials but also the least likely to be understood. They feature a sketch of a male and a female human, a map of Earth’s surface, a diagram of our solar system and the radio frequency that the extraterrestrials should use to respond to the message. Plus, they offer the coordinates of our solar system, referenced to the locations of globular clusters—stable and tightly packed groups of thousands to millions of stars that would likely be familiar to space-watching entities anywhere in the galaxy.

The researchers propose sending their communication from either California’s Allen Telescope Array or China’s Five-Hundred-Meter Aperture Spherical Radio Telescope (FAST). Since the recent destruction of the Arecibo telescope in Puerto Rico, these are the world’s only radio telescopes actively courting SETI researchers. For now, however, both can only listen to the cosmos; Jiang acknowledges that outfitting either telescope with transmission equipment would not be a trivial project. But it is possible, and Jiang says he and his co-authors are discussing ways to work with FAST researchers to make it happen.

A far deeper question is whether we

should send a message at all, a controversy among many SETI researchers: Could this entire effort be a waste of time, or could it invite attack by malicious entities? “I don’t live in fear of an invading horde, but other people do. And just because I don’t share their fear doesn’t make their concerns irrelevant,” says Bowling Green State University researcher Sheri Wells-Jensen, an expert on the linguistic and cultural issues associated with interstellar message design. But “just because it would be difficult to achieve global consensus on what to send, or whether we should send, doesn’t mean we shouldn’t do it. It is our responsibility to struggle with this and clue as many people in as possible.”

Many insist that the potential rewards of “active SETI” far outweigh the risks. First contact would be one of the most momentous occasions in the history of our species, the argument goes—and if we just wait around for someone to call us, it may never happen. As for the risk of annihilation by malevolent space aliens, we blew our cover long ago. Any extraterrestrial capable of traveling to Earth would likely be more than capable of detecting evidence of life in the chemical signatures of our atmosphere or the electromagnetic radiation that has been leaking from our radios, televisions and radar systems for the past century.

“This is an invitation to all people on Earth to participate in a discussion about sending out this message,” Jiang says. “We hope, by publishing this paper, we can encourage people to think about this.”

—Daniel Oberhaus

“A Beacon in the Galaxy: Updated Arecibo Message for Potential FAST and SETI Projects,” by Jonathan H. Jiang et al., in *Galaxies*; March 25, 2022

GENETICS

Flying Frogs

Analysis and flight test probe how “parachute frogs” glide

A few frog species in the jungles of East Asia take hopping to the extreme. These daredevil amphibians, dubbed parachute frogs, leap from treetops and soar through the rain-forest canopy to evade predators. Some can cover more than 50 feet in a single glide.

Although they lack the true wings of birds and bats, these frogs use extensive webbing between their toes as a winglike surface to slow their descent. They also have oversized feet, as well as flaps of loose skin along their limbs and sticky toe pads to help them safely land.

University of Texas at Austin evolutionary biologist David Hillis and his colleagues at China’s Chengdu Institute of Biology collected several specimens of black-webbed tree frogs—a lime-green parachute frog species with black and yellow webbing—from rain forests in southern China to pick apart the genetics behind the impressive adaptations.

The researchers compiled the tree frog’s genome and compared it with a closely related frog incapable of gliding. For a study in the *Proceedings of the National Academy of Sciences USA*, they pinpointed 455 modified genes. “Many of the genes we identified are associated with various aspects of webbing, foot and limb development,” Hillis says. “All are consistent with the strong morphological adaptation of flying frogs for

gliding behavior.” The researchers found some genes produced longer limbs and stickier toe pads for climbing. They also identified the network of genes likely responsible for extra webbing by tracking foot development in each species’ tadpoles.

To observe these differences in action, the researchers conducted a controlled flight test. They placed frogs from each species on perches and recorded any jumps and subsequent glides—positioning soft sponges below in case frogs fared badly in the air. This proved important for the nongliding frogs, which plummeted into the sponges. But the parachute frogs splayed their heavily webbed toes to glide horizontally before touching down.

According to biomechanist Mimi Koehl of the University of California, Berkeley, who has studied flying frogs’ biodynamics and was not involved in the work, the extra webbing both slows their fall and helps them steer through the rain-forest canopy. The frogs dodge trees by using oversized back feet like rudders as they descend toward puddles on the forest floor, congregating to mate and lay eggs. “If they can’t maneuver through this complicated environment, they’re going to miss the orgy,” Koehl says.

The researchers say understanding these frogs’ adaptations may help illuminate how other animals—such as flying squirrels and flying lizards—took to the sky. Koehl and her colleagues have even used flying frogs to help model dinosaur flight. Flying dinosaurs “had feathered tails and feathers on their hind legs,” she says. “They had the same maneuverable body design as flying frogs.” —Jack Tamisiea



Parachute frog

Arun Roisri/Getty Images

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— Julia Sweeney

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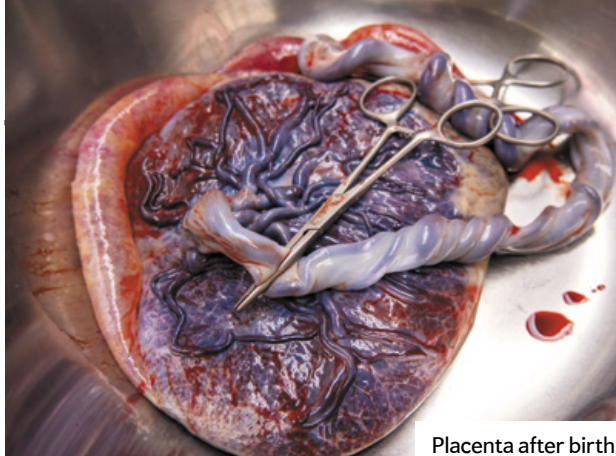


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Placenta after birth

BIOLOGY

Body Invader

Placenta genetics offer ideas for anticancer drugs

To obtain nutrients for a growing fetus, a placenta embeds itself into the uterus—an “invasion” that resembles the way a tumor takes over healthy tissue. Now researchers have identified genes that help to regulate placental embedding and may prove instructive in developing anticancer drugs, according to a new study in the *Proceedings of the National Academy of Sciences USA*.

Scientists knew that the amount a placenta embeds varies across species. In some, such as humans and apes, placenta cells push deep into the uterine wall with relative ease. But in animals like cows and horses, the uterus has evolved to resist such intrusions more strongly. This capability may help protect the maternal immune system and lessen uterus damage when giving birth.

In 2019 cellular biologists Günter Wagner of Yale University and Kshitiz of the University of Connecticut Health found that this cellular resistance extends beyond the uterus. They observed a direct correlation between how deeply a species’ placenta embedded and the rate of tumors that spread beyond their primary site in that species’ body. Species with highly embedded placentas were associated with higher rates of metastatic cancer; cellular material connecting tissues and organs in these species was less resistant to invasion by both placentas and tumors. The question was why.

For the new study, Kshitiz, Wagner and their colleagues examined nine mammal species for differences in protein production that might explain how some species’ tissues resist invasion more strongly. The team identified two proteins that, when produced in abundance, made tissues more susceptible to cellular intrusion—whether from a placenta or a tumor. When the protein-producing genes were removed, cells blocked invasion more effectively.

“A mutation that helps the uterus keep the placenta out also [could affect] the biology of cancer in, say, the skin,” Wagner says.

To Wellcome Sanger Institute cancer biologist Sam Behjati, who was not involved in the study, this finding suggests new ways to target tumor growth and spread. “This is a hard-core, comparative biological study,” he says. Scientists know a lot about the molecular steps required for implantation—and “it would be nice to employ that line of pharmacological thinking for metastases.”

Still, Amy Boddy, a comparative oncologist at the University of California, Santa Barbara, who was also not involved, cautions that this specific invasion process probably does not tell the whole story. Cancers have a variety of causes and contributors. “Everything that is multicellular is vulnerable to cancer,” Boddy says. “We’ve just started probing the potential mechanisms.” —Carrie Arnold

ECOLOGY

Into the Mucosphere

Tiny organisms trap prey with carbon-rich slime

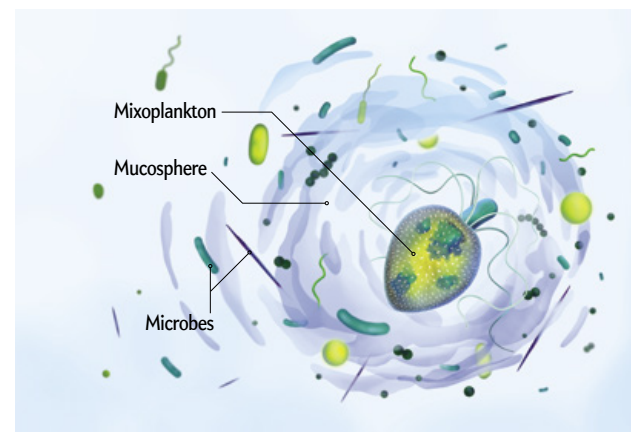
Ocean oddities called mixoplankton are organisms that can get energy both through photosynthesis and by eating other microbes. Now new research published in *Nature Communications* suggests that one such species, *Procoentrum cf. balticum*, displays a bizarre and clever hunting technique—one that significantly contributes to the crucial cycling of carbon through land, atmosphere and oceans.

Study lead author Michaela Larsson, a marine biologist at the University of Technology Sydney, and her colleagues were studying marine mixoplankton in the laboratory when they noticed the creatures twisting and turning as they exuded mucus. The researchers found that beyond photosynthesizing in the daytime, these organisms also form a carbon-rich “mucosphere” around themselves at night—then use chemical cues to lure other microbes into it. The mixoplankton then eat the microbes and shed the mucus package, which sinks to the ocean floor and deposits a rich store of carbon.

The study “is evidence that our thinking around how carbon is cycled in the ocean must be revised to include the sophisticated behaviors of microbes,” Larsson says. Identifying *P. balticum* DNA in a global marine microbe data set shows the organisms’ prevalence across the ocean, suggesting they contribute considerably to the planetary carbon cycle. The authors estimate these plankton could sequester up to 0.15 gigaton of carbon every year—about 0.5 percent of the world’s annual carbon emissions.

According to Aditee Mitra, a marine systems modeler at Cardiff University in Wales, who was not involved in the research, the paper “is yet another indication of how little we know about [ocean] organisms that collectively have generated around half of the oxygen in Earth’s atmosphere and continue to play a pivotal role in planetary biogeochemical cycling.”

Since the study’s publication, scientists have observed that other mixoplankton species can form and release mucospheres. Researchers are also investigating how microbe behaviors might vary in different marine conditions. “Discovering this microbial behavior and evaluating the broader implications for ocean biogeochemical cycling really are just the beginning,” Larsson says. —Susan Cosier



IN THE NEWS

Quick Hits

By Joanna Thompson

SCOTLAND

New analysis of the famous “bodies in the bog” found near Edinburgh indicates that at least two—a man and a woman—were born far from their final resting place. Scientists used traces of chemical isotopes from the individuals’ teeth to determine their status as Medieval ramblers.

SPAIN

Archaeologists studying Paleolithic cave art in Cantabria found that up to a quarter of the ochre handprints placed there were made by children. The prints were likely made by blowing red pigment through a hollow reed or bone over a hand used as a stencil.

CANADA

Although caribou populations are declining across most of the Canadian wilderness, research suggests British Columbia’s Klinse-Za herd has tripled in size in nine years. The herd is protected through a program led by two First Nations groups.

ECUADOR

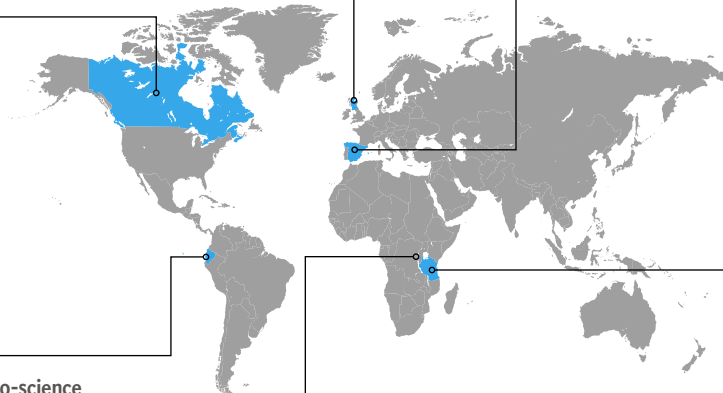
Researchers described two new-to-science species of glass frog—tiny, transparent amphibians living in the Andes foothills. Despite looking nearly identical and living on opposite sides of a river valley, the two species have surprisingly different genomes.

RWANDA

Scientists in Nyungwe National Park recently captured a Hill’s horseshoe bat, a species last spotted by scientists in 1981. The researchers recorded the critically endangered bat’s call before release so they can monitor its population in the future.

TANZANIA

A program on the semiautonomous islands of Zanzibar combines drones and a smartphone app to map malaria-carrying mosquito hotspots. The mosquitoes breed in tiny bodies of standing water, which are difficult to survey on foot—but one drone can cover more than 70 acres in about 20 minutes.



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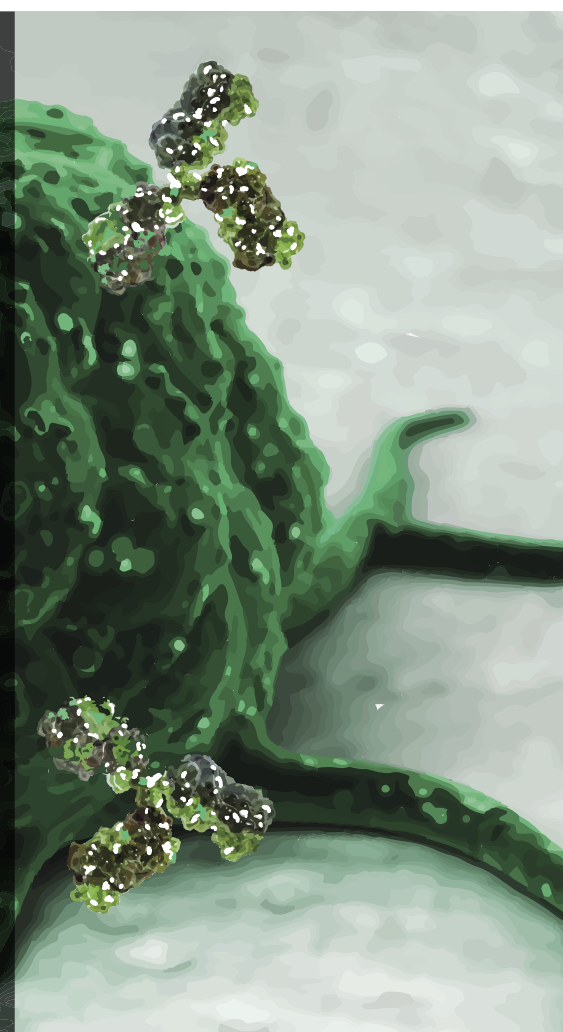
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CHEMISTRY

Science in Images

By Joanna Thompson

Photographer Justin Zoll shoots stunning landscapes—without setting foot outside. Instead he peers through a secondhand Olympus BH2 microscope into a hidden world of psychedelic crystal vistas.

Zoll has more than 15 years of photography experience, mostly capturing weddings and concerts. Around six years ago a friend introduced him to the world of micrography. “I got hooked right away,” Zoll recalls. He fell in love with a trial-and-error process of combining solvents and crystalline salts, creating aesthetically pleasing compositions too small to be seen with the naked eye. When the COVID pandemic struck and his workaday event venues shut down, he suddenly found himself with ample time to experiment in his makeshift bedroom lab. He ordered a plethora of powdered substances online and busted out a hot plate.

The vibrant colors in Zoll’s photographs are the product of each crystal’s structure—not added by a computer. “If you look through the microscope, this is pretty much exactly what you see,” he says, although he does take multiple shots of each slide to create a panoramic effect.

The amino acids L-glutamate and beta-alanine, combined to form this tableau, are both produced in the body and are commonly sold as supplements for athletes and body builders. To create this type of image, Zoll dissolves the compounds—typically in high-proof vodka—and dries the mixture, with or without heat. The aquamarine and gold colors on display here are relatively rare for amino acid crystals, he says.

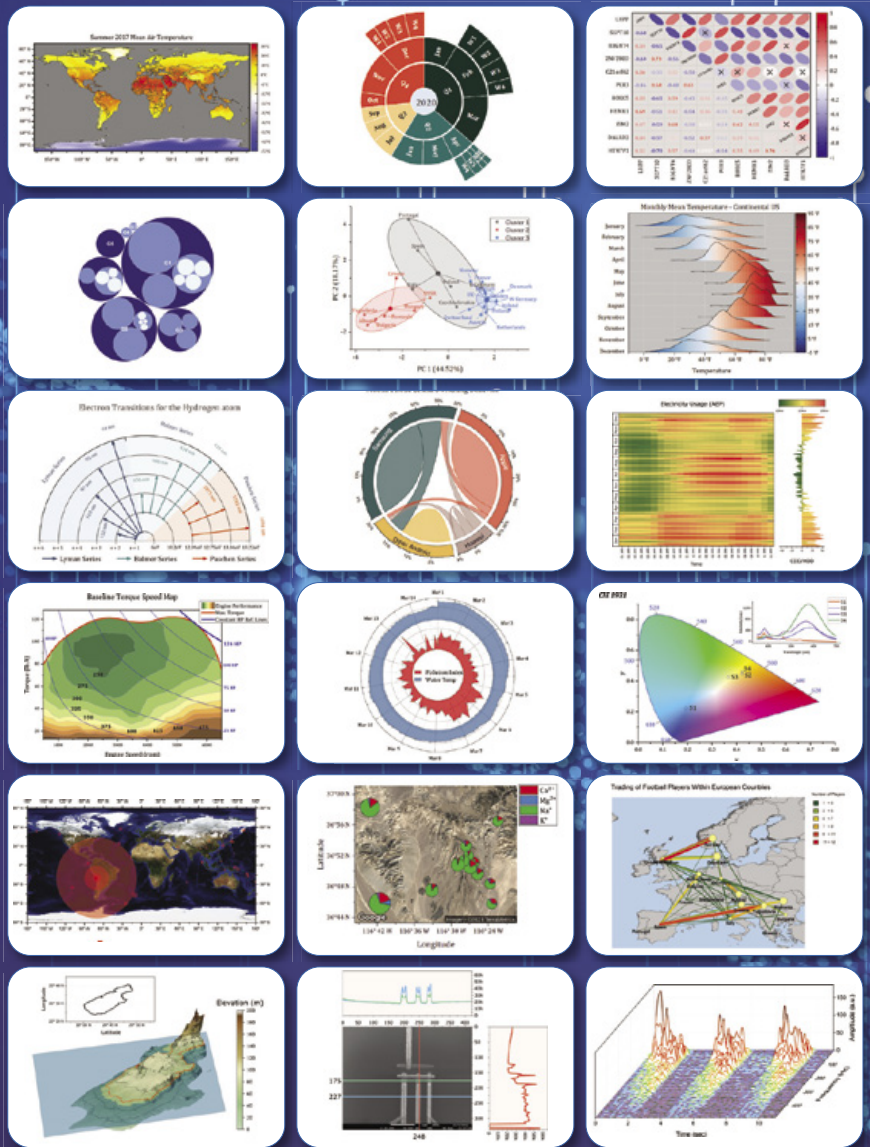
Zoll does not have a background in chemistry or physics, but he harbors a deep appreciation for the beauty science can illuminate. “Simple math creates similar structures, from the cosmic down to what I’m looking at in my bedroom under a microscope,” he says. “I think that’s really cool. And I think it’s important for us to share that perspective.”

Justin Zoll





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TECH

Vitamin Map

AI can pinpoint nutrient deficiencies from space

Micronutrient deficiencies afflict more than two billion people worldwide, including 340 million children. This lack of vitamins and minerals can have serious health consequences. But diagnosing deficiencies early enough for effective treatment requires expensive, time-consuming blood draws and laboratory tests.

New research provides a more efficient approach. Computer scientist Elizabeth Bondi and her colleagues at Harvard University used publicly available satellite data and artificial intelligence to reliably pinpoint geographical areas where populations are at high risk of micronutrient deficiencies. This analysis could potentially pave the way for early public health interventions.

Existing AI systems can use satellite data to predict localized food security issues, but they typically rely on directly observable features. For example, agricultural productivity can be estimated from views of vegetation. Micronutrient availability is harder to calculate.

After seeing research showing that areas near forests tend to have better dietary diversity, Bondi and her colleagues were inspired to identify lesser-known markers for potential malnourishment. Their work shows that combining data such as vegetation cover, weather and water presence can suggest where populations will lack iron, vitamin B₁₂ or vitamin A.

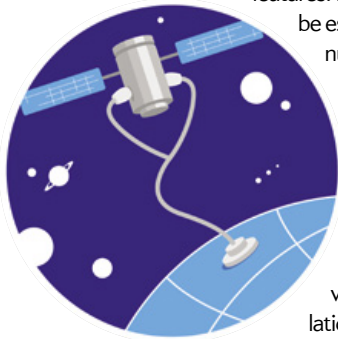
The team examined raw satellite measurements and consulted with local public health officials, then used AI

to sift through the data and pinpoint key features. For instance, a food market, inferred based on roads and buildings visible, was vital for predicting a community's risk level. The researchers then linked these features to specific nutrients lacking in four regions' populations across Madagascar. They used real-world biomarker data (blood samples tested in labs) to train and test their AI program.

Predictions of regional-level micronutrient deficiency in populations outside the training data sets met, and sometimes exceeded, the accuracy of estimates based on surveys administered by local public health officials. "Our work showcases a method that allows for identification and targeting of vulnerable populations for nutritional support that may supplement ... expensive and invasive procedures," Bondi says. The study was detailed at the Association for the Advancement of Artificial Intelligence's 2022 virtual meeting.

"This is a novel contribution that highlights AI's potential to advance public health," says Emory University epidemiologist Christine Ekenge, who was not involved with the study. Collecting health data in low-resource settings can be difficult because of cost and infrastructure constraints, she adds, and "the authors have validated a method that can overcome these challenges."

The researchers aim to develop a software application that extends this analysis to other countries that have public satellite data. "We hope that this application could allow public health officials to interact with the insights our system can provide and help to inform interventions," Bondi says. —Rachel Berkowitz



ECOLOGY

Smart Leaves

Thirsty redwoods pull water out of thin air

Coastal California's redwood forests—with their lush ferns, towering trees and damp petrichor scent—might not seem to want for water, but they do face dry summers. To survive them, the trees, *Sequoia sempervirens*, grow specialized shoots with leaves that scrape moisture from the air.

Many plants (including redwoods) are known to drink through their leaves, but "no one ever really figured out how the water gets in there," says ecologist Alana Chin, now at ETH Zürich. Exposing leaves to moisture has costs: even a thin film of water can block the flow of carbon dioxide into leaf openings called stomata, hindering photosynthesis.

To see how the trees solve this dilemma, Chin and her colleagues climbed redwoods in various climate zones and snipped two samples. Back in the laboratory, they generated fog with a humidifier and measured how much water these leafy shoots absorbed. They also examined leaf surfaces and cross sections, then modeled water movement to see which traits affect uptake.

Their analysis, published in the *American Journal of Botany*, revealed two distinct redwood shoot types. Resembling asparagus stalks with leaves bunched close to the twig, "axial" shoots make up a small portion of the canopy but absorb water at about four times the rate of ordinary-looking "peripheral" shoots. The team estimated a tall redwood absorbs up to 13 gallons of water in the hour after it gets wet. Meanwhile peripheral leaves power photosynthesis with dense stomata and waxy, water-repellent coatings.

The study found that redwoods in drier, southern areas have more axial shoots that are located higher up than on northern trees, which helps the former pull extra water from summer fog and light rain. Other tree species may have similarly specialized shoots; pines, for example, have two types that might be analogous to those on redwoods, Chin says. Such versatility could be important in the context of climate change, notes Wake Forest University ecologist Carter Berry, who was not involved in the study. "In a drier world," he says, "the ability to subsidize your water source with water from the air becomes more important." —Ula Chrobak

Alana Chin/University of California, Davis

ENVIRONMENT

Mainstream Drugs

Many of the world's rivers are coursing with pharmaceuticals

For more than 20 years scientists have known that the drugs we take, for maladies ranging from headaches to diabetes, eventually make their way into our waterways—where they can harm the ecosystem and potentially promote antibiotic resistance.

But most research on pharmaceutical contaminants has been done in North America, Europe and China and has examined just a small subset of compounds. The studies also use a variety of sampling and analysis methods, making it hard to compare results. Such limitations mean scientists may be missing a big piece of the pollution puzzle.

A new paper published in the *Proceedings of the National Academy of Sciences USA* provides a more comprehensive look. A network of 127 scientists sampled 258 rivers in 104 countries for 61 different chemicals, producing “a sort of ‘pharmaceutical fingerprint’ of nearly half a billion people across all the world’s continents,” says study lead author John L. Wilkinson, an environmental chemist at the University of York in England.

Many of the most drug-polluted rivers were in Africa and Asia, “in areas and countries that have been largely forgotten by the scientific community” on this issue, Wilkinson says. Waterways with the biggest pharmaceutical concentrations also tended to be in lower-middle-income countries; the authors say this could stem from improved medication access in places that still lack sufficient wastewater infrastructure.

Four compounds—caffeine, nicotine, acetaminophen and cotinine (a chemical produced by the body after exposure to nicotine)—showed up on every continent, including Antarctica. Another 14, including antihistamines, antidepressants and an antibiotic, were traced on all continents except Antarctica. Some drugs were detected only in specific places, such as an antimalarial found in African samples.

Overall, the study shows that “more of this kind of global assessment of aquatic pollution” is needed, particularly for other

chemicals that pose more of a human health risk, says Elsie Sunderland, a Harvard University environmental scientist who was not involved with the new research. It also suggests, she adds, that “we need wastewater treatment.”

—Andrea Thompson

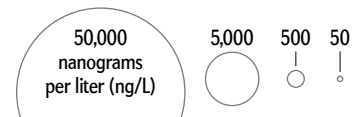
KEY

Each circle represents a sampling campaign consisting of water collection from sites within a city, town or local area. Most campaigns included 5 to 11 sites.

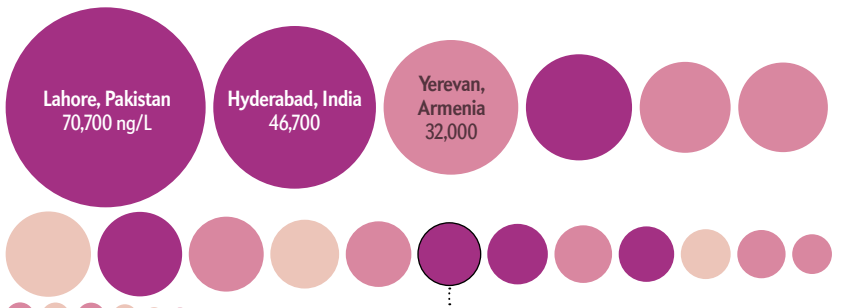
Color shows country's income level (per the World Bank)

- Low
- Lower-middle
- Upper-middle
- High
- Not listed

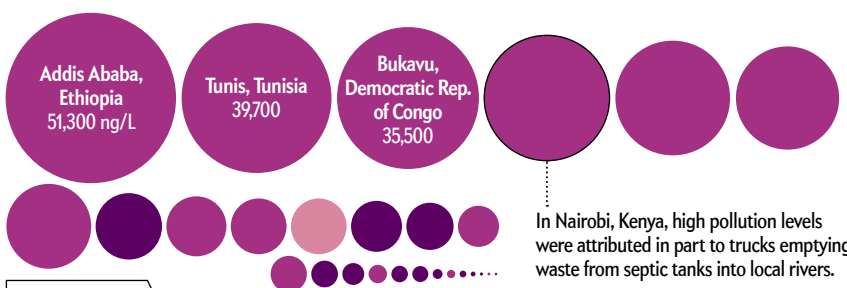
Circle size shows mean cumulative concentration of pharmaceuticals found in each campaign



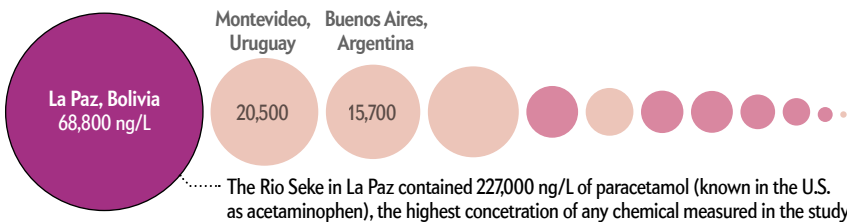
Asia



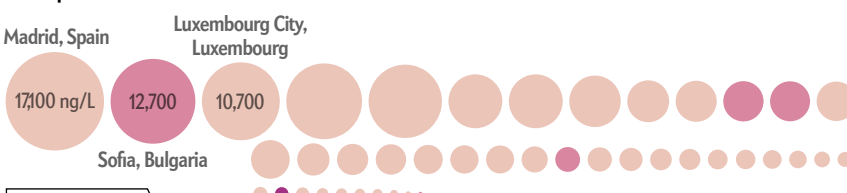
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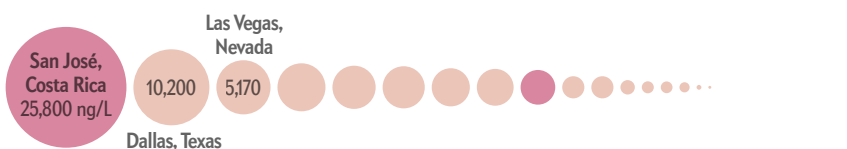
South America



Europe



North America

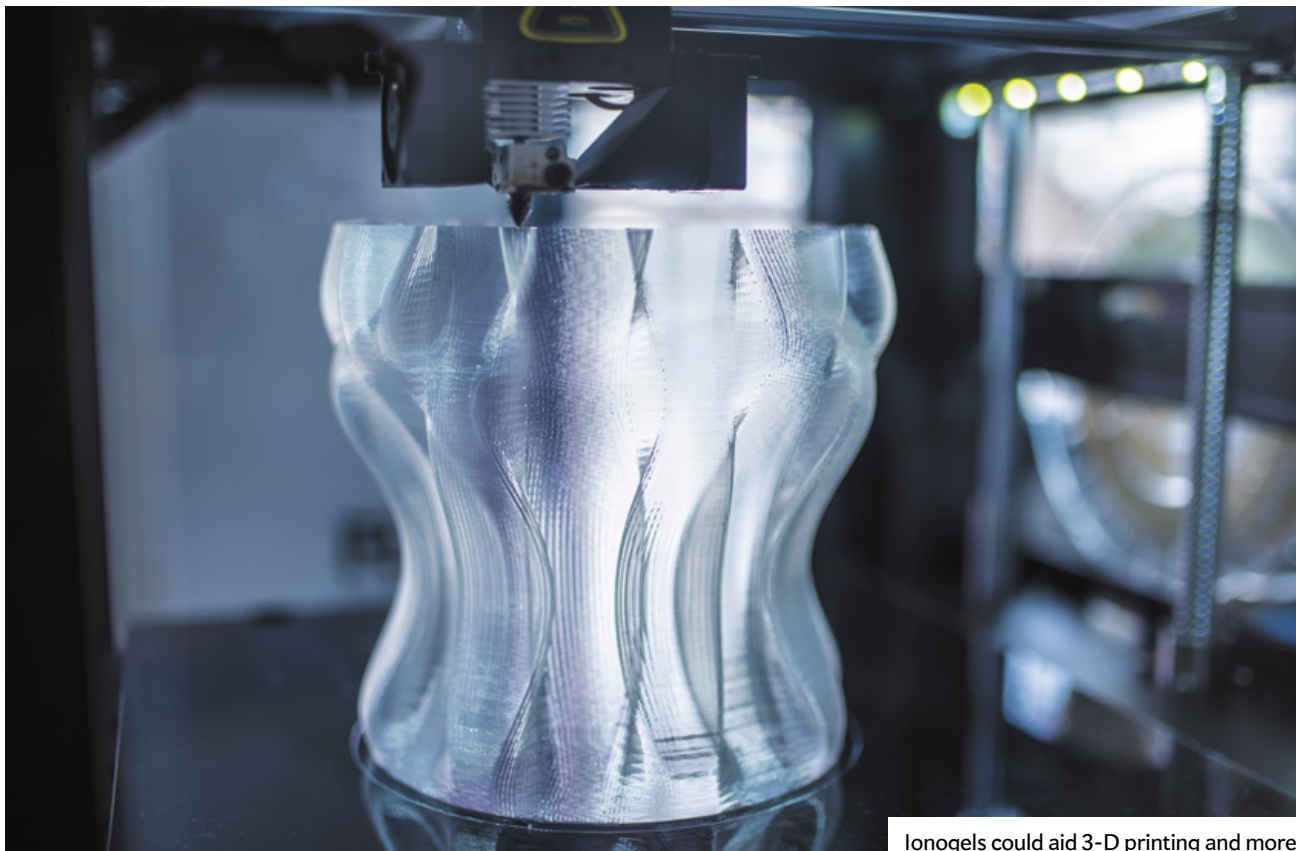


Oceania

Antarctica



Source: “Pharmaceutical Pollution of the World’s Rivers,” by John L. Wilkinson et al., in *Proceedings of the National Academy of Sciences USA*, Vol. 119, February 22, 2022



Ionogels could aid 3-D printing and more.

MATERIALS SCIENCE

Super Gels

New ionogels are tough, stretchable and easy to make

Flexible, squishy hydrogel materials are used in a dizzying array of applications, from soft contact lenses to *Jell-O*. But all share a common structure: a tangled network of polymer chains soaked in water. Now researchers have developed their own version of a hydrogel cousin that is tougher and could perhaps find even more uses, including longer-lasting batteries. Meet a new ionogel.

Instead of water, ionogel polymers are inundated with an ionic liquid. This fluid is made up of positively and negatively charged ions—like the composition of *table salt*. But an ionic liquid does not assemble into a crystalline solid at room temperature. Nevertheless, the strong bonds between ions ensure the liquid does not evaporate like water does. And thanks in part to the sticking power of ions, polymers soaked in an ionic liquid can be tougher than hydrogels are.

Michael Dickey, a chemical engineer at North Carolina State University, and his colleagues have devised a new method for creating ionogels with mechanical properties he describes as “best in class.” They are harder to break than either cartilage or natural rubber while remaining soft and stretchy. (One type of ionogel can stretch up to seven times its length—more than twice as far as a rubber band can, Dickey says.) Like other ionogels, his team’s new ones conduct electricity and remain stable amid shifting temperatures. If heat is applied, they can self-heal a cut or tear. The new material is described in a recent study published in *Nature Materials*.

“These transparent ionogels have remarkably tough mechanical properties and are distinguished by how easy they are to prepare,” says Xuanhe Zhao, a mechanical engineer at the Massachusetts Institute of Technology, who reviewed the study but was not directly involved in the work. Other researchers have developed their own ionogels, but making them typically involved multiple steps or complex chemistry. Using the new formula, Dickey and his colleagues simply mixed an ionic liquid

with the building blocks (called monomers) of two different types of polymers, and then they shone light on the liquid to trigger the monomers to link up into polymer chains. “In this case, one plus one equals 100,” Dickey says. “You take these two materials that, by themselves, are [common], but then you put them in this new environment, and you get something remarkably tough.”

Easy-to-make ionogels could have many applications. Their toughness and stretchiness make them a good candidate for cushioning to protect against car accidents or explosions. They solidify when exposed to light, so an ionogel formulation could be used to 3-D print hard-to-break objects. And because their ions can carry a charge, the gels could be used in a rechargeable battery, where the researchers say they would resist degradation better than the liquid electrolytes currently in use.

Those are just a few possibilities, Dickey says. “When you have a material that’s so easy to make and has such great properties,” he adds, “it’s bound to find applications that are probably even beyond my imagination.”

—Sophie Bushwick

Azaman/Getty Images

BIOLOGY

Pimple Patrol

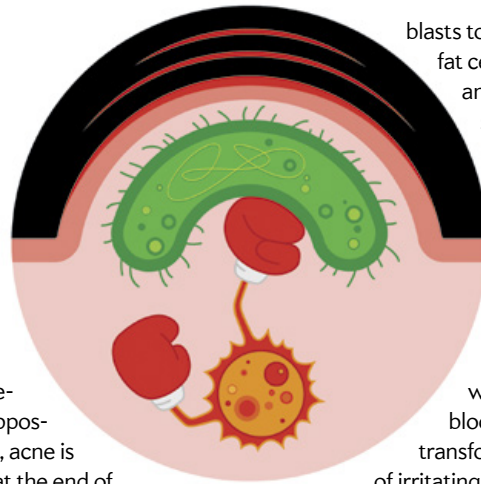
New dermatology research gets to the root of acne

If **pimples** are caused by oily skin, why doesn't a good washing prevent all break-outs? A recent study offers an answer—and maybe a new line of defense.

Pimples contain tiny and discrete bacterial infections. The most commonly involved bacteria are *Cutibacterium acnes*, which live innocuously on skin cells but can grow out of control when the skin's oily sebum increases and boosts bacterial food supply. What we think of as acne—the pustules, redness and swelling—is a battle between our immune system and these rapidly multiplying bacteria, says dermatologist Richard Gallo of the University of California, San Diego, who led the new study. “For most people, it’s not that you’re dirty, or you’re not washing your face enough,” Gallo explains. “This is a problem with the way your body’s immune system

is dealing with the bacteria that are supposed to be there.”

If one imagines the immune system and bacteria as being on opposing soccer teams, acne is the beat-up turf at the end of the game. The new study identifies a previously unknown, and particularly turf-mangling, immune system player. Gallo and his colleagues showed in *Science Translational Medicine* that a structural cell type called a fibroblast (which is not typically considered an immune cell) contributes to the facial face-off. Working with mice and with human skin samples, the scientists found that *C. acnes* triggers fibro-



blasts to transform into fat cells that secrete an antimicrobial substance—along with inflammation-causing proteins. The researchers also discovered that retinoids, a powerful and commonly used class of pimple-fighting drug, work partially by blocking fibroblasts’ transformation and release of irritating proteins.

Jonette Keri, a clinical dermatologist at the University of Miami Miller School of Medicine, who was not involved in the research, calls the finding an “exciting” new way to think about acne. Because retinoids can have undesirable side effects, she says, pursuing a more targeted way to stop the fibroblasts’ transformation would be “fantastic” for clinical treatment.

—Maddie Bender

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Vaulted Seeds

After the Svalbard Global Seed Vault

Hoarded at the heart of an Arctic mountain,
within an archipelago of snow: an ark of seeds.
Cocooned against soil, nuclear bodies hunker
and wait for some future hungerscape. A gathering

of crops, varied faces folded into foil,
shuttered from the earth. Lentil, dark and round
and pebble-smooth. Barley's slender husk of an eye.
Each wrinkled chickpea the embryonic head of a bird.

Sister seeds, in Aleppo, shelter abandoned
in the rubble of war. The snow is a silence
except for how the seeds call out to one another
across landmasses that shift and warm.

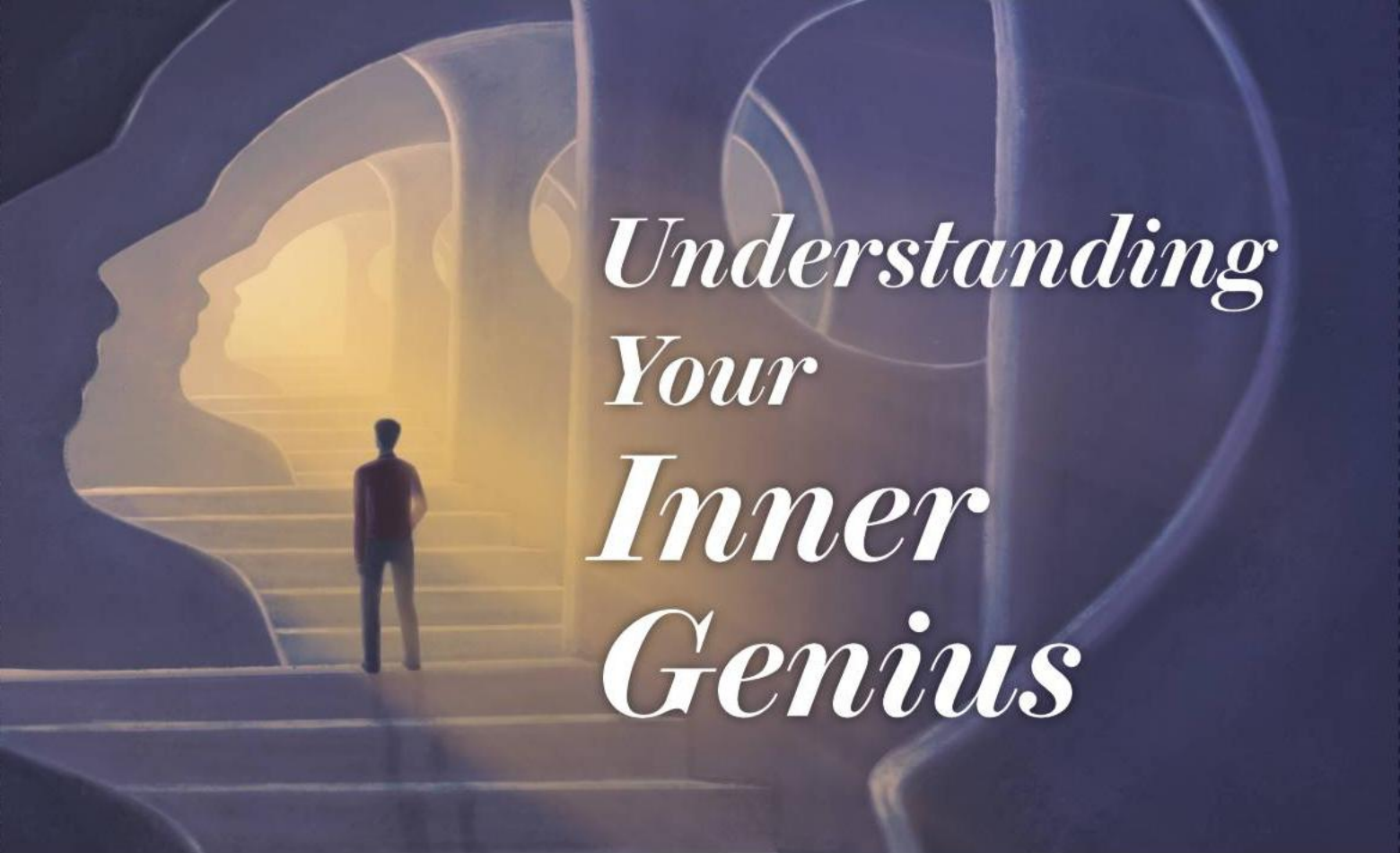
Svalbard reindeer swivel their ears to listen.
Foxes pause ghostlike on the permafrost. With one
quadrate eye, the vault reflects a frigid blue sea.
Ringed seals bob and dive among the glassy floes.

The vault's stone hull juts like a shipwreck in the drifted
ice while polar bears chuff and lumber past the door.
Inside, thousands upon thousands of promises to feed
what may remain. Doomsday, its other name.

Because we've already planted what's to come.



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Claudia Wallis is an award-winning science journalist whose work has appeared in the *New York Times*, *Time*, *Fortune* and the *New Republic*. She was science editor at *Time* and managing editor of *Scientific American Mind*.



Regenerating Damaged Joints

New research on arthritis and cartilage opens up growing possibilities

By Claudia Wallis

“Cartilage doesn’t heal.” That’s what doctors often tell us when we injure the flexible tissue that lines our hips, knees and shoulders or when osteoarthritis has eroded it so that our joints hurt when we move. I’ve certainly heard it myself from orthopedic surgeons who explain that cartilage has no blood supply to bring repair cells and nutrients to an injury site. Yet it’s always struck me as improbable that a living tissue could not replace damaged cells. As it turns out, recent research suggests that articular cartilage—the type in our joints—does have some limited repair capacity. New insights into this ability are raising hopes for treatments that could enhance healing or protect damaged cartilage from further deterioration.

To picture articular cartilage, envision the tough, white coating on the end of a chicken bone. Most of it is a spongy material called extracellular matrix, a mixture of water and fibrous proteins pumped out by cells called chondrocytes. “There is intrinsic regeneration—with new tissue being formed and old tissue chewed up and washed away—just as there is for every tissue with the exception of tooth enamel,” explains rheumatologist Virginia Kraus of the Duke University School of Medicine. But, she emphasizes, the renewal process in cartilage is sluggish. And it

is true that in adults the tissue has no blood supply. Instead cartilage gets help from what experts call dynamic loading—putting stress or weight on the joint, which causes nutrient-carrying synovial fluid to flow in and out. “That’s why exercise is so critical to joint health,” Kraus notes. “The way you get nutrients to cartilage is through movement.”

Kraus is one of a small number of scientists who studies the slow turnover in this tissue. In a surprising discovery, she and her team [reported in 2019](#) that the production of proteins associated with repair and regeneration differs by joint: It is greater in the ankle than in the knee and greater in the knee than the hip. Kraus refers to this gradient as “our inner salamander,” explaining that in salamanders and other animals that can regenerate a lost limb, this capacity is more robust in the foot than higher up in the leg.

Her study also showed that genetic material associated with repair is more abundant in arthritic joints than healthy ones. Just as a limb injury launches a repair program in a salamander, osteoarthritis is turning it on in humans, Kraus suspects, although “obviously the program we have is not sufficient.” Still, the repair process may be working in the ankle, which, she notes, is far less prone to severe arthritis than the knee or hip.

There is other evidence that human cartilage can regenerate. A procedure called joint distraction is being tested as a way to promote healing in patients who have bone-on-bone knee arthritis and are too young to be good candidates for total knee replacement. (Prosthetic knees last 15 to 20 years, after which they must be replaced in a complex surgery.) The procedure involves placing pins above and below the knee and using an external device for six weeks to separate the upper and lower leg bones by five millimeters. This opens up the joint space. Patients are encouraged to walk, but the device reduces stress, so the knee is bathed in nutrient-laden fluid without being overburdened.

Dutch researchers have shown that the procedure leads to a [small increase in cartilage in the joint and less pain](#)—benefits that last [at least two years](#) and as many as 10 in some patients. Larger clinical trials of the technique are needed, “but it’s a fascinating model,” says rheumatologist Philip Conaghan of the University of Leeds in England.

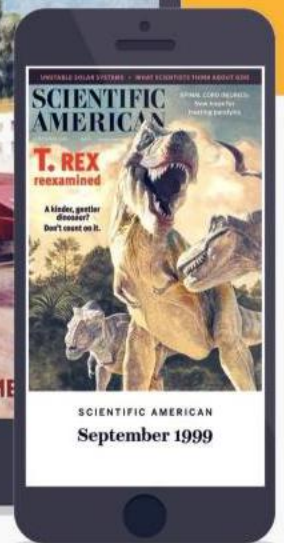
Conaghan investigates new drugs for arthritis, including a growth factor called sprifermin that [appears to slow the loss of cartilage in some patients](#). He is also looking at canakinumab, an inflammation inhibitor that was tested as a cardiovascular drug and showed a surprising side effect: [dramatically fewer joint replacements](#) in recipients than in a placebo group. But Conaghan warns that the quest for drugs that can thicken cartilage is a tough one because of the slow and uncertain nature of repair: “The change is so small, and it’s hard to pick it up, even with the best imaging.”

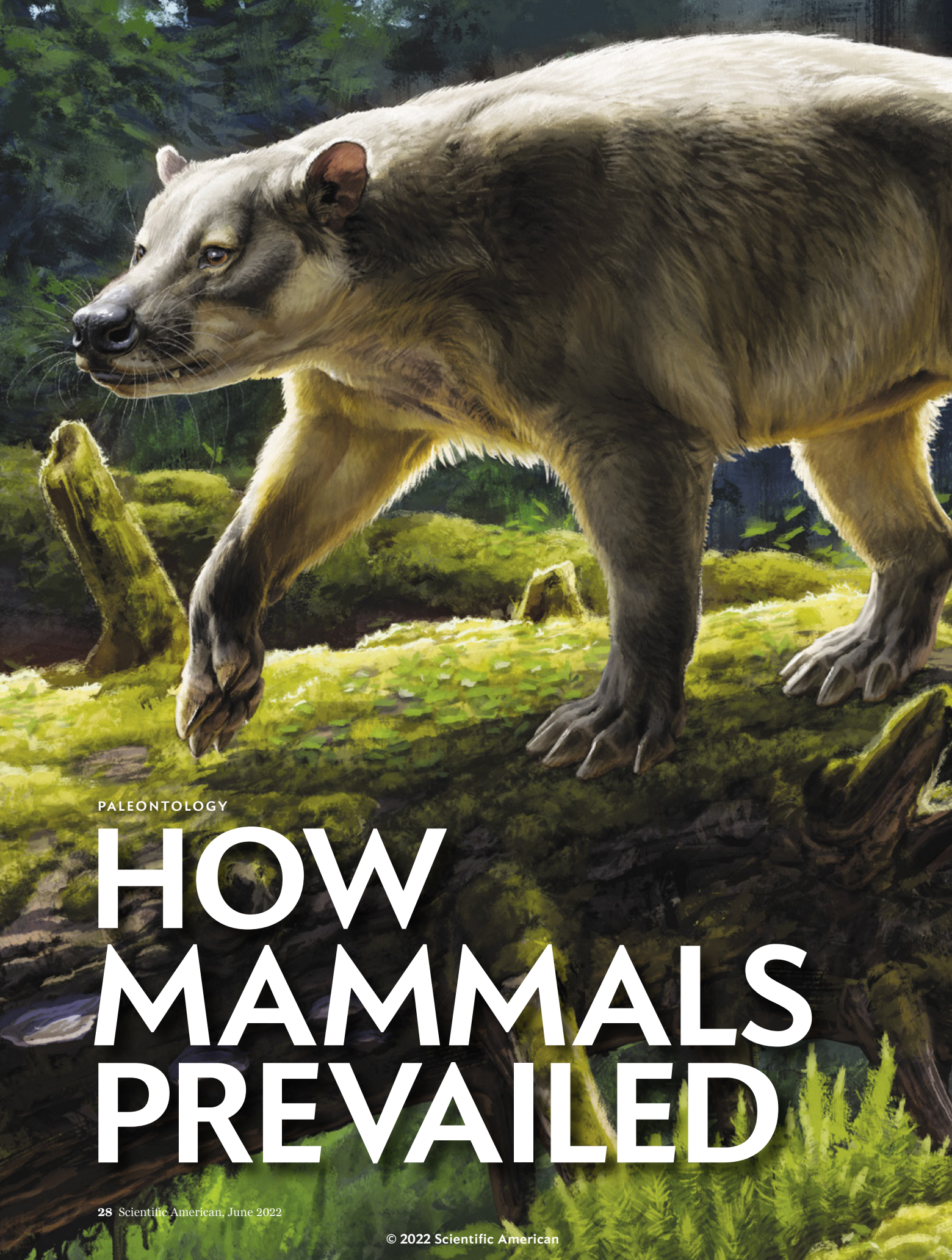
For now, strength-building exercise remains the best strategy for those of us with fraying joints. Conaghan recommends walking in a swimming pool. “Strong quads reduce knee pain a lot, no matter what you’ve got going on,” he says. “All of life is about strong muscles.” ■

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PALEONTOLOGY

HOW MAMMALS PREVAILED

An artistic illustration of a prehistoric forest scene. In the foreground, two small, furry mammals with dark stripes on their bodies are shown. One is on the left, looking towards the right with its mouth slightly open. The other is in the center, looking forward. To the left, the large, furry tail and hind leg of a much larger animal are visible. The background is filled with dense green foliage, including ferns and other plants, creating a lush, shaded environment. The lighting is dramatic, with strong highlights and deep shadows.

They scurried in the shadows of dinosaurs
for millions of years until a killer asteroid created
a new world of evolutionary opportunity

By Steve Brusatte

Illustration by Beth Zaiken

**EARLY PLACENTAL
MAMMAL** *Ectoconus*
gave birth to live, well-
developed young.

Steve Brusatte is a professor at the University of Edinburgh and author of *The Rise and Reign of the Mammals*, a new narrative history of mammal evolution (Mariner Books, 2022).



EVERY SPRING I BRING MY STUDENTS TO THE DESERT OF NORTHWESTERN NEW MEXICO, just north of Chaco Canyon, where the ancestral Pueblo people built a great city out of rocks a millennium ago. As we hike across the pastel-striped badlands, we can't help but tread on dinosaur bones. The ground is littered with busted *Tyrannosaurus rex* limbs and chunks of vertebrae that anchored the lofty necks of sauropods some 66.9 million years ago during the Cretaceous period. And then, suddenly, the bones disappear.

As we continue walking up through the rock layers, we begin to notice a new type of fossil. Jaws filled with teeth. Not the steak knives of *T. rex*, but teeth with complex cusps and valleys. They are the molars of mammals. On one trip, in 2014, I followed their trail into a dry creek bed sacred to the Navajo called Kimbeto—the “sparrowhawk spring.” From the other end of the wash, I heard a victory yelp. My colleague Tom Williamson had found a skeleton—one belonging to a big animal, weighing around 100 kilograms. We could tell from its pelvis that it gave birth to live, well-developed young. It was a placental mammal, like us.

This fossil mammal, *Ectoconus*, was a revolutionary. It lived a mere 380,000 years after the worst day in Earth history, when a six-mile-wide asteroid ended the Age of Dinosaurs in fire and fury, ushering in a new world. Textbooks often tell a simple tale: the dinosaurs died, but mammals survived and quickly took over. Yet this account has glossed over a troubling reality: we actually know very little about the mammals that endured the extinction and persevered during the next 10 million years, during the Paleocene epoch. How were they able to persist when 75 percent of species died, and how did they set the foundation for the more than 6,000 species of placental mammals that thrive today, from the aerial bats to the aquatic whales to humans?

Scientists have debated these questions since the 1870s, when the first fossils of Paleocene placental mammals emerged in New Mexico. Finally, over the past two decades, new discoveries and research techniques have unmasked these placental pioneers. They nearly went the way of the dinosaurs, but after barely surviving the brimstone, they rapidly inflated their bodies from rat-sized to cow-sized, diversified their diets and behaviors—and eventually expanded their brains—and rang in a new Age of Mammals.

TRIASSIC ORIGINS

REWIND BACK to the Triassic period. People often assume that mammals followed dinosaurs in the evolutionary past, but in fact, both groups trace their origins to the same time and place: around 225 million years ago, when all of Earth's land was gathered into the

supercontinent Pangea. At this time, the planet was recovering from the worst mass extinction in history, when mega volcanoes in Siberia spewed lava and carbon dioxide for millions of years, causing a global heat spike that killed up to 95 percent of all species. After the volcanoes shut off, dinosaurs, mammals, and many other new groups arose to fill the vacuum.

For the next 160 million years dinosaurs and mammals went their own separate ways, but both were successful. Dinosaurs became giants and excluded mammals from large-bodied niches. Mammals did the opposite: with their small body sizes, they could exploit ecological niches that the bigger dinosaurs couldn't access. Having attained a competitive edge in those habitats, they effectively prevented *T. rex*, *Triceratops* and kin from becoming small. Between 201 million and 66 million years ago, during the Jurassic and Cretaceous periods, a bounty of pint-sized mammals—none larger than a badger—lived underfoot of the dinosaurs. Among them were scurriers, climbers, diggers, swimmers and gliders. It was these animals that developed the classic mammalian blueprint: hair, warm-blooded metabolism, a complex lineup of teeth (canines, incisors, premolars, molars), and the ability to feed their babies milk.

These early mammals grew into a verdant family tree. There were dozens of subfamilies distinguished by different types of teeth, diets and reproductive styles. One such group—the multituberculates—flourished in the Cretaceous underworld, using their saw-blade premolars and gnawing incisors to devour a new type of food: fruits and flowers. Scores of their fossils came to light during the 1963–1971 Polish-Mongolian expeditions to the Gobi Desert, one of the first major female-led paleontological fieldwork projects, captained by one of my heroes, the late Polish paleobiologist Zofia Kielan-Jaworowska.

Meanwhile, as multituberculates prospered, three other groups quietly branched off on their own. These trailblazers gave rise to the three mammal lineages that persist today: the egg-laying monotremes; the marsupials, which give birth to feeble young that develop further in a pouch; and the placentals, like *Ectoconus* and us, which birth larger young. The molecular clock—a technique that



uses DNA differences among modern species and back calculates to estimate when they diverged—predicts that some placental lineages, including primates, lived alongside the dinosaurs. Although paleontologists are desperate to recover fossils of such early placentals, they have yet to be found.

Then one day 66 million years ago this primeval tableau—of dinosaurs thundering across the land and mammals scampering in the shadows—ended in chaos. An asteroid the size of Mount Everest was hurtling through the heavens, traveling faster than a jet airliner. By chance, it smashed into what is now the Yucatán Peninsula of Mexico, striking with the force of more than a billion nuclear bombs, and punched a hole in Earth's crust more than 10 miles (16 kilometers) deep and more than 100 miles (160 kilometers) wide. Tsunamis, wildfires, earthquakes and volcanic eruptions raged around the planet. Dust and soot clogged the atmosphere, turning the world dark for years. Plants couldn't photosynthesize, forests collapsed, herbivores died, carnivores followed. Ecosystems crumbled. It was the end of the Age of Dinosaurs.

A CLOSE CALL

THE ASTEROID WAS APOCALYPTIC, and it changed the course of Earth's history. Unable to cope, three out of every four species succumbed to extinction. Dinosaurs were the most famous victims: all the long-necked, horned, duck-billed, dome-headed and sharp-toothed ones died, with only a handful of birds carrying on the dinosaur legacy to the present day.

And what about mammals? In most tellings of the end-Cretaceous extinction, they are heralded as the great survivors, the winners who seized the crown from the dinosaurs. In a sense, this is true—mammals did persevere, or else we would not be here. But

ROCKS OF TORREON WASH in northwestern New Mexico contain fossils of mammals that lived in the Paleocene epoch.

new research shows that it was a close call, and their fate hinged on what happened in the days, decades and millennia after the asteroid impact. For mammals, the asteroid was both their moment of greatest peril and their big break.

The best record of those mammals that faced the asteroid and its aftermath comes from the northern Great Plains of the U.S. For nearly half a century William Clemens of the University of California, Berkeley, who passed away in 2020, explored the sagebrush-scented ranchlands of northeastern Montana. Sculpting these hills are rocks formed by rivers that drained the ancestral Rocky Mountains and flowed through forests, during a three-million-year stretch spanning the end of the Cretaceous, the fallout from the asteroid and the dawn of the Paleocene. Tens of thousands of fossils from these layers, studied statistically by Clemens's former student and current University of Washington paleontologist Gregory Wilson Mantilla, reveal what lived, what died and why.

Perhaps surprisingly, mammals were doing well in the latest Cretaceous. At least 30 species lived in Montana back then, filling many ecological roles at the base of the dinosaur-dominated food chain, including bone crunchers, flower eaters, insectivores and omnivores. The vast majority of these creatures were metatherians (early members of the marsupial line) or multituberculates. Early cousins of placentals called eutherians were present, though rare. This situation was stable throughout the final two million years of the Cretaceous. There was no sign of serious trouble.

Then everything changes. Looking at the sedimentary rocks that formed 66 million years ago, we see that a thin line appears, satu-

rated with iridium, an element that is rare on the surface of Earth but common in outer space. This is the chemical fingerprint of the asteroid. Dinosaurs—including *T. rex* and *Triceratops*—abruptly disappear. The Cretaceous has given way to the Paleocene.

The earliest Paleocene scene is dire. There is a fossil locality in Montana dated to approximately 25,000 years after the asteroid hit, called the Z-Line Quarry. It reeks of death. Almost all the mammals that flourished in the region in the Cretaceous are gone; only seven species remain. Several other fossil sites divulge what was happening over the next 100,000 to 200,000 years. If you pool together all mammals from this time, there are 23 species. Only one of these is a metatherian; these marsupial ancestors, once so abundant in the Cretaceous, were nearly extinguished. All told, if you consider the entire Montana fossil record, along with other data from across western North America, the statistics are grim. A paltry 7 percent of mammals survived the carnage. Imagine a game of asteroid roulette: a gun, with 10 chambers, nine of which hold a bullet. Even those odds of survival are slightly better than what our ancestors faced in the brave new world of the Paleocene.

This bleak state of affairs raises a question: What allowed some mammals to endure? The answer became apparent when Wilson Mantilla looked at the victims and survivors. The survivors were smaller than most of the Cretaceous mammals, and their teeth indicate they had generalist, omnivorous diets. The victims, on the other hand, were larger, with more specialized carnivorous or herbivorous diets. They were supremely adapted to the latest Cretaceous world, but when the asteroid unleashed disaster, their adaptations became hardships. The smaller generalists, in contrast, were better able to eat whatever was on offer in the postimpact chaos, and they could have more easily hunkered down to wait out the worst of the bedlam.

As ecosystems recovered in the earliest Paleocene, many of the mammals that started to multiply were eutherians, the placental antecedents that were once bit players in the Cretaceous. Their tiny bodies, flexible diets, and perhaps faster ways of growing and reproducing allowed them to commandeer open niches and start building new food webs. Around 100,000 years postasteroid a new eutherian appeared in Montana and swiftly became common. *Purgatorius*, with gentle molar cusps for eating fruits and highly mobile ankles for clinging and climbing in the trees, was an early member of the primate line. It, or perhaps another closely related eutherian, was our ancestor.

THE FIRST PLACENTALS

THESE PLUCKY SURVIVORS forged a new world—an Age of Mammals, in which placentals, more than all the others, became ascendant. Some of the best fossils of the first true placentals to form diverse Paleocene communities come from New Mexico, particularly Kimbeto. *Ectoconus*, whose skeleton we excavated in 2014, was one of these trailblazers. When it was bounding through swampy rain forests and snacking on leaves and beans 65.6 million years ago, it was the largest mammal that had ever lived there. It was one of dozens of new placentals in its environment, already turning dinosaurs into ancient history.

We have known about these Paleocene placentals for nearly 150 years. Their fossils were reported during surveys in the 1870s and 1880s, when geologists joined cartographers and soldiers to chart lands then recently seized from Native Americans. One such explorer, David Baldwin, found a cache of mammals at Kimbeto and

other sites of similar age, which were sandwiched between older fossils of Cretaceous dinosaurs and younger mammals from the Eocene epoch, which lasted from 56 million to 34 million years ago, that could readily be classified into familiar groups such as horses, monkeys and rodents. The Paleocene mammals were not so easily categorized, however. They were clearly much larger than any Cretaceous mammals, and they lacked epipubis bones at the front of their pelvis, suggesting they had large placentas to nourish their young in utero. Thus, they were assuredly placentals. But their skeletons seemed peculiar—stocky and muscle-bound, with mashups of features seen in various groups of modern-day mammals.

These Paleocene oddballs garnered a troublesome reputation, and scholars began to dismiss them as “archaic” placentals. What were their relationships with their Cretaceous forebears and modern-day mammals, and how did they move, eat and grow? These questions flummoxed paleontologists for generations. Enter Thomas Williamson, curator at the New Mexico Museum of Natural History and Science. For more than a quarter of a century, he has scoured the badlands, training his twin sons, Ryan and Taylor, and many local Navajo students to become ace fossil collectors. Over the last decade my students and I have joined Tom’s team.

Tom and his crew have collected thousands of fossils, which paint a vivid picture of Paleocene life within the first million years of the asteroid. Among the roster of archaic placentals are animals like *Ectoconus*, which are shoehorned into a nebulous group called condylarths. Members of this group were mainly plant eaters or omnivores with sturdy builds; many of them had hooves. They shared the herbivore niches with pantodonts—barrel-chested leaf gobblers with enormous hands and feet, which achieved sizes comparable to modern cows. Another group, the taeniodonts, were gargoyle-esque diggers, which used their huge clawed forearms to tear through dirt and their massive jaws and enlarged canines to root out tubers. All these mammals would have feared the triisodontids, the terrors of the Paleocene, which looked like wolves on steroids and smashed the bones of their prey with crushing molars.

Untangling the genealogical relationships of these archaic placentals is challenging. My research group is currently working with Williamson, Carnegie Museum of Natural History mammalogist John Wible and other colleagues on this Gordian knot of phylogeny. We are building a vast data set of fossil and extant mammals, and their anatomical and genetic features, so that we can construct a master family tree. Our preliminary results are encouraging. Some of the archaic species, such as taeniodonts, might have stemmed from Cretaceous eutherian ancestors and thus would be among the most primitive placentals on the trunk of the family tree. Others, including some of the condylarths, share features with today’s hoofed mammals and are probably proto-horses and proto-cattle. The archaic placentals, therefore, seem to be a diverse menagerie, some of which formed their own idiosyncratic subgroups and others the ancestral stock from which today’s placentals arose.

A HEAD START

ALTHOUGH THE PRECISE LOCATIONS of condylarths and taeniodonts and their archaic ilk in the family tree remain to be worked out, we are already grasping what they were like as living, breathing animals. Fossils collected by our team and studied using new technologies reveal how these placentals developed novel features and behaviors, helping them adapt to the early Paleocene mayhem and take advantage of open niches. Many placental trademarks evolved

The Rise of Mammals

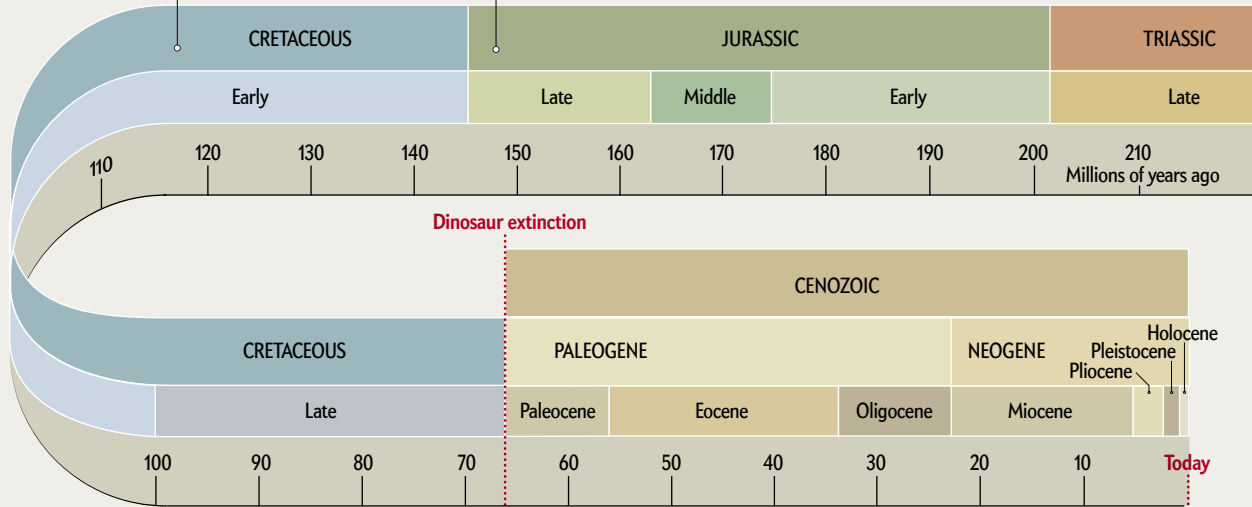
Mammals lived underfoot of the dinosaurs for tens of millions of years. It wasn't until after a six-mile-wide space rock crashed into what is now the Gulf of Mexico 66 million years ago, wiping out 75 percent of species—including the nonbird dinosaurs—

that the mammals began to take center stage. Recent findings reveal how they survived the mass extinction and went on to usher in the Age of Mammals, giving rise to a host of diverse species that inhabit sea, land and sky.

The ancestors of the egg-laying monotremes, pouched marsupials, and placentals, which birth large young, make their debut.

Mammals evolve an array of body types to exploit various ecological niches, but in contrast to dinosaurs, they remain small.

Mammals and dinosaurs both originate around 225 million years ago on the supercontinent of Pangea.



BODY SIZE

Small body size helped some mammals survive the asteroid impact that extinguished the dinosaurs. But in the aftermath, the forerunners of placentals began to increase their body size from rat-sized to cow-sized and larger.

Maximum Body Size (kilograms)

1 10 100 1,000 10,000



ECOLOGICAL DIVERSITY

Placentals evolved traits that allowed them to exploit the wide array of ecological niches open to them. Some had bodies and teeth specialized for climbing trees and eating fruit, for instance; others were purpose built for digging down underground and munching tubers.

Relative Diversity

Low ↔ High



SPECIES RICHNESS

As the Cretaceous period gave way to the Paleocene epoch, and ecosystems recovered from the devastation from the asteroid, the numbers of mammal species in local communities abruptly surged.

Relative Diversity

Low ↔ High

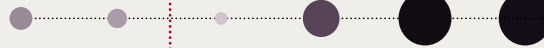


INTELLIGENCE/BRAIN SIZE

Of all the backboned animals, mammals have the largest brains relative to body size. Conventional wisdom holds that their brains grew steadily over time. But recent findings show that they did not become especially brainy until after they had attained big bodies.

Relative Size

Small ↔ Large



Computed tomography scans of fossil skulls reveal that brain size decreased in the earliest placentals and then later increased independently in several lineages through pronounced growth of brain regions involved in sensory function.



Sources: "The Evolution of Maximum Body Size of Terrestrial Mammals," by Felisa A. Smith et al., in *Science*, Vol. 330; November 26, 2010 (body size data); "Untangling the Multiple Ecological Radiations of Early Mammals," by David M. Grossnickle et al., in *Trends in Ecology and Evolution*, Vol. 34; October 2019 (ecological diversity data); "Diversity Dynamics of Phanerozoic Terrestrial Tetrapods at the Local-Community Scale," by Roger A. Close et al., in *Nature Ecology and Evolution*, Vol. 3; February 2019 (species diversity data); "Brain before Brains in Placental Mammals after the End-Cretaceous Extinction," by Ornella C. Bertrand et al., in *Science*, Vol. 376; March 31, 2022 (brain size data)



during this time—assets that helped to mold generalist extinction survivors into new and diverse specialists. These traits underpinned the success of placentals over the next 66 million years and are part of the foundation of our own human biology.

Chief among these hallmarks of placental mammals is the capacity to birth well-developed young, which gestate for a prolonged period inside the mother before being born in an advanced state. This arrangement differs markedly from how the other two types of extant mammals reproduce. Monotreme babies hatch from eggs, and marsupials are born so premature that they must shelter in their mother's pouch for months to complete development. Prolonged gestation allows some placentals to get a head start in life: babies can often start moving, socializing and even procuring their own food shortly after birth.

To figure out how Paleocene archaic placentals grew, Gregory Funston, a postdoctoral scholar working in my laboratory at the University of Edinburgh, cut a variety of their teeth, including the milk teeth of babies, into thin slices that he could examine under a microscope. By counting daily lines of growth and identifying chemically distinctive stress markers in the enamel caused by birth, he could tell that some of these mothers nurtured babies in their wombs for around seven months—more than twice as long as marsupials. This observation confirms the evidence from pelvic anatomy that these Paleocene species really were placentals. More important, this growth strategy unlocked a superpower. Larger off-

spring could more easily grow into larger adults, which may have enabled the first placentals to rapidly balloon in stature within a few hundred thousand years of the dinosaurs' demise, after 160 million years of being stuck at tiny sizes.

As the Paleocene placentals grew larger, they diversified in other ways. My former Ph.D. student and current postdoc Sarah Shelley, who has been a key member of our New Mexico field crews, studied the skeletons of archaic species in detail, paying particular attention to how the muscles attached. She performed a statistical analysis of a large data set of measurements, comparing the Paleocene species with their Cretaceous precursors and modern-day descendants. What she found was unexpected: the archaic placental skeletons were highly diverse, and their ankles were capable of many types of locomotion. Their skeletons were indeed stocky and generalized at quick glance, one reason they were long stereotyped as archaic. But their muscular frames were highly adaptable, and different species were able to burrow, trot and climb. These species could also acquire different types of food. Such intense diversification is indicative of what biologists call an adaptive radiation, which occurs when many new species rapidly proliferate from an ancestor, changing aspects of their appearance and behavior to take advantage of new environments or opportunities.

For all their specializations, however, the Paleocene archaic placentals were not especially intelligent. This was the surprising revelation of a study led by Ornella Bertrand, a postdoc in my lab, who

Thomas Williamson



AT KIMBETO WASH, also in northwestern New Mexico (left), field crews have recovered fossil jaw bones belonging to plant-eating *Ectoconus* (top right) and fearsome meat eaters known as triisodontids (bottom right).

is a wizard at using CT scans to digitally reconstruct the brains, ears and other neurosensory structures of extinct species. She scanned several skulls of archaic placentals from New Mexico, along with stunning new fossils recently discovered near Denver by Tyler Lyson and Ian Miller and their team. Compared with their minuscule Cretaceous predecessors, the Paleocene mammals did have larger brains in terms of absolute size. Yet as lab and field studies of modern mammals show, it is relative brain size—the ratio of brain volume to body mass—that truly matters. The relative brain sizes of the archaic placentals were laughably small compared with not only those of today's mammals but even those of the Cretaceous species living with the dinosaurs.

The first placentals, it seems, got so big so fast that their brains couldn't initially keep pace. This finding counters a long-standing convention that mammal brains got progressively larger over time, in both absolute and relative size. It also, perhaps, defies expectations: Shouldn't the mammals that founded the placental dynasty have used their wits to navigate the obstacle course of postasteroid survival? Apparently not. Growing bigger bodies was more important than growing bigger brains, at least at first, when there

were so many vacant niches to fill. In such a fickle world of abundant opportunity, large brains may have even been detrimental because of their higher energetic costs.

Eventually, as ecosystems stabilized and competition among the many new placentals increased, their brains expanded. Much of the growth was in the neocortex, a sublime region of the cerebrum involved in higher cognition and sensory integration. But this burgeoning would have to wait until the next time interval after the Paleocene: the Eocene, when the archaic placentals slowly declined and the modern placental groups—including horses, bats and whales—took over the planet.

THE MODERN WORLD

THE PALEOCENE was a greenhouse world; the New Mexican mammals frolicked in jungles, and crocodiles basked in the high-latitude sun. Then, about 56 million years ago, the greenhouse got even hotter. Magma began to pool under the northern continents and migrated upward as a plume. As it percolated through the crust, it baked the rocks of the deep Earth. Like an engine burning gasoline, this activity released carbon dioxide—trillions of tons of it, which warmed the atmosphere between five and eight degrees Celsius within, at most, 200,000 years. Earth has not been hotter since.

This sudden global warming event, called the Paleocene-Eocene Thermal Maximum, was yet another hurdle that mammals had to overcome. But this time, unlike the asteroid 10 million years earlier, very few mammal species were extinguished. Instead they went on the move, following new high-latitude migration corridors that opened as temperatures warmed. Some of the migrants boasted new adaptations, notably much larger brains. They debuted other new traits, too: primates evolved nails on their fingers and toes to grip branches, even-toed artiodactyls developed pulley-shaped ankles that facilitated fast running, and odd-toed perissodactyls acquired big hooves that made them champion gallopers. These more modern-style mammals swarmed across the interlinked continents of North America, Europe and Asia, and their mass migration overwhelmed the archaic placentals. Condylarths, taeniodonts, pantodonts and triisodontids would survive only a little longer.

South of the equator, where Cretaceous and Paleocene mammal fossils are much rarer, the story was different. Both Africa and South America were island continents, which incubated their own unusual placentals in isolation: elephants and kin in Africa; sloths and armadillos in South America. It was also down south where the other two mammal lines managed to hold on. Monotremes, such as the platypus and echidna, took refuge in Australia and New Guinea, where a scant five species remain today. Marsupials were wiped out on the northern continents but won a reprieve by immigrating to South America and then hopping across Antarctica to Australia, where they diversified into kangaroos and koalas. (One group later returned to North America as immigrants: opossums.)

But the future mostly belonged to the placentals. Before long, as the warming spike abated, some were swinging from trees, others flapping their wings, and others trading arms for flippers and supersizing their bodies into marine behemoths. From here today's rich tapestry of placentals—including us—can trace our heritage. ■

FROM OUR ARCHIVES

Ascent of the Mammals, Stephen Brusatte and Zhe-Xi Luo; June 2016.

scientificamerican.com/magazine/sa



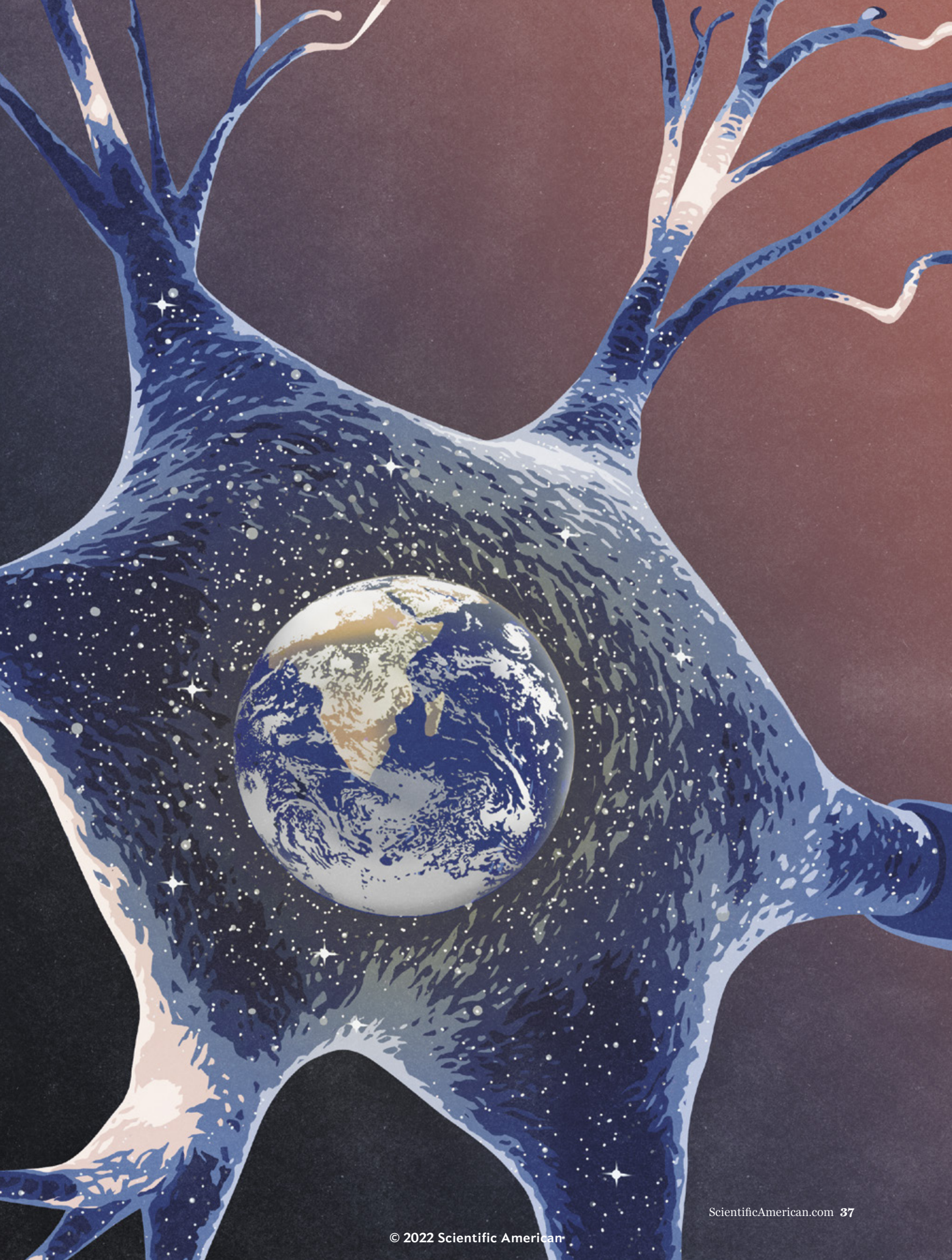
NEUROSCIENCE

Constructing the World from Inside Out

The brain probes
your physical
surroundings
to select just
the information
needed to survive
and flourish

By György Buzsáki

Illustration by Islenia Milien



György Buzsáki is a systems neuroscientist whose work has focused on the ways memories form and how brain rhythms segment neural information to support cognition. He was a co-recipient of the 2011 Brain Prize from the Lundbeck Foundation. Buzsáki is author most recently of *The Brain from Inside Out* (Oxford University Press, 2019).



AS A YOUNG COURSE INSTRUCTOR IN SEMINARS FOR medical students, I faithfully taught neurophysiology by the book, enthusiastically explaining how the brain perceives the world and controls the body. Sensory stimuli from the eyes, ears, and such are converted to electrical signals and then transmitted to the relevant parts of the sensory cortex that process these inputs and induce perception. To initiate a movement, impulses from the motor cortex instruct the spinal cord neurons to produce muscular contraction.

Most students were happy with my textbook explanations of the brain's input-output mechanisms. Yet a minority—the clever ones—always asked a series of awkward questions. “Where in the brain does perception occur?” “What initiates a finger movement before cells in the motor cortex fire?” I would always dispatch their queries with a simple answer: “That all happens in the neocortex.” Then I would skillfully change the subject or use a few obscure Latin terms that my students did not really understand but that seemed scientific enough so that my authoritative-sounding accounts temporarily satisfied them.

Like other young researchers, I began my investigation of the brain without worrying much whether this perception-action theoretical framework was right or wrong. I was happy for many years with my own progress and the spectacular discoveries that gradually evolved into what became known in the 1960s as the field of “neuroscience.” Yet my inability to give satisfactory answers to the legitimate questions of my smartest students has haunted me ever since. I had to wrestle with the difficulty of trying to explain something that I didn't really understand.

Over the years I realized that this frustration was not uniquely my own. Many of my colleagues, whether they admitted it or not, felt the same way. There was a bright side, though, because these frustrations energized my career. They nudged me over the years to develop a perspective that provides an alternative description of how the brain interacts with the outside world.

The challenge for me and other neuroscientists involves the weighty question of what, exactly, is the mind. Ever since the time of Aristotle, thinkers have assumed that the soul or the mind is initially a blank slate, a *tabula rasa* on which experiences are painted. This view has influenced thinking in Christian and Persian philosophies, British empiricism and Marxist doctrine. In the past century it has also permeated psychology and cognitive science. This “outside-in” view portrays the mind as a tool for learning about the true nature of the world. The alternative view—one that has defined my research—asserts that the primary preoccupation of brain networks is to maintain their own internal dynamics and perpetually generate myriad nonsensical patterns of neural activity. When a seemingly random action offers a benefit to the organism's survival, the neuronal pattern leading to that action gains meaning. When an infant utters “te-te,” the parent happily offers the baby “Teddy,” so the sound “te-te” acquires the meaning of the Teddy bear. Recent progress in neuroscience has lent support to this framework.

DOES THE BRAIN “REPRESENT” THE WORLD?

NEUROSCIENCE INHERITED the blank slate framework millennia after early thinkers gave names like *tabula rasa* to mental operations. Even today we still search for neural mechanisms that might relate to their dreamed-up ideas. The dominance of the outside-in framework is illustrated by the outstanding discoveries of the legendary scientific duo David Hubel and Torsten Wiesel, who

introduced single-neuronal recordings to study the visual system and were awarded the Nobel Prize in Physiology or Medicine in 1981. In their signature experiments, they recorded neural activity in animals while showing them images of various shapes. Moving lines, edges, light or dark areas, and other physical qualities elicited firing in different sets of neurons. The assumption was that neuronal computation starts with simple patterns that are synthesized into more complex ones. These features are then bound together somewhere in the brain to represent an object. No active participation is needed. The brain automatically performs this exercise.

The outside-in framework presumes that the brain's fundamental function is to perceive "signals" from the world and correctly interpret them. But if this assumption is true, an additional operation is needed to respond to these signals. Wedged between perceptual inputs and outputs resides a hypothetical central processor—which takes in sensory representations from the environment and makes decisions about what to do with them to perform the correct action.

So what exactly is the central processor in this outside-in paradigm? This poorly understood and speculative entity goes by various names—free will, homunculus, decision maker, executive function, intervening variables or simply just a "black box." It all depends on the experimenter's philosophical inclination and whether the mental operation in question is applied to the human brain, brains of other animals or computer models. Yet all these concepts refer to the same thing.

An implicit practical implication of the outside-in framework is that the next frontier for progress in contemporary neuroscience should be to find where the putative central processor resides in the brain and systematically elaborate the neuronal mechanisms of decision-making. Indeed, the physiology of decision-making has become one of the most popular focuses in contemporary neuroscience. Higher-order brain regions, such as the prefrontal cortex, have been postulated as the place where "all things come together" and "all outputs are initiated." When we look more closely, however, the outside-in framework does not hold together.

This approach cannot explain how photons falling on the retina are transformed into a recollection of a summer outing. The outside-in framework requires the artificial insertion of a human experimenter who observes this event [see box at right]. The experimenter-in-the-middle is needed because even if neurons change their firing patterns when receptors on sensory organs are stimulated—by light or sound, for instance—these changes do not intrinsically "represent" anything that can be absorbed and integrated by the brain. The neurons in the visual cortex that respond to the image of, say, a rose have no clue. They do not "see" the appearance of a flower. They simply generate electrical oscillations in response to inputs from other parts of the brain, including those arriving along multiple complex pathways from the retina.

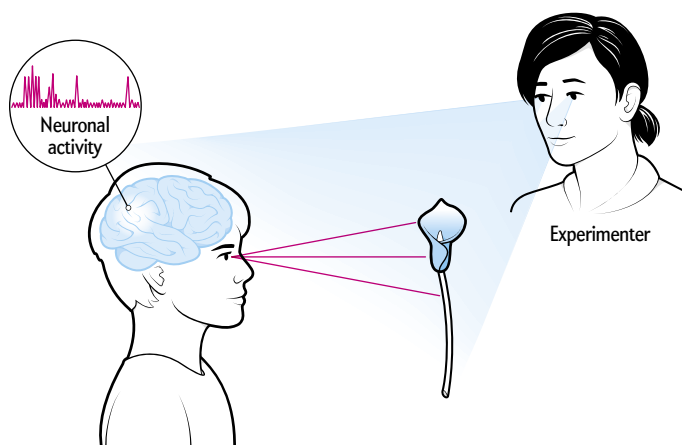
In other words, neurons in sensory cortical areas and

Outside In vs. Inside Out

The idea of the brain as a blank slate onto which experience is written has existed since ancient times—and persists today in modified form. Some neuroscientists have begun to question this theory because it requires a hard-to-justify assumption about the way we perceive and process events from the outside world—in particular, the need to involve a hypothetical "interpreter" to explain what is happening.

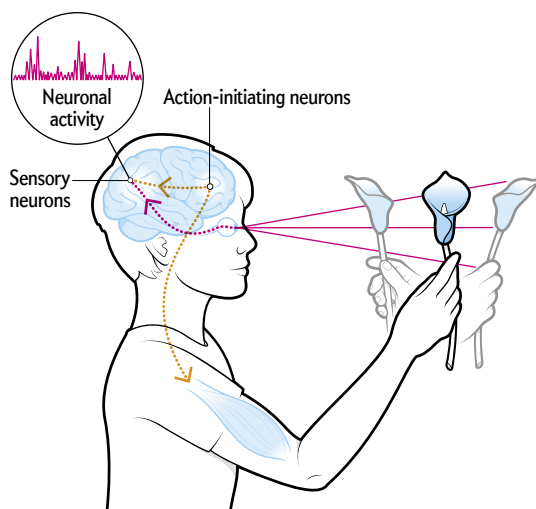
Outside-In Framework

A stimulus—the image of a flower—reaches the eyes, and the brain responds by causing neurons to fire. This theory is plausible only with the involvement of an "experimenter" to observe and establish a relation between the flower and the neuronal responses it induces. Absent the experimenter, neurons in the sensory cortex do not "see" the flower.



Inside-Out Framework

The alternative, inside-out theory does away with the experimenter. It presumes instead that we come to understand the external world by taking actions—moving a flower, for instance—to learn about an object. To accomplish this task, inputs from action-initiating neurons combine with sensory inputs to provide an understanding of the object's size, shape and other attributes. A meaningful picture arises, allowing the neurons to "see" the flower.



even in the hypothetical central processor cannot “see” events that happen in the world. There is no interpreter in the brain to assign meaning to these changes in neuronal firing patterns. Short of a magical homunculus watching the activities of all the neurons in the brain with the omniscience of the experimenter, the neurons that take this all in are unaware of the events that caused these changes in their firing patterns. Fluctuations in neuronal activity are meaningful only for the scientist who is in the privileged position of observing both events in the brain and events in the outside world and then comparing the two perspectives.

PERCEPTION IS WHAT WE DO

BECAUSE NEURONS HAVE NO direct access to the outside world, they need a way to compare or “ground” their firing patterns to something else. The term “grounding” refers to the ability of the brain’s circuits to assign meaning to changes in neuronal firing patterns that result from sensory inputs. They accomplish this task by relating this activity to something else. The “dah-dah-dit” Morse code pattern becomes meaningful only when it has previously been linked to the letter “G.” In the brain, the only available source of a second opinion appears when we initiate some action.

We learn that sticks that look bent in water are not broken by moving them. Similarly, the distance between two trees and two mountain peaks may appear identical, but by moving around and shifting our perspective we learn the difference.

The outside-in framework follows a chain of events from perception to decision to action. In this model, neurons in dedicated sensory areas are “driven” by environmental signals and thus cannot relate their activity to something else. But the brain is not a serial processing unit; it does not proceed one by one through each of these steps. Instead any action a person takes involves the brain’s motor areas informing the rest of the cerebral cortex about the action initiated—a message known as a corollary discharge.

Neuronal circuits that initiate an action dedicate themselves to two tasks. The first is to send a command to the muscles that control the eyes and other bodily sensors (the fingers and tongue, among others). These circuits orient bodily sensors in the optimal direction for in-depth investigation of the source of an input and enhance the brain’s ability to identify the nature and location of initially ambiguous incoming signals from the senses.

The second task of these same action circuits involves sending notifications—the corollary discharges—to sensory and higher-order brain areas. Think of them as registered mail receipts. Neurons that initiate eye movement also notify visual sensory areas of the cortex about what is happening and disambiguate whether, say, a flower is moving in the wind or being handled by the person observing it.

This corollary message provides the second opinion sensory circuits need for grounding—a confirma-

tion that “my own action is the agent of change.” Similar corollary messages are sent to the rest of the brain when a person takes actions to investigate the flower and its relationship to oneself and other objects. Without such exploration, stimuli from the flower alone—the photons arriving on the retina connected to an inexperienced brain—would never become signals that furnish a meaningful description of the flower’s size and shape. Perception then can be defined as what we *do*—not what we passively take in through our senses.

You can demonstrate a simple version of the corollary discharge mechanism. Cover one of your eyes with one hand and move the other eye gently from the side with the tip of your finger at about three times per second while reading this text. You will see immediately that the page is moving back and forth. By comparison, when you are reading or looking around the room, nothing seems to move. This constancy occurs because neurons that initiate eye movements to scan sentences also send a corollary signal to the visual system to indicate whether the world or the eyeball is moving, thus stabilizing the perception of your surroundings.

LEARNING BY MATCHING

THE CONTRAST BETWEEN outside-in and inside-out approaches becomes most striking when used to explain the mechanisms of learning. A tacit assumption of the blank slate model is that the complexity of the brain grows with the amount of experience. As we learn, the interactions of brain circuits should become increasingly more elaborate. In the inside-out framework, however, experience is not the main source of the brain’s complexity.

Instead the brain organizes itself into a vast repertoire of preformed patterns of firing known as neuronal trajectories. This self-organized brain model can be likened to a dictionary filled initially with nonsensical words. New experience does not change the way these networks function—their overall activity level, for instance. Learning takes place, rather, through a process of matching the preexisting neuronal trajectories to events in the world.

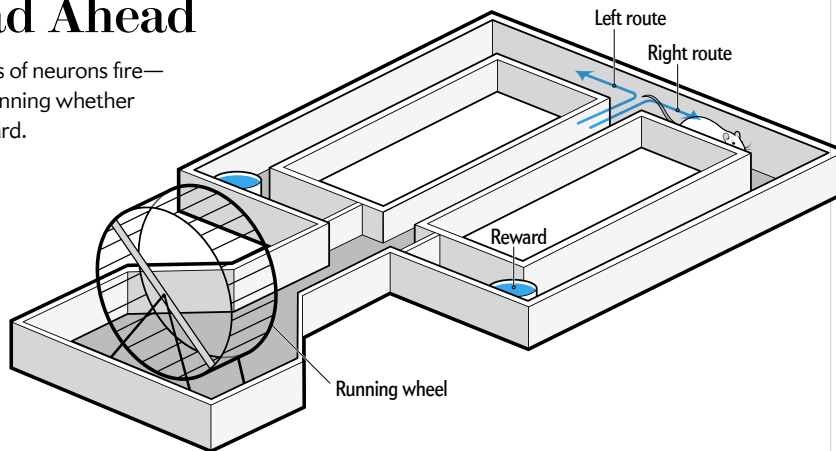
To understand the matching process, we need to examine the advantages and constraints brain dynamics impose on experience. In its basic version, models of blank slate neuronal networks assume a collection of largely similar, randomly connected neurons. The presumption is that brain circuits are highly plastic and that any arbitrary input can alter the activity of neuronal circuits. We can see the fallacy of this approach by considering an example from the field of artificial intelligence. Classical AI research—particularly the branch known as connectionism, the basis for artificial neural networks—adheres to the outside-in, tabula rasa model. This prevailing view was perhaps most explicitly promoted in the 20th century by Alan Turing, the great pioneer of mind modeling: “Presumably the child brain is something like a notebook as one buys it from the stationer’s,” he wrote.

Imagining the Road Ahead

An experiment demonstrates that distinct sets of neurons fire—each set in a different order—when a rat is planning whether to take the left or right route to receive a reward.

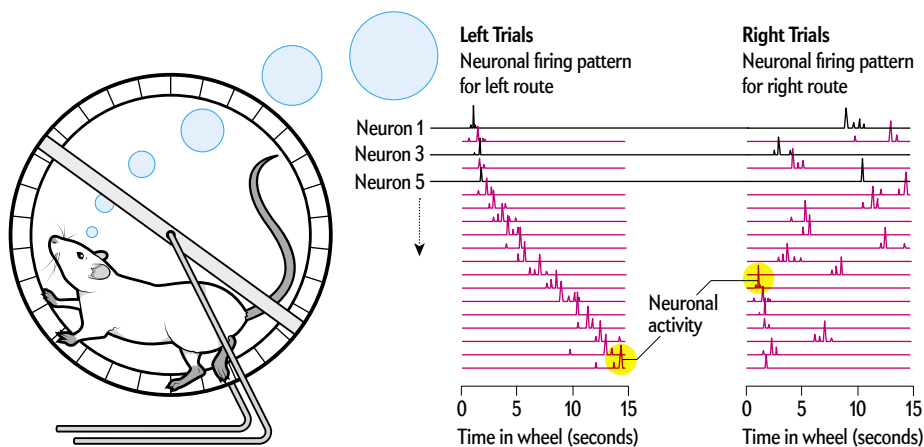
Experimental Setup

A running wheel is located at the entrance to a maze with two route options, both of which lead to a reward. The rat is free to choose a path through the maze after a 15-second run on the wheel. Neuronal firing patterns are recorded during both maze and wheel activity.



Results

Neuronal activity while the rat was running in the wheel predicted the direction it would take in the maze many seconds later, as if the animal were imagining the path to come. The “left trials” panel represents a sequence of neuronal firing that differs from the one for the right trials. When the “left” pattern occurred while the rat was in the wheel, it took the left route in the maze moments later.



Artificial neural networks built to “write” inputs onto a neural circuit often fail because each new input inevitably modifies the circuit’s connections and dynamics. The circuit is said to exhibit plasticity. But there is a pitfall. While constantly adjusting the connections in its networks when learning, the AI system, at an unpredictable point, can erase all stored memories—a bug known as catastrophic interference, an event a real brain never experiences.

The inside-out model, in contrast, suggests that self-organized brain networks should resist such perturbations. Yet they should also exhibit plasticity selectively when needed. The way the brain strikes this balance relates to vast differences in the connection strength of different groups of neurons. Connections among neurons exist on a continuum. Most neurons are only weakly connected to others, whereas a smaller subset retains robust links. The strongly connected minority is always on the alert. It fires rapidly, shares information readily within its own group, and stubbornly resists any modifications to the neurons’ circuitry. Because of the multitude of connections and their high communication speeds, these elite subnetworks, some-

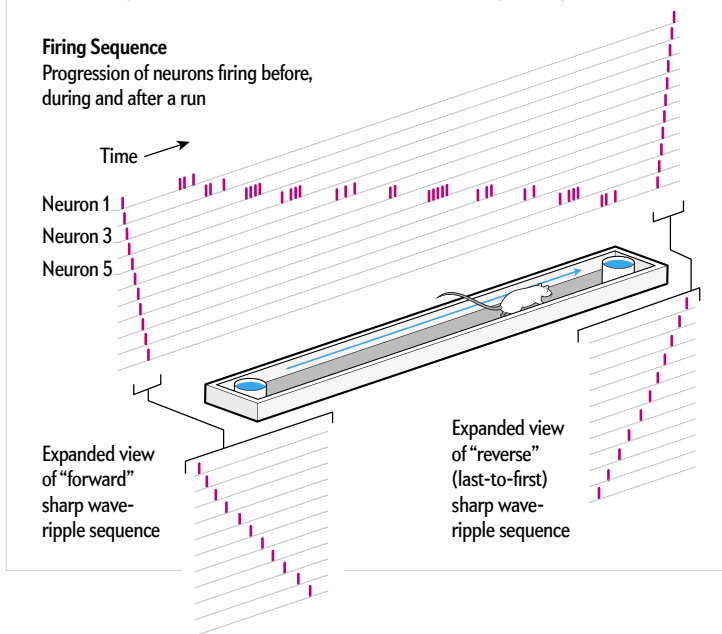
times described as a “rich club,” remain well informed about neuronal events throughout the brain.

The hard-working rich club makes up roughly 20 percent of the overall population of neurons, but it is in charge of nearly half of the brain’s activity. In contrast to the rich club, most of the brain’s neurons—the neural “poor club”—tend to fire slowly and are weakly connected to other neurons. But they are also highly plastic and able to physically alter the connection points between neurons, known as synapses.

Both rich and poor clubs are important for maintaining brain dynamics. Members of the ever ready rich club fire similarly in response to diverse experiences. They offer fast, good-enough solutions under most conditions. We can make good guesses about the unknown not because we remember it but because our brains always make a surmise about a new, unfamiliar event. Nothing is completely novel to the brain because it always relates the new to the old. It generalizes. Even an inexperienced brain has a vast reservoir of neuronal trajectories at the ready, offering opportunities to match events in the world to preexisting brain patterns without requiring substantial reconfiguring of connections. A brain that

Rehearsal and Playback

A group of neurons fire before, during and after a rat runs a lap on an elevated track. Neurons firing rapidly at the beginning and end of the run (*insets*) are the same ones active during the run, constituting either a rehearsal or a playback (the latter in reverse) of the rat's trajectory. These early and late events are known as sharp wave ripples and enable a mental process that selects and remembers an optimal path.



remakes itself constantly would be unable to adapt quickly to fast-changing events in the outside world.

But there also is a critical role for the plastic, slow-firing-rate neurons. These neurons come into play when something of importance to the organism is detected and needs to be recorded for future reference. They then go on to mobilize their vast reserve to capture subtle differences between one thing and another by changing the strength of some connections to other neurons. Children learn the meaning of the word "dog" after seeing various kinds of canines. When a youngster sees a sheep for the first time, they may say "dog." Only when the distinction matters—understanding the difference between a pet and livestock—will they learn to differentiate.

COGNITION AS INTERNALIZED ACTION

AS AN EXPERIMENTER, I did not set out to build a theory in opposition to the outside-in framework. Only decades after I started my work studying the self-organization of brain circuits and the rhythmic firing of neuronal populations in the hippocampus did I realize that the brain is more occupied with itself than with what is happening around it. This realization led to a whole new research agenda for my lab. Our experiments, along with findings from other groups, revealed that neurons devote most of their activity to sustaining the brain's perpetually varying internal states

rather than being controlled by stimuli impinging on our senses.

During the course of natural selection, organisms adapt to the ecological niches in which they live and learn to predict the likely outcomes of their actions in those niches. As brain complexity increases, more intricate connections and neuronal computations insert themselves between motor outputs and sensory inputs. This investment enables the prediction of planned actions in more complex and changing environments and at lengthy time scales far in the future. More sophisticated brains also organize themselves to allow computations to continue when sensory inputs vanish temporarily and an animal's actions come to a halt. When you close your eyes, you still know where you are because a great deal of what defines "seeing" is rooted in brain activity itself. This disengaged mode of neuronal activity provides access to an internalized virtual world of vicarious or imagined experience and serves as a gateway to a variety of cognitive processes.

Let me offer an example of such a disengaged mode of brain operation from our work on the brain's temporal lobe, an area that includes the hippocampus, the nearby entorhinal cortex and related structures involved with multiple aspects of navigation (the tracking of direction, speed, distance traveled, environmental boundaries, and so on).

Our research builds on leading theories of the functions of the hippocampal system, such as the spectacular Nobel-winning discovery of John O'Keefe of University College London. O'Keefe found that firing of hippocampal neurons during navigation coincides with the spatial location of an animal. For that reason, these neurons are known as place cells.

When a rat walks through a maze, distinct assemblies of place cells become active in a sequential chain corresponding to where it is on its journey. From that observation, one can tentatively conclude that continually changing sensory inputs from the environment exercise control over the firing of neurons, in line with the outside-in model.

Yet other experiments, including in humans, show that these same networks are used for our internal worlds that keep track of personal memories, engage in planning and imagine future actions. If cognition is approached from an inside-out perspective, it becomes clear that navigation through either a physical space or a landscape that exists only in the imagination is processed by identical neural mechanisms.

Fifteen years ago my lab set about to explore the mechanisms of spatial navigation and memory in the hippocampus to contrast the outside-in and inside-out frameworks. In 2008 Eva Pastalkova, a postdoctoral fellow, and I trained rats to alternate between the left and right arms of a maze to find water. At the beginning of each traversal of the maze, the rat was required to run in a wheel for 15 seconds, which helped to ensure that memory alone of the maze routes, and not environmental and body-derived cues, allowed it to choose a par-

ticular arm of the maze. We reasoned that if hippocampal neurons “represent” places in the maze corridors and the wheel, as predicted by O’Keefe’s spatial navigation theory, a few neurons should fire continuously at each spot whether the rat is in the corridors or the wheel. In contrast, if the neurons’ firing is generated by internal brain mechanisms that can support both navigation and memory, the duration of neuronal firing should be similar at all locations, including inside the wheel.

The findings of these experiments defied outside-in explanations. Not a single neuron among the hundreds recorded fired continuously throughout the wheel running. Instead many neurons fired transiently one after the other in a continuous sequence.

Obviously these neurons could not be called place cells, because the animal’s body was not displaced while at the single location of the running wheel. Moreover, the firing patterns of individual neurons in this neuronal trajectory could not be distinguished from neurons active when the rat was traversing the arms of the maze.

When we sorted individual trials according to the rat’s future choice of left or right arms, the neuronal trajectories were uniquely different. The distinct trajectories eliminated the possibility that these neuronal sequences arose from counting steps, estimating muscular effort or some other undetected feedback stimuli from the body. Also, the unique neuronal trajectories allowed us to predict the animal’s maze arm choice from the moment it entered the wheel and throughout wheel running, a period in which the rat had to keep in mind the previously visited arm. The animals needed to correctly choose the alternate maze arm each time to get their rewards [*see box on page 41*].

These experiments lead us to the idea that the neuronal algorithms that we can use to walk to the supermarket govern internalized mental travel. Disengaged navigation takes us through the series of events that make up personal recollections, known as episodic memories.

In truth, episodic memories are more than recollections of past events. They also let us look ahead to plan for the future. They function as a kind of “search engine” that allows us to probe both past and future. This realization also presages a broadening in nomenclature. These experiments show that progressions of place cell activity are internally generated as preconfigured sequences selected for each maze corridor. Same mechanism, multiple designations—so they can be termed place cells, memory cells or planning cells, depending on the circumstance.

Further support for the importance of disengaged circuit operations comes from “offline” brain activity when an animal is milling around doing nothing, consuming a reward or just sleeping. As a rat rests in the home cage after a maze exploration, its hippocampus generates brief, self-organized neuronal trajectories. These sharp wave ripples, as they are known, occur in

100-millisecond time windows and reactivate the same neurons that were firing during several seconds of maze running, recapitulating the neuronal sequences that occurred during maze traversals. Sharp wave-ripple sequences help to form our long-term memories and are essential to normal brain functioning. In fact, alteration of sharp wave-ripple events by experimental manipulations or disease results in serious memory impairment [*see box on opposite page*].

Clever experiments performed in human subjects and in animals over the past decade show that the time-compressed ripple events constitute an internalized trial-and-error process that subconsciously creates real or fictive alternatives for making decisions about an optimal strategy, constructing novel inferences and planning ahead for future actions without having to immediately test them by undertaking a real exploit. In this sense, our thoughts and plans are deferred actions, and disengaged brain activity is an active, essential brain operation. In contrast, the outside-in theory does not make any attempt to assign a role to the disengaged brain when it is at rest or even in the midst of sleep.

THE MEANING OF INSIDE OUT

IN ADDITION TO its theoretical implications, the inside-out approach has a number of practical applications. It may help in the search to find better diagnostic tools for brain disease. Current terminology often fails to describe accurately underlying biological mechanisms of mental and neurological illnesses. Psychiatrists are aware of the problem but have been hindered by limited understanding of pathological mechanisms and their relation to symptoms and drug responses.

The inside-out theory should also be considered as an alternative to some of the most prevalent connectionist models for conducting AI research. A substitute for them might build models that maintain their own self-organized activity and that learn by “matching” rather than by continual adjustments to their circuitry. Machines constructed this way could disengage their operations from the inputs of electronic sensors and create novel forms of computation that resemble internal cognitive processes.

In real brains, neural processes that operate through disengagement from the senses go hand in hand with mechanisms that promote interactions with the surrounding world. All brains, simple or complex, use the same basic principles. Disengaged neural activity, calibrated simultaneously by outside experience, is the essence of cognition. I wish I had had this knowledge when my smart medical students asked their legitimate questions that I brushed off too quickly. ■

FROM OUR ARCHIVES

Where Am I? Where Am I Going? May-Britt Moser and Edvard I. Moser; January 2016.

scientificamerican.com/magazine/sa

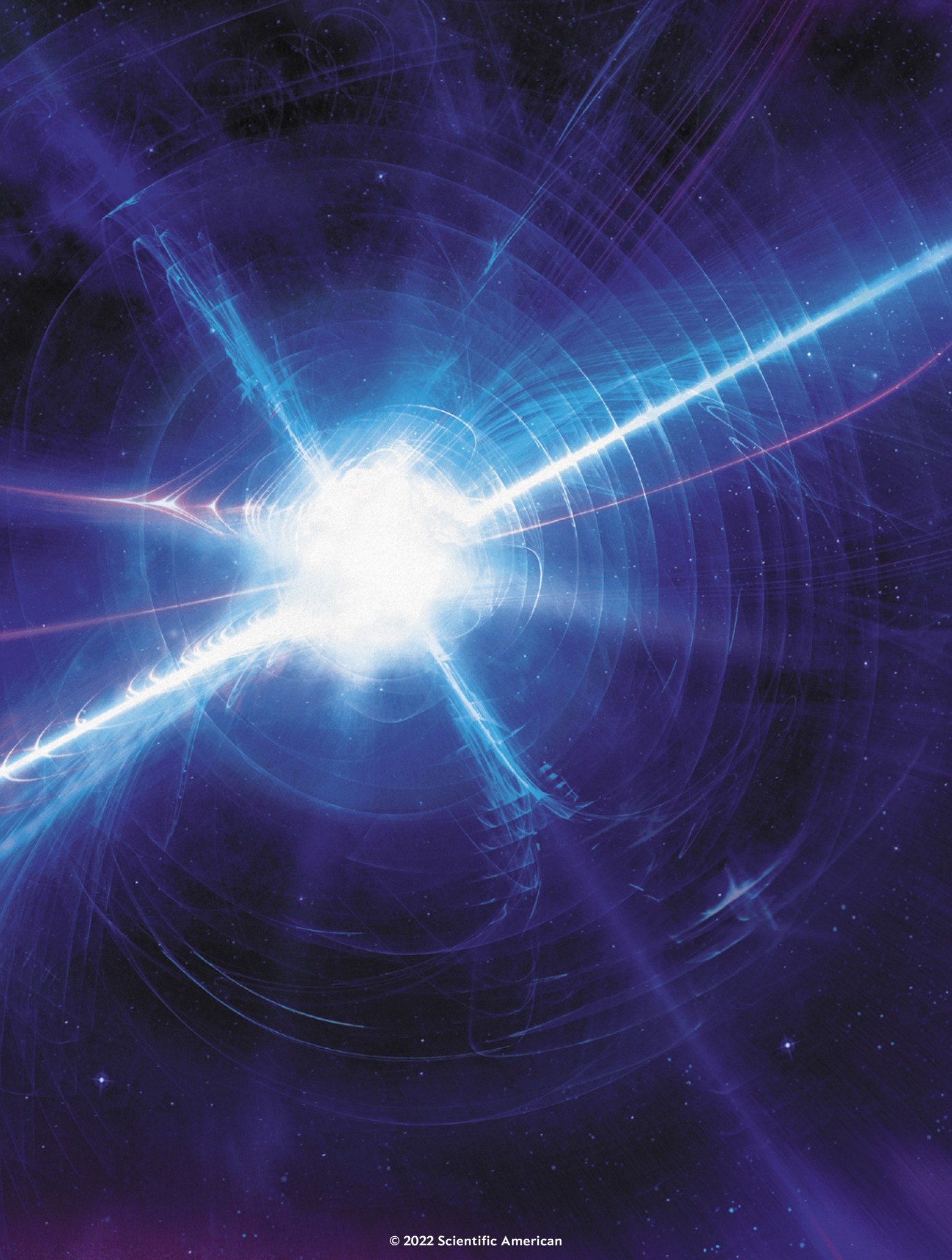
ASTRONOMY

Mysterious Cosmic Detonations

Twenty years after their discovery,
fast radio bursts are coming into focus

By Adam Mann

Illustration by Mark Ross



Adam Mann is a journalist specializing in astronomy and physics. His work has appeared in *National Geographic*, the *Wall Street Journal*, *Wired*, and elsewhere.



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NOBODY NOTICED WHEN AN AUSTRALIAN RADIO TELESCOPE CAPTURED a fleeting explosion coming from far beyond the Milky Way in 2001. Records of the powerful flare sat unseen for more than half a decade until a group of scientists sifting through archival data spotted the eruption—a so-called fast radio burst (FRB). According to one of those scientists, astrophysicist Duncan Lorimer of West Virginia University, the burst produced as much energy in a few thousandths of a second as the sun does in a month.

Today researchers know that these explosions happen at least 800 times a day all over the sky, and they are one of the most active topics in astrophysics. Although much about FRBs remains unknown, in just the past year a clearer picture has started to emerge. “I think we’re closer to understanding what some FRBs are,” says Ziggy Pleunis, an astrophysicist at the University of Toronto. “But as we’ve been going on this quest, new discoveries have led to new questions.”

The study of FRBs is now at an inflection point. A torrent of new detections and deeper studies have elevated certain models of their inner workings while eliminating others, and several upcoming projects should help further narrow the possibilities. Meanwhile scientists have learned that the bright light of an FRB carries within it a record of the contents of the intergalactic depths it traversed along its way to Earth, providing information about galaxies and the material between them that no other mechanism can.

MAGNETIC MOMENTS

IN APRIL 2020 THREE SEPARATE research teams detected an enormous blast of radio energy coming from a magnetar located in the Milky Way. Magnetars are an extreme kind of neutron star, a city-sized remnant left behind when a massive star dies in a supernova. A magnetar’s magnetic field can be so strong that approaching within 1,000 kilometers of one would disrupt your body’s atomic nuclei and electrons, causing you to effectively dissolve.

Magnetars were already a leading candidate for the source of FRBs. But the few dozen known magnetars in our galaxy had never been observed to produce eruptions that might resemble the phenomena. The discovery of a short and formidable radio burst from a galactic magnetar called SGR 1935+2154 was exactly

what researchers had been missing. If the same burst had come from another galaxy, its signature would have been indistinguishable from a typical FRB. “That was a huge moment for the field,” says Kenzie Nimmo, an astronomer at the University of Amsterdam. “It alleviated all doubt that at least some FRBs come from magnetars.”

How, exactly, a magnetar can produce an FRB is still the subject of debate. Most theories involve some kind of jarring starquake or an explosion caused when a magnetar’s twisting magnetic field lines snap and reconnect. Events such as these could directly generate an FRB’s flash, or they might make a shock wave that heats up surrounding material, incinerating dust and turning gas into plasma to produce light as it travels outward.

Several telescopes saw an x-ray flash arriving just after SGR 1935+2154’s radio signal, suggesting that whatever released the radio energy also generated more complicated side effects. Many details are still unclear. “Did this happen on the surface of the star, or in the magnetosphere, or in the material around the magnetar?” asks Emily Petroff, an astrophysicist also at the University of Amsterdam. “We still don’t really agree on that.”

COSMIC CURIOSITIES

BECAUSE FRBS CAN VARY in brightness, duration and other properties, it is unlikely that any single observation can explain them all. In the summer of 2021 the Canadian Hydrogen Intensity Mapping Experiment (CHIME), a dedicated FRB-hunting telescope in British Columbia, released a catalog of 536 FRBs that it had detected during the first year of its operation, quadrupling the number known. The bursts were already known to come in two distinct flavors—those that repeatedly flash their signals and those that are one-off events. CHIME’s data showed that nonrepeaters

were far more common than repeaters and that each had different characteristics.

On average, the bursts from repeaters lasted longer than their one-off counterparts and emitted their light in a narrower range of frequencies. Whether the disparity represents a different mechanism for these flashes or something else about their progenitors' ages or environments remains to be seen. The situation resembles an earlier mystery surrounding another class of cosmic explosions: gamma-ray bursts, which were shown in the 1990s to arise from three separate types of events. Scientists hope to discover whether FRBs also fall into distinct populations with their own origin stories.

CHIME's catalog includes large numbers of FRBs from a variety of galaxies, muddying the link to magnetars, which emerge almost exclusively in galaxies that are churning out massive, short-lived stars. CHIME's FRB haul, however, includes many sources from quieter galaxies that are barely forming any new stars at all. "Magnetars can explain some fraction of FRBs. Nobody would dispute that," says Shami Chatterjee, an astronomer at Cornell University. "But is that all of them? Almost certainly not."

A paper published in *Nature* in February 2022 adds support to this assertion. Using an array of radio telescopes called the European Very Long Baseline Interferometry (VLBI) Network, a team determined the position of a repeating burst designated FRB 20200120E with extreme precision. The object had originally been localized to the nearby spiral galaxy M81, but VLBI zoomed in farther and revealed that it lives within an ancient hive of densely packed stars known as a globular cluster. Such collections mainly host stars around 10 billion years old—yet magnetars are thought to endure for only 10,000 years or so before lapsing into more sedate neutron stars. "This is a game changer," says Mohammadtaher Safarzadeh, a theoretical astrophysicist at Harvard University. "Whatever is causing the FRB signal likely has the same age as the globular cluster and is definitely not a magnetar."

Magnetars might occasionally arise from two neutron stars crashing into each other—a production mechanism that has never been confirmed—which could potentially explain one in a globular cluster, says theoretical astrophysicist Bing Zhang of the University of Nevada, Las Vegas. But nobody knows exactly how often such events occur or how long the resulting magnetars would remain active.

Further complicating the magnetar picture is another curiosity: FRB 20180916B, also known as R3 because it was the third repeating FRB ever discovered. Originally pinpointed to a region toward the star-forming center of a spiral galaxy around half a billion light-years away, R3 was subsequently shown to be in the galaxy's outskirts, suggesting that it is either an older object or one somehow kicked away from its birthplace. Even stranger, this burst produces explosions only during a four- to five-day window of activity that occurs every 16.35 days, making it a so-called periodic repeater.

Researchers have been scratching their heads over its peculiar regularity. A magnetar that spins around on its axis like a top, sometimes pointing its blasts toward Earth and other times facing away, is one possible explanation. Another is a bursting object orbiting a second structure, such as a black hole surrounded by a disk of material, that cyclically obscures the explo-

sive events. Scientists have even suggested it comes from a pair of orbiting neutron stars whose magnetospheres periodically interact, creating a cavity where eruptions can take place. "What makes the field so fun right now is that there are so many exciting possibilities," Chatterjee says.

APPROACHING ANSWERS

FRB ASTRONOMERS ARE STILL pursuing major questions. Are non-repeaters really one-time events, or could they burst again if we watch for long enough? The magnetar in our galaxy appears to be fairly quiet. But was it significantly more active in its younger years? Could other esoteric scenarios, such as asteroids hitting a black hole, somehow produce FRB-like signals? Scientists are publishing new observations and theories all the time.

The CHIME collaboration is building a set of smaller telescopes that will help triangulate the exact positions of many FRBs. In a few years researchers expect to know the precise locations of hundreds or even 1,000 events. In addition to elucidating FRBs, these data will allow scientists to perform important measurements of the universe.

Astronomers first knew FRBs were coming from outside the Milky Way because their light was dispersed, meaning the higher frequencies arrived a few milliseconds before the lower ones. This pattern offers information about the matter the radio waves traveled through as they made their way through space. Astronomers believe there is much more regular matter in the universe than what we see in stars and galaxies, and they suspect that the missing matter lies in the intergalactic medium. In 2020 a team studied a handful of FRBs to estimate how much material their light passed through and showed it was almost exactly equivalent to the amount of matter expected there.

The ultimate goal is to use FRBs to map the matter throughout the universe. And light from some FRBs is highly polarized—its waves have been rotated by magnetic fields during its flight—potentially revealing information about magnetic conditions in other galaxies or the spaces between them. In the meantime, the mystery of FRBs' origins remains. "I fully anticipate, within the next decade, we'll get one or two more surprises, like the galactic magnetar that we didn't even know we should be looking for, which will push our understanding forward in a massive way," Petroff says.

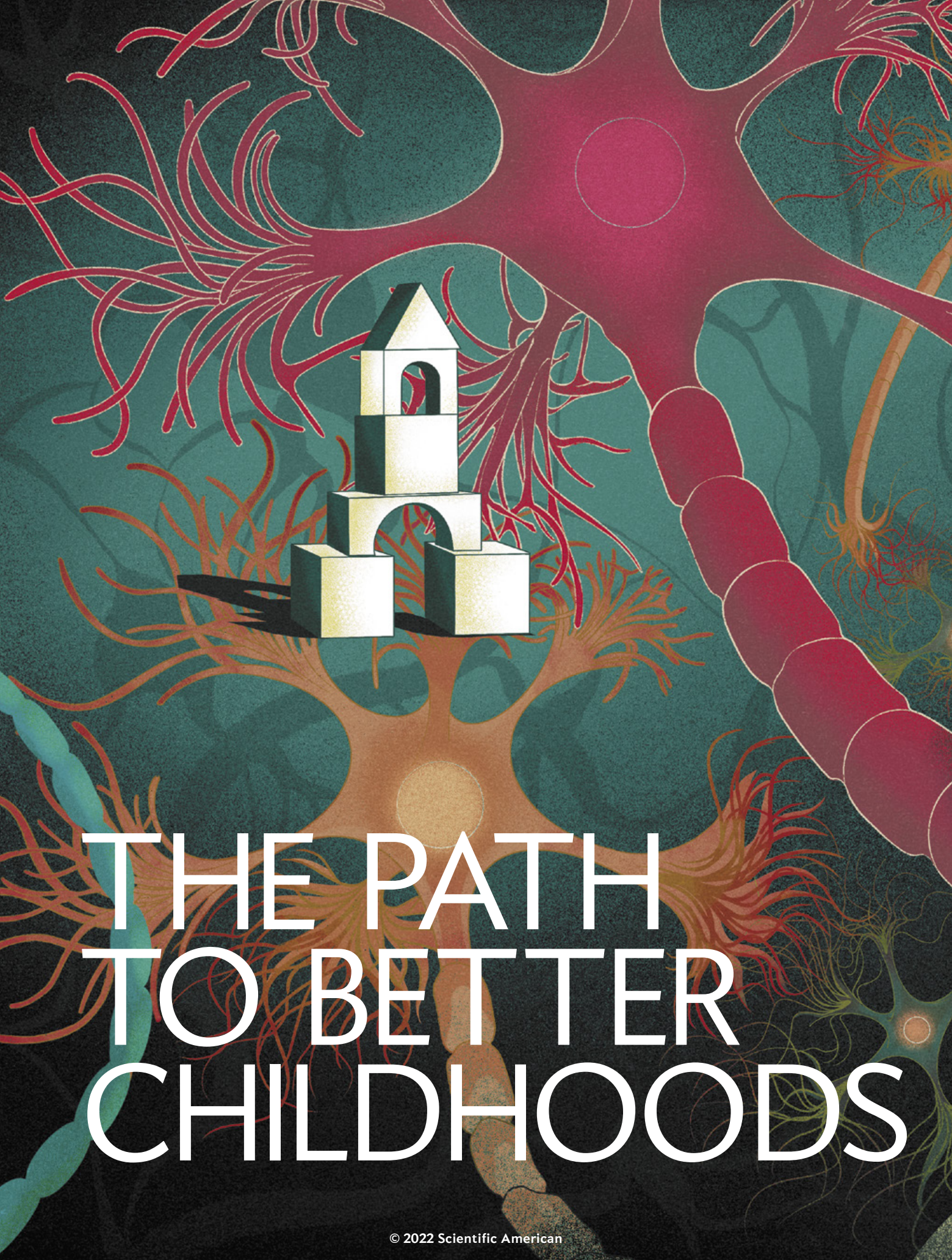
If some nonrepeating FRBs arise from cataclysmic events such as neutron stars crashing together, as many astronomers suspect, they would also create gravitational waves. Were a radio telescope to see a blast at the same time as the Laser Interferometer Gravitational-wave Observatory (LIGO) or its counterparts around the world, it would sway some toward that possibility. And if such a collision produced a magnetar, could the initial cataclysmic one-off FRB give rise to a distinct, repeating FRB source? Time will tell.

Given recent history, more FRB excitement is likely in the coming years, Lorimer says: "Just when you think things are settling down, you have a year with all these remarkable discoveries." ■

FROM OUR ARCHIVES

Flashes in the Night. Duncan Lorimer and Maura McLaughlin; April 2018.

scientificamerican.com/magazine/sa



THE PATH TO BETTER CHILDHOODS



CHILD DEVELOPMENT

Brain science provides a clear road map for policies that give children more learning abilities and brighter futures—yet the U.S. continues to wander off course

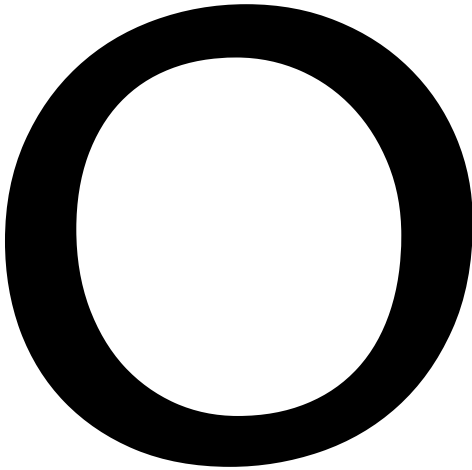
*By Dana Suskind and
Lydia Denworth*

Illustration by Islenia Milien

Dana Suskind, a childhood-learning researcher and pediatric cochlear implant surgeon at the University of Chicago Medical Center, is co-director of the TMW Center for Early Learning + Public Health. She is co-author of *Parent Nation: Unlocking Every Child's Potential, Fulfilling Society's Promise* (Dutton, 2022).



Lydia Denworth is a Brooklyn, N.Y.-based science writer and a contributing editor for *Scientific American*. She wrote about the neuroscience of stuttering in our August 2021 issue. She is co-author of *Parent Nation*.



N VITAL MEASURES THAT PREDICT LATER SUCCESS IN SCHOOL AND life, small children in the U.S. do worse than kids in comparable countries. This distressing information comes from an Organisation for Economic Cooperation and Development (OECD) study of five-year-olds. For years the OECD has been examining the academic achievement of 15-year-old students

from around the world, and recently it extended this work to the younger group. On average, American children had lower literacy and numeracy scores, poorer self-regulation skills, and engaged in fewer acts of cooperation, kindness and other prosocial behaviors than did children in England and Estonia, the other countries studied. Just about the only bright spot was that U.S. children were roughly equivalent to their international peers on some—but not all—social-emotional measures.

These findings did not get the attention they deserved, because they were announced in March 2020, a few days after the World Health Organization declared that COVID had become a pandemic. But they did not come as a surprise—other recent research has shown that about half of American children are not “on track” in at least one critical area of school readiness. Because the OECD report looked at kids who were just starting school, it was a powerful reminder that we have lost sight of something basic: Learning begins on the first day of life—and not the first day of class. The earliest years of a child's life are full of opportunity. A child's brain will never be more receptive to experience, more plastic, than it is during this pivotal time. Nearly 85 percent of brain growth occurs between birth and the age of three. During this period one million neural connections per second are formed.

Two decades of child development research tell us that small kids need two things above all else to get off to the best possible start: nurturing interaction with caregivers and protection from toxic stress. Over the past five years a new wave of neuroscientific studies, highlighting the neurobiological effects of early experience, has strongly pointed toward ways of accom-

plishing these goals. Such research provides an early peek at what is happening in young children's brains. The studies show that environments and relationships we know benefit development are also associated with higher levels of activation and connectivity in parts of the brain that underpin language and cognitive development.

One of us (Suskind) is a pediatric physician and early-learning researcher who has been tracking the way emerging science on brain development can inform not just what we do as parents but as a society. For instance, paid leave gives parents time to develop nurturing relationships. Child allowances and tax credits can alleviate the poverty known to be detrimental to development. When parents work outside the home, as a considerable majority of American mothers and fathers must, access to quality child care provides young children with responsive, engaged caregivers.

Yet there is a disconnect between what science tells us children need and what we as a society do to help them. The U.S. is the only developed country in the world that does not mandate paid leave for a parent after childbirth. In 2020 four in 10 children in the U.S. had families who were struggling to afford basic necessities.

Congress just allowed an expanded child tax credit to lapse—a credit that helped millions of families weather the pandemic and had dramatically cut the number of poor children. Further, approximately half of Americans live in so-called **child care deserts**, where there aren't nearly enough facilities or caregivers, and fewer than 10 percent of existing child care programs are considered high quality. The pandemic highlighted these gaps. Like a powerful earthquake with lingering aftershocks, it showed just how shaky our nation's support for parents and their children really is.

The science of brain development is rarely part of any public discussion of ways to fix these gaps. But it should be at the center of that conversation because it lays out a road map to improve national and local policies that can make children's lives much better.

THE MANY EFFECTS OF LANGUAGE

WEARING his ever present Chicago Bulls cap, Randy settled onto the soft carpet of his living room and pulled his two-year-old son, Julian, into his lap.

"Want to play?" he asked.

Julian grinned and began to stack some blocks. Father and son counted together ("one ... two ... three ... four ... five ...") until a tall and precarious tower stood in front of them.

"Drop it, drop it." Randy nudged Julian, encouraging him to tip the tower over. Julian gazed at his dad, his eyes twinkling with delight as Randy added a few more blocks. When the stack—and the counting—reached 16, the tower came crashing down.

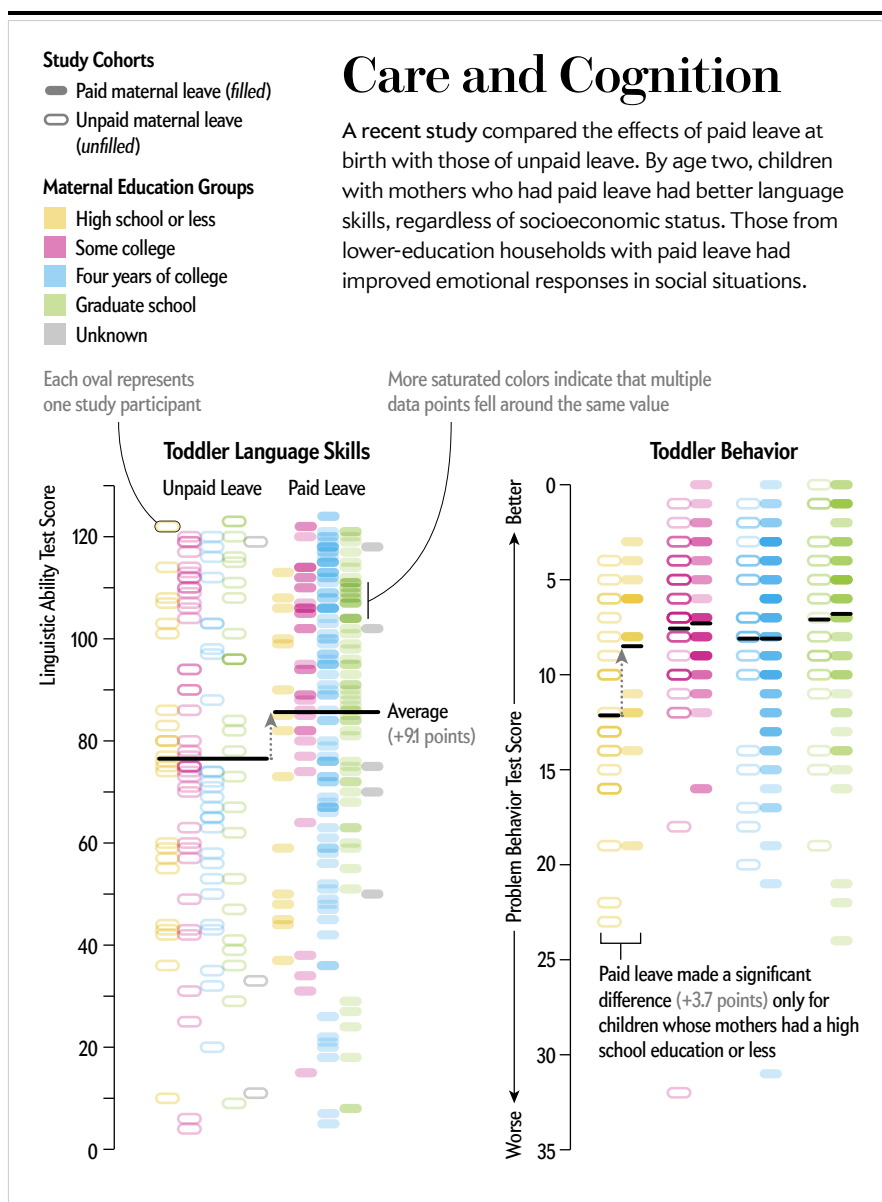
"Boom!" Randy shouted.

"Boom!" Julian echoed.

Randy fully embraced his role as a responsive parent—so much so that he signed up for a home-visiting research program in the Chicago area to learn more about child development. (We are using only first names to protect the family's privacy.) He was tuning in to his child, talking to him, and taking turns in their ongoing conversation even though Julian couldn't say much yet. This kind of **rich language input** is central to the importance of nurturing relationships. For years researchers focused on the quantity of words a child heard—the so-called 30-million-word gap—as the best predictor of language development. The newest research reveals that quality of language exposure matters even more. Overhearing conversation isn't enough. Children must participate, just as Randy encouraged Julian to do.

Care and Cognition

A recent study compared the effects of paid leave at birth with those of unpaid leave. By age two, children with mothers who had paid leave had better language skills, regardless of socioeconomic status. Those from lower-education households with paid leave had improved emotional responses in social situations.



In a 2018 study, which was the first of its kind, researchers at Harvard University and the Massachusetts Institute of technology put 36 four- to six-year-old children in a brain scanner and told them stories about playing hide-and-seek and opening birthday presents. While the kids listened, the scientists looked at brain structure and function. Previously the researchers had recorded everything the children heard for two days, to get a sense of their language environment.

Children who typically experienced not just more language but more conversational turn taking showed more activation in key language areas of the brain as they heard stories in the scanner. These kids also showed stronger connections *between* language areas that govern speech perception and speech production. "At every socioeconomic level, more conversation was related to more mature brain development," says speech language pathologist and neuroscientist Rachel Romeo, who

Source: "Paid Maternal Leave Is Associated with Better Language and Socioemotional Outcomes during Toddlerhood," by Karina Kozak et al., in *Infancy*, Vol. 26, July/August 2021

led the study and is now at the University of Maryland.

Other research indicates that important connections between very young children and caregivers actually occur on a neural level. [Their brains sync up](#). Elise Piazza and her colleagues at the Princeton University Neuroscience Institute found this out when they used a method called functional near-infrared spectroscopy that can track the activity of neurons. The scientists looked at adults and infants between nine and 15 months old, in a variety of situations. The brain waves of the infants and the adult synchronized when the two were directly playing together or jointly paying attention to the same object. They did not sync when the adult spoke to someone else in the room, affirming that overheard language does not count. This kind of [synchrony](#) has been

Paid leave after the birth of a child was associated with lower infant mortality and hospitalizations and improved infant attachment.

linked to social learning, problem-solving skills and vocabulary development. And when in sync, the adult turned out to be following the baby's lead, anticipating smiles and interest, rather than the other way around.

"We already knew that infant-directed speech is very important for babies' learning and that a variety of communicative cues could be important for them," says Piazza, who is now at the University of Rochester. But "even before they're fully verbal, there are a lot of ways in which [babies'] brains are picking up on these different cues in the environment."

Such research strongly supports the need for parents to have time with their children. It also underlines why parents also need access to high-quality, affordable child care. The problem faced by Randy, and millions like him, was that there was rarely enough time to parent the way he wished. To make ends meet, he was holding down multiple jobs. His wife, Mayra, worked full-time, too. Most days Randy saw his kids for all of 30 minutes. And the only child care Randy could afford was custodial—at pickup he often found Julian in front of a blaring television. "Here we have this body of research showing over and over that the core adult-child interactions in the early years of life are critical for brain development and social development," Romeo says. "Anything we can do as a society to create an environment where [those] relationships can flourish, that's the best investment we can make in children's futures."

EARLY HELP FOR PARENTS

LANGUAGE is just one dimension of the powerful nurturing interactions between children and caregivers. For infants, connections begin on the first day of their lives. That is why paid leave at the birth of a child is consis-

tent with policy centered on early brain development. But few Americans have such leave. Randy and Mayra didn't have it. When their two children were born, Mayra was one of the roughly one quarter of mothers who return to work within two weeks, and Randy took only a day or two off each time.

Traditionally research on paid leave has focused on the economic side of the equation—assessing the impact on employers or on household incomes. Yet more recently, studies of the effects of paid leave on [the health of mothers and children](#) found it was associated with lower levels of postpartum depression, improved infant attachment, decreases in infant mortality and rehospitalizations, as well as increases in pediatric visits, timely immunizations and the duration of breastfeeding. When fathers took paid leave at the birth of a child, it benefited both parents' mental health, lowering depressive symptoms and stress. Plus, married parents who both take leave are less likely to divorce.

To this already persuasive evidence, the newest studies add positive impacts of paid leave on infants' cognitive development. In 2021 developmental psychologist Natalie Brito of New York University and her colleagues published a study of 328 mothers and babies from across the socioeconomic spectrum, some of whom had paid leave and some of whom had unpaid leave at the birth of their child. When the children were two years old, the researchers asked the mothers to report on their children's language abilities, as well as their emotional responses in social situations. [Paid leave was associated with higher language skills](#) for the toddlers at all socioeconomic status (SES) levels and with better emotional skills among children whose mothers had lower education levels. "It seems as though paid leave was beneficial for every family, but it may have an outsize effect for lower-SES families," Brito says.

Paid leave actually [changes patterns of brain activity](#). In a second study of 80 mothers and babies published this past April in *Child Development*, Brito and her colleagues used electroencephalography (EEG) to eavesdrop on babies' brain waves three months after birth. Interactions between neurons create these waves, or oscillations. Everyone has high- and low-frequency waves, and both types are important. But as children get older, the relative amount of high-frequency activity tends to increase. Previous studies suggested that young children with more high-frequency waves, when tested a little later on in life, tend to have higher scores on skills necessary for learning and thinking.

In the work by Brito and her co-workers, infants whose mothers could take paid leave tended to have more higher-frequency waves, and fewer low-frequency ones, than babies whose mothers had unpaid leave. Although the sample was relatively small and not a truly random selection of babies, the researchers did control for a range of potentially confounding variables, such as gestational age at birth, number of children in the home, maternal relationship status, education and occupational prestige. The association between paid

leave and brain-wave patterns persisted, explaining 12 to 30 percent of the variance in infant brain activity.

It is hard to disentangle the reasons for these differences, but stress among the mothers could be one factor. The study measured levels of a stress-related hormone, cortisol, in the mothers' hair; those levels tend to go up as psychological and physical stress accumulates. Mothers who had paid leave had lower cortisol levels than mothers with unpaid leave. They also had higher parent-child interaction scores on tests of maternal sensitivity. Because paid leave provides resources and financial stability, Brito suggests, "it is likely to reduce stress and probably indirectly impacts the way that they parent or that they interact with their kids." These are the first studies of their kind and don't prove cause and effect. But, as Brito says, "some of these dots have started to be connected."

SOLUTIONS FOR THE FUTURE

WE KNOW that very young children do best when they are protected from toxic stress and when their lives are stable and predictable. Brand-new research has turned up [higher risks of developmental delays](#) in babies born during the COVID pandemic, which some experts suspect may be related to [higher stress levels in their mothers](#). We have known for decades that children growing up in families with lower incomes are more likely to face these types of unpredictable and distressing situations.

More recently, neuroscientists began exploring [what poverty does to children's brains](#). In a 2015 study of more than 1,000 children between the ages of three and 20, neuroscientist Kimberly G. Noble of Teachers College at Columbia University and her colleagues found a consistent relationship between cortical surface area (which is associated with cognitive ability) and socioeconomic factors. That study and others have found that the largest differences appear in areas of the brain that handle language, executive function and memory.

For instance, in 2019 Noble and her colleagues, also using hair cortisol levels as markers of chronic stress, showed that higher levels were associated with smaller hippocampi, a part of the brain integral for memory. These changes may be an adaptive response: The young brain is waiting for instructions from the environment, and if a child grows up in an environment of toxic stress, that child's brain will organize itself to be highly reactive to stress. But such changes can cost children later in educational and employment settings.

Tax credits for families with young children have the most potential to reduce rates of childhood poverty, according to [a 2019 National Academy of Sciences report](#). The benefits of these credits became clear during the pandemic, when a historic expanded tax credit brought about an immediate reduction in childhood poverty rates. For the first time ever, the credit was independent of earnings—a provision that benefited those who were working and those who wished to stay home with their children. More than 90 percent of American children were eligible.

But at the end of 2021 the closely divided U.S. Senate refused to extend this program. When the credits ran out, between December 2021 and January 2022, the childhood poverty rate spiked from 12 to 17 percent, higher than before the pandemic. That pushed an additional 3.7 million children into poverty. According to the NAS report, the long-term effects of childhood poverty on adult employment, crime rates and population health cost the U.S. between \$800 billion and \$1.1 trillion annually, whereas a set of policies centered on tax credits plus nutritional supplements and a few other programs would cut childhood poverty by 50 percent and ultimately cost the country less.

We also know a lot about what works in child care. The U.S. already supports a high-quality, universal system of centers, run by the Department of Defense for military families. About 30 years ago military child care was as bad as the worst we see today. People in the armed forces, doing demanding jobs, had to worry about who was watching their children, and this could detract from their performance. So the Pentagon completely revised these programs, increasing professional development and pay, enforcing high standards of care, capping the costs to families and improving access. Widespread access to quality care is a hallmark of European countries. For example, England and Estonia, the other countries in the OECD study of five-year-old children, both have generous paid leave and near-universal preschool programs.

Instituting something similar in the U.S. won't be cheap. Last year Congress did not pass legislation that would have subsidized child care costs for most working families as well as adequate wages for child care providers. The price tag would have been \$400 billion. That might sound steep, but it is not when compared with the price of inaction. A report by ReadyNation, a not-for-profit group started by business executives to research education, found that child care problems cost the U.S. \$57 billion a year in lost earnings, productivity and revenue. It has also been estimated that if American women stayed in the workforce at a rate similar to that of Norway, which has paid leave and government-subsidized child care, the U.S. could add \$1.6 trillion to the gross domestic product.

With no paid leave, no child care and limited child credits, it is glaringly obvious that a devastating divide exists between what science tells us children need and what U.S. policy actually does for them. It is time to start using our wealth of scientific evidence to guide our policies and practices. Healthy brain maturation represents the foundation of our country because it represents our future. That means there is nothing more important we can do as a society than foster and protect the brain development of our children. ■

FROM OUR ARCHIVES

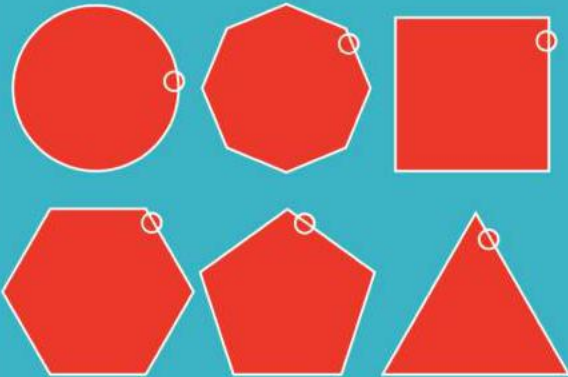
Brain Trust. Kimberly G. Noble; March 2017.

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An Untold Cost

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AS THE FIRST WAVE of the COVID pandemic washed across the world, it left devastation in its wake. The novel coronavirus rent holes in our social safety nets, nets already worn and tattered even before the pandemic took hold. And what quickly became evident was that the resulting devastation was persistently most acute among disadvantaged people and in marginalized communities.

COVID made obvious what many already knew: Inequity—whether because of race, culture, skin color, income or caste—can be lethal. On a global level, vaccines were slow to reach poor and developing nations, which didn't have the resources to produce, pay for or distribute the jabs. The vaccines they did finally receive were less effective against evolving waves of the virus, with mRNA technology proving difficult to procure. But disparities afflicted wealthy countries, too. In the U.S., mental health care lost providers even as the need for their services skyrocketed. Treatment, already hard to find, dwindled until it was largely accessible only to those with money and resources.

Infectious disease also thrives on inequity. It spreads fastest in areas of dense crowding, and because it typically affects impoverished and relatively powerless communities, it is underfunded and undertreated. Before COVID, tuberculosis killed more people globally than any other communicable disease. The pandemic made this worse as people crowded together inside their homes and became infected by one airborne virus while trying to avoid another.

Bias can also prove deadly in noninfectious illnesses. Cardiovascular disease, which was the leading cause of death worldwide in 2019, was originally pegged as a disease of the rich, linked to too much indulgence and too little exercise. More recently, it has also emerged as a problem in low-income and marginalized areas. In fact, even as screening and treatment have decreased mortality linked to heart attacks in some groups, others remain overlooked or unable to make substantive enough changes to their diets or lives to see much improvement at all.

Solutions makers at all levels have been working hard to change the status quo. Whether they're quantifying social determinants of health—assessing how life stressors such as financial need, food availability, childhood stress, and more contribute to someone's well-being—or finding women the care they need through pregnancy and postpartum, these change makers are creating paths toward more equitable care. We need only look to the AIDS pandemic to see why their efforts are important. Today, 40 years after the first cases of HIV were described, we have made great strides in both preventive and therapeutic treatments. But those medications often can't reach those who need them most acutely. We have come so far, and we have so far yet to go.

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Discrimination Is Heartbreaking

Heart disease, once thought to be a malady of the rich, has a global impact. Today its victims are those most affected by inequity

By Jyoti Madhusoodanan

SHANTAQUILLETTE CARTER-WILLIAMS was on the gym treadmill when she first felt an odd flutter in her heart. “I remember stopping and thinking, ‘That doesn’t feel right,’” says the now 43-year-old Dallas resident. But she knew the importance of exercise—she walked or ran almost every day—so she got back to it and finished her workout.

She followed up with a doctor who diagnosed her with exercise-induced arrhythmia and told her to be careful with increasing her heart rate, says Carter-Williams, a retired accountant. She switched to different kinds of workouts. That was in 2012. Over the next six years worrying symptoms such as chest pain took her to the emergency room a dozen times. Each time doctors there sent her home with no diagnosis and no way to prevent it from happening again. In June 2018 lingering back pain, stomachache and nausea led Carter-Williams to think she had the flu. She was working from home and planned to go to bed early, instead of making another inconclusive trip to the hospital. She was just wrapping up a phone call when her college-aged daughter stepped into the room. Carter-Williams turned to speak, and a bizarre pain shot down the left side of her jaw and neck. “I’d never felt anything like it before,” she says.

Her daughter drove her to the hospital. As they waited to be seen, Carter-Williams began to vomit. An intense pressure, “like someone stepping on my chest,” overwhelmed her. She was handed a pill to place in her mouth. Then her heart started to race. She remembers that hospital staff gave her an injection in her belly and administered other drugs. A brown-skinned doctor came into the room shortly after. He leaned over, held her hand and said, “I don’t want to scare you, but you’re having a heart attack.”

After the specialist left, her own cardiologist, who was a resident at the hospital, took over her care. She was discharged a few days later with no medication to prevent another incident—contrary to common clinical recommendations. As it turns out, that’s not an uncommon situation. “Unfortunately, guideline-based therapies are not uniformly applied to all patients,” says Roxana Mehran, a cardiologist at Mount Sinai’s Icahn School of Medicine in New York City. “Women and underrepresented minorities are less often treated with guideline-directed medical and interventional treatments.”

Nine months later, at age 40, Carter-Williams had a stroke.

As a Black woman, Carter-Williams was at high risk of having a heart attack. Despite that, she is also among the patients most likely to be overlooked in screening tests or have symptoms dismissed as not heart-related. Outdated thinking holds that overeating or a sedentary lifestyle are the main risk factors. But discrimination is also deadly: both within the U.S. and around the world, people who experience gender, race, socioeconomic or other discrimi-

nation are far more likely to suffer and die from heart disease.


Understanding of heart disease has dramatically expanded over the past half a century. In the 1940s heart disease caused around half the deaths in the U.S. The epidemic precipitated a flood of research that resulted in landmark, lifesaving discoveries. Researchers found, for example, that inactivity, smoking, alcohol consumption, and diets rich in fatty foods or salt raised a person’s risk of heart disease. They discovered how conditions such as diabetes and high lipid levels increased the chances of heart attack or stroke and designed drugs to stave off these dangers. And for those who wound up in emergency rooms despite these measures, surgical advances such as balloon catheters, stents or artificial valves made heart attacks less deadly.

Over time deaths dropped—at least in higher-income, majority communities in industrial nations. But as research on cardiovascular disease risk adopted a more global approach, heart disease again emerged as the number-one killer worldwide. These new studies revealed that the same risk factors drove heart attacks no matter where a person lived or what their socioeconomic status was. The difference was that now about 80 percent of heart attack victims lived in lower- and middle-income countries.

“For far too long, we didn’t have high-quality studies of cardiovascular disease that included people” from lower- and middle-income countries, says Amitava Banerjee, a cardiologist at University College London. Within the U.S., research centered on higher-income communities. And in the rest of the world, the focus was more on the differences between Western and Eastern countries than on their similarities—something that, Banerjee says, stems from “a history of colonialism in medicine” that aimed to serve expats instead of local communities.

Now researchers have focused on bridging these gaps. They are showing that, at every level, advances in reducing the burden of heart disease are less likely to reach or help people who experience discrimination. Long-standing biases have resulted in medical treatments that are less available or, when available, less useful to historically marginalized communities. Not only do these people face barriers of access, they are also often disproportionately burdened by risk factors such as air and water pollution.

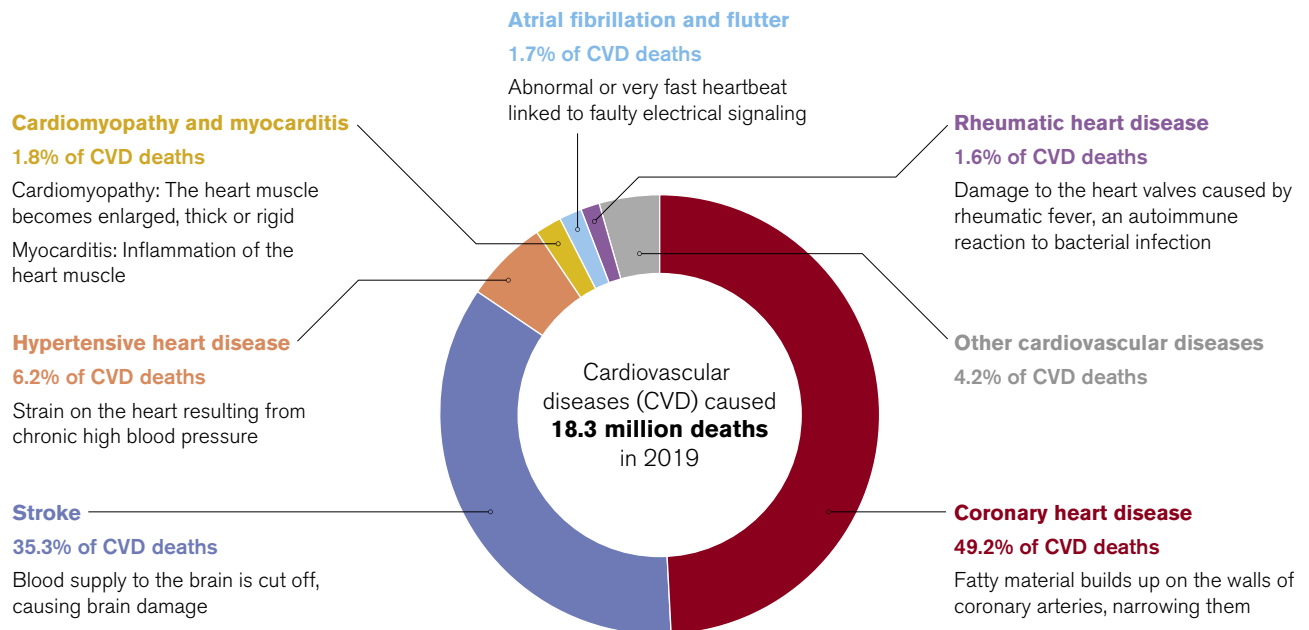
The biology of heart disease is universal. Tests, drugs, and other interventions for reducing heart attack risk are the same everywhere in the world. Despite this shared foundation, solutions ad-



THE THREE CHILDREN
of ShantaQuilette Carter-
Williams place their hands
over their mother's heart.

What Is Heart Disease?

Cardiovascular conditions don't just affect the heart. They can manifest as diseases that strike blood vessels or restrict blood supply to the brain, as well as various disorders that lessen the heart's ability to circulate blood.



Addressing the problem were mostly developed within a limited, Western context. They fail to account for social circumstances that can make diagnostics, preventive medicine and treatments inaccessible to the rest of the world. “We can’t just transport what we find in high-income countries and assume it’s going to work in low-income countries,” says Shivani Patel, a social epidemiologist at Emory University. “There are powerful social influences that need to be included in the constellation of risk factors.”

OVERLOOKED AND UNDERREPRESENTED

IN 1947 THE U.S. PUBLIC HEALTH SERVICE (now the National Institutes of Health) launched a study that tracked both the health and life habits of residents of the town of Framingham, Mass., and then looked at how those corresponded to heart health. Thanks to the Framingham Heart Study—which continues today—and others conducted in the U.S. and Europe, clinicians now know precisely how heart disease begins, worsens and kills. And they know, to a great extent, how to stop it.

In 1990 William Kannel, a former director of the Framingham Study, gave a lecture in which he reported that the study linked

heart disease to a “lifestyle typified by a faulty diet, sedentary living, unrestrained weight gain and cigarette smoking.” Therefore, people could improve heart health by changing how they lived. Public health campaigns around the world spread the message. In the U.S., the American Heart Association launched a campaign, called Life’s Simple 7, defining seven different things—such as smoking, diet and physical activity—that could decrease cardiovascular risk.

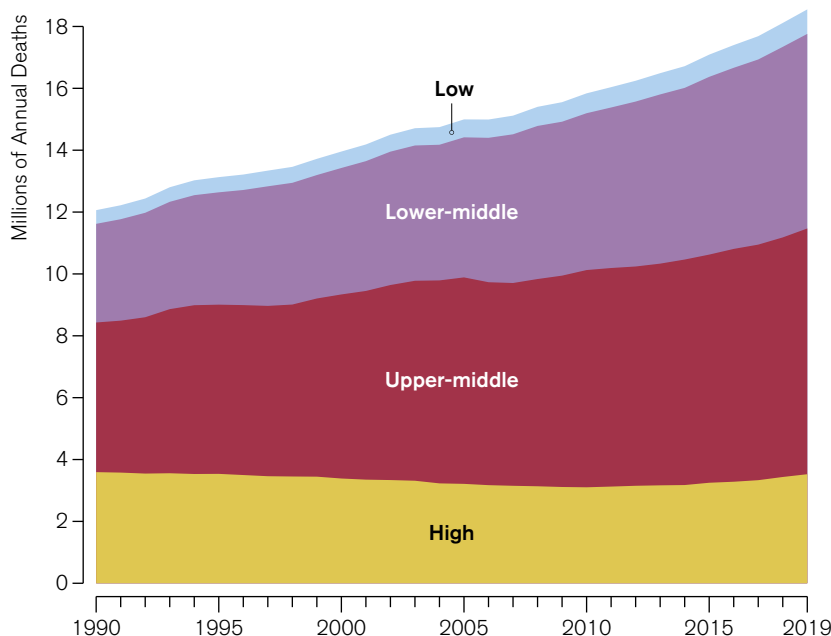
Despite the name, these measures are anything but simple. The advice to eat healthier foods and be physically active is rooted in strong evidence, but it does not account for people around the world whose lives look nothing like those of the mostly white, mostly well-off residents of a Boston suburb. “The current recommendations have fallen short because of the lack of focus on social determinants of health and structural drivers” that influence a person’s health practices, says LaPrincess Brewer, a cardiologist at the Mayo Clinic in Minnesota. “Unfortunately, Life’s Simple 7 aren’t necessarily delivered in the [appropriate] sociocultural context.”

Consider exercise. Even when feasible, it is not enough by itself to ensure a healthy heart. Carter-Williams knew exercise was

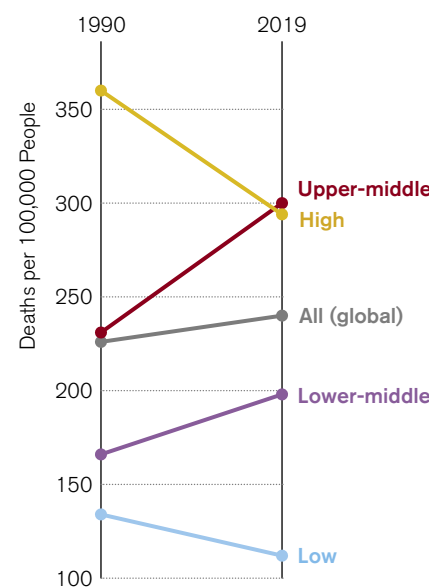
Heart Disease in Middle-Income Countries

In 1990 the highest rates of heart disease mortality occurred in high-income countries. But by 2019 death rates in middle-income countries had caught up. Cases continue to rise globally, particularly in lower- to middle-income countries.

Total Heart Disease Deaths by Country Income Level



Heart Disease Death Rates by Country Income Level



important, particularly because her job came with a lot of desk time. But a treadmill habit wasn't enough to prevent her heart attack. For others, just walking out the door is a difficult ask. A lack of access to safe spaces for exercise, smog-filled air or cultural barriers to women walking alone frequently hinder or prevent physical activity. Patel points to India as an example, where persistent colorism drives women, particularly adolescent girls, to stay indoors (and thus be less active) to prevent sun-darkened skin.

Other times recommending exercise is simply absurd, says Andre Pascal Kengne, an internist and researcher at the South African Medical Research Council. In rural areas of South Africa, he points out, people at risk of heart disease often work physically demanding jobs, making planned exercise superfluous: "Think of a farmer who spends six to eight hours a day working on a farm," he says. "If you tell him at a consult to exercise, what do you expect to achieve?"

Western dietary recommendations also fail to account for how diets vary by culture. So-called heart-healthy foods described in public campaigns reflect a small subset of norms from industrial nations while excluding most culinary traditions around the

world, including in the U.S. Public campaigns aim for awareness, but Brewer points out that the problem for most people is not a lack of understanding or knowledge.

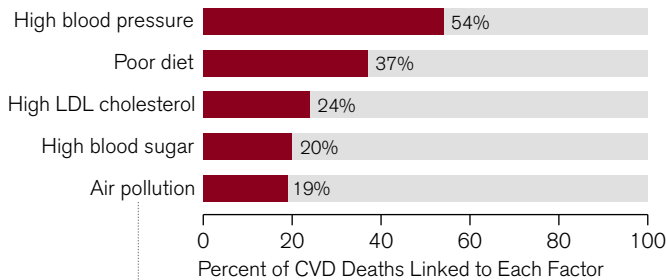
Translating awareness into a change in habits is stymied by many factors: a lack of culturally relevant guidelines, financial insecurity or an inability to access affordable, nutritious food. "Whether it's their ability to place food on the table or lack of outlets to purchase healthy food," Brewer says, community members are aware they face these issues. The problem, she says, is that they find it tough to act on diet or exercise recommendations given their financial or social circumstances.

Around the world, people of low socioeconomic status or those who live in food deserts are the most likely to have diets high in sodium and saturated fats and low in fresh produce. In a study of 195 countries published in the *Lancet*, researchers found that such diets remain the leading cause of heart disease. People eat this way out of necessity, not choice. "The reality is that wherever you are, the cheapest way to eat is often the least healthy," Banerjee says. Across the world, highly processed foods have grown more common and accessible—more so than fresh fruits and vegeta-

Risk Factors for Heart Disease

Some causes of heart disease, such as high blood pressure or cholesterol, are universal. The burden of these risks, however, falls disproportionately on people of certain races and ethnicities.

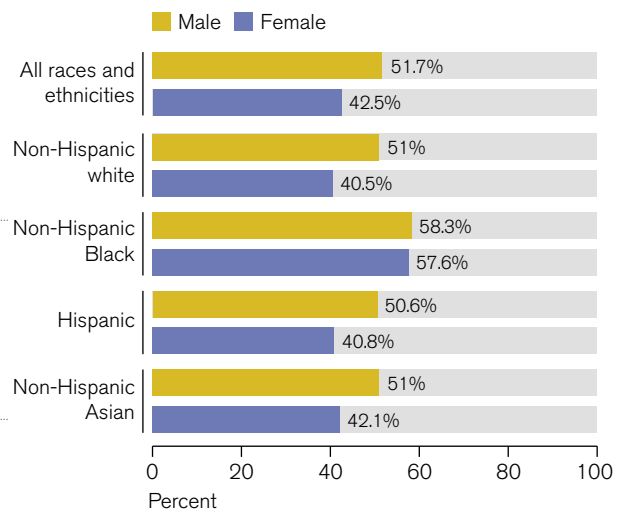
Top Five Risk Factors for Heart Disease



Poor air quality contributes to 3.5 million fatal strokes and heart attacks each year, almost all of them in middle-income countries.

According to recent research, lifetime experience of discrimination is associated with higher blood pressure among people of color.

Prevalence of High Blood Pressure by Sex and Race or Ethnicity in the U.S.



bles—at least in part due to subsidies that often make junk food cheaper even in the poorest communities.

In many low- and middle-income countries, rates of obesity and diabetes initially rose fastest in urban areas. Now rates are rising in rural areas as well, Patel says. These shifting trends, which are likely to result in more instances of heart disease, mean the condition has moved firmly beyond being a disease of affluence or sedentary lifestyles associated with city living.

Over the past two decades Patel's work has focused on tribal communities in rural India. She spent a few years in the village of Juna Mozda, in the western Indian state of Gujarat, and now focuses on understanding heart disease risk factors among its residents. Most of Juna Mozda's residents are Adivasis, members of tribal communities. "Some of the highest rates of high blood pressure are among these Indigenous communities, who are often the poorest," Patel says.

Ishwar Vasava, a farmer and social activist who has lived in Juna Mozda all his life, says he has noticed a shift in people's diets over the years: more sugar spooned into tea, traditional grains replaced with rice, and desserts and fried treats now a part of daily routines. Alcohol use is a concern, too, Vasava says, especially in young men who return to the village after years of working in

adjacent industrial towns. "I don't see much of a difference between our life in the village and that of the city anymore," he says.

Urban or rural, simply telling people to eat better and drink less alcohol is unlikely to address rising rates of cardiovascular disease. "We tell the story that people can change their risk themselves," says Joel Kaufman, an epidemiologist at the University of Washington. "But people can't change their diet and lifestyle as much as we'd like to think."

BIASED BENEFITS

IN HIGH-INCOME countries, lifestyle-based changes have clearly helped cut rates of heart disease: Smoking bans, awareness campaigns and other policies limiting tobacco use have made large contributions to the decrease in deaths from cardiovascular disease. So have advances such as better screening tests and prescription drugs. Medications for treating diabetes, hypertension, high cholesterol, and other conditions have proved so effective that they are now on the World Health Organization's list of essential medicines for all countries.

The blood tests most often used to prescribe these drugs unfortunately do not work equally well for everyone, because they were developed using data from men of European ancestry. The

Sources: Institute for Health Metrics Evaluation. Used with permission. All rights reserved. (risk factor data); "Heart Disease and Stroke Statistics—2022 Update: A Report from the American Heart Association," by Connie W. Tsao et al., in *Circulation*, Vol. 145, February 22, 2022 (hypertension prevalence data)

SHOWN CLOCKWISE with their mother, ShantaQuilette, and father, Roy Williams, are daughters Sanaa and Nyaira and son Adysaan.



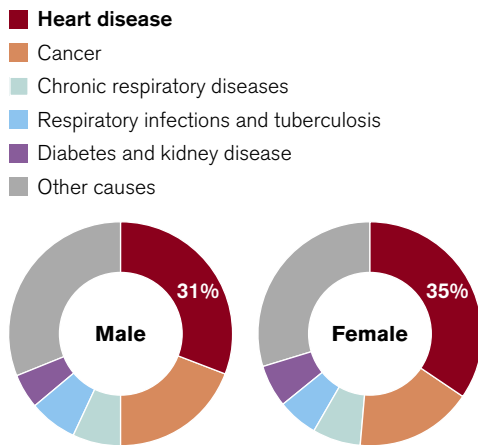
Photograph by Gioncarlo Valentine

Heart Disease Affects Both Men and Women

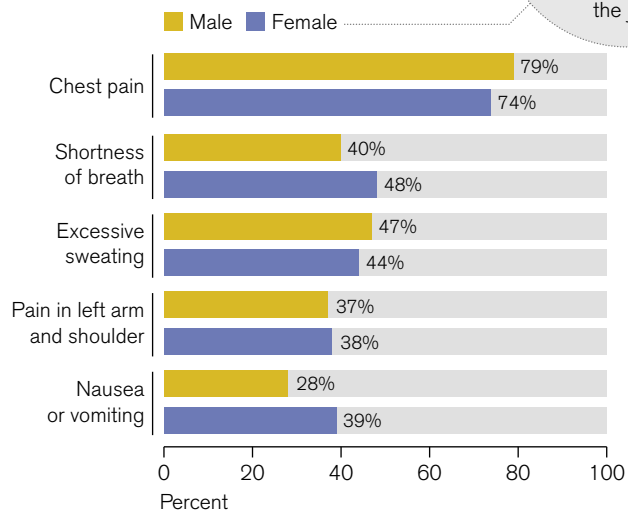
Heart disease is too often thought to be a problem only for men. But globally, it causes 35 percent of deaths among women every year. Symptoms of heart attacks differ by sex, with women more likely to experience nausea or shortness of breath than men.

Besides differing rates of these symptoms, women are much more likely than men to experience pain between the shoulder blades or in the jaw.

Top Five Causes of Death in 2019 by Sex



Top Five Heart Attack Symptoms by Sex



hemoglobin A1C test for diabetes (which, untreated, is a risk factor for heart attacks) does not work for people who are of Asian or African descent if they are anemic or are not overweight. And the most commonly used cholesterol and triglyceride assessments do not work as well to assess risk among Black individuals in the U.S. Even when test results show normal levels of triglycerides, statistics from the Centers for Disease Control and Prevention show that Black people experience higher rates of hypertension than white, Hispanic or Asian groups, says Anne Sumner, an endocrinology researcher at the National Institute of Diabetes and Digestive and Kidney Diseases. “Health disparities are not just related to not having access to care. You have to have access to the right screening tools, too.”

Precisely how much harm is caused by inaccurate screening tools is tough to know for certain. Shortly after her heart attack, Carter-Williams looked through her old medical records and found some numbers highlighted as abnormal. When she asked her doctors about the results, she says, “they really could not give me an explanation other than ‘it’s not high enough for us to be concerned.’” She only began to receive cholesterol medication 10 months later, after her stroke.

Even when test results are accurate, barriers to treatment per-

sist, particularly in low- and middle-income countries. It can prove nearly impossible for some people—like the farmer who spends his days doing manual labor—to get to a clinic in the first place. In South Africa, subsidized health care ensures that patients at many clinics do not pay for preventive drugs, says Kengne of the South African Medical Research Council. “If they can get to the clinic, the medication is free,” he says. “But the transportation cost to get there” is the problem.

The cost of medications as well as their availability hinders access to drugs in many low- and middle-income countries. In a 2020 study of 21 countries published in *BMJ Global Health*, researchers linked the inaccessibility of necessary medicines to higher odds of disability and death from heart disease. Drugs that treat diabetes or hypertension are available to only about 50 to 60 percent of the population in both high-income countries and low- and middle-income countries. In the latter case, a month’s worth of brand-name medication typically costs six days’ wages, whereas generics cost about two days’ worth. “The most common reason people give me for stopping their medicines is financial,” says Jaideep Menon, a cardiologist at the Amrita Institute of Medical Sciences and Research Center in Kochi, India. “Another is because the drugs aren’t available in a pharmacy near them.”

Sources: Institute for Health Metrics Evaluation. Used with permission. All rights reserved. (death rate data); “Sex Differences in Symptom Presentation in Acute Coronary Syndromes: A Systematic Review and Meta-Analysis,” by Roos E. M. van Oosterhout et al., in *Journal of the American Heart Association*, Vol. 9, May 5, 2020 (heart attack symptom data)

Gender, age, caste and socioeconomic status all determine who gets care, Menon says. Discrimination based on these factors results in what researchers call “social deprivation”: restrictions in a person’s ability to access health care.

Those biases are not limited to low-income countries. They frequently prevent access to quality care in high-income countries, too, particularly if someone is Black or female. “The places where we start to see a gender divide and increased heart disease rates in women” is in places where they experience discrimination, says Mount Sinai cardiologist Mehran. “That includes right here in the U.S., where there’s discrimination against them based on income, education, and other factors.”

Women in cardiac distress are less likely to be noticed or given timely care. Heart disease and stroke cause 35 percent of deaths in women, but their symptoms are different from men’s, and surveys show that physicians are less confident diagnosing heart attacks in women than they are in men. They are more likely to attribute a woman’s heart attack symptoms to stomach upset or mental health issues. And women—particularly young Black women—are less likely to receive treatment, either preventive or once a heart attack has already occurred.

For her part, even after she had been diagnosed with cardiovascular issues, Carter-Williams was told nothing was wrong and to “stop stressing out over her job,” she says. She was never tested for blocked blood vessels, something that increases someone’s odds of another heart attack. Despite a family history of heart disease and earlier blood tests showing high cholesterol levels and elevated blood pressure, she received no prescription medications.

Nine months after her first hospital stay, Carter-Williams collapsed at work, unable to walk or remember her name. This time the hospital physician suspected seizures. Carter-Williams and her husband were not convinced. After she was discharged, the couple found a new neurologist, a Black woman, who diagnosed her as having had a stroke.

The stroke left Carter-Williams unable to walk or keep up with her job. She took early retirement at the age of 42. And although she is on the mend, she has also taken steps to reduce her odds of experiencing discrimination. After eight years of missed diagnoses, she says, “I fired every one of my doctors who didn’t look like me.” Her new care team are either Black or members of other minority groups, she says. “I wanted people who could understand that there is bias.”

GROUND REALITIES

INEQUITY ENDURES because it is rooted in so many sources: unconscious and conscious bias, centuries of racism marginalizing people of color, a history of forcing those of least means and power into environments that are the most polluted.

That legacy remains a reality for people of color or low socioeconomic status around the world. Research on social determinants of health lags behind progress in drug development for di-

Global policies continue to prioritize economic development over the health of the most vulnerable communities.

abetes and hypertension. Starting in 1988, 40 years after the Framingham study began, researchers launched three similar efforts to understand high rates of heart disease in Black, Hispanic and Native American communities. Over the years these and other studies have begun to reveal the importance of discrimination as a risk factor for disease. One study in 2017 in *JAMA Internal Medicine* found that Black people who lived in more segregated neighborhoods experienced greater rates of hypertension. When they moved to less segregated communities, their blood pressure improved.

“Segregation is a good proxy for a lot of the things we think of when we think of structural racism, including education, earning potential and wealth,” says Kiarri Kershaw, the social epidemiologist at Northwestern University who led the work. The brunt of discrimination is borne out in other research, too. Studies in Brazil, the U.S. and other countries have shown that people who experience everyday discrimination, such as being passed over for a promotion or being harassed by neighbors, tend to have higher rates of hypertension. These social experiences are layered over long-standing regulations and policies that exacerbate inequity. Discriminatory practices in housing and the development of freeways, mines or factories usually result in low-income neighborhoods or marginalized communities bearing the impact of both air and water pollution.

Food policy is similarly biased. Governments in many countries impose lower taxes on the sale of highly processed foods such as refined sugar or oils. Recipients of government subsidies—who are usually poorer—are more likely to consume such products. They are also less likely to be able to afford medicines for chronic conditions such as hypertension or diabetes that result from excess consumption of these foods. Funding to improve medical care for these precursors to heart disease has failed to keep up with the surge in cases, in part because the burden of infectious diseases has yet to wane.

Changing the social and political systems that exacerbate heart disease is a complex, unwieldy process. Global policies continue to prioritize economic development over the health of the most vulnerable communities in the world. Which means, Menon says, “marginalized groups tend to lose out on all fronts.”

Jyoti Madhusoodanan is an independent journalist based in Portland, Ore. She covers the life sciences, health equity and bioethics for *Science*, the *Guardian*, *Undark*, and other outlets.



Mental Health Care's Great Divide

The stress of COVID fractured a system that was already cracked

By Sarah Sloat

FOR MORE THAN 25 years, Richard Youins struggled to find help with his drug addiction. Youins is from New Haven, Conn., home to both Yale University and a number of less affluent neighborhoods—his community has been shaken by murders and drug-related crimes during the pandemic. Substance use clinics and treatment sites were available, but he felt the care they provided overlooked who he was as a person. The needs “of our community weren’t being addressed,” says Youins, who is Black. “It wasn’t realistic.”

Youins felt that traditional mental health care ignores the social, economic, emotional and faith-based needs of underserved communities. “After hanging out and spending all my money on a Saturday night, I would feel so ashamed I wanted to go and talk to

God,” but doing so felt out of reach because he felt unwelcome in church settings, and the services available to him did not cultivate that type of much needed support network, he says. Now sober, Youins works as a peer-support specialist with the Connecticut Mental Health Center and has seen how COVID worsened mental health challenges in his city. “It’s a trying time,” he says.

Rates of mental illness were already high in the U.S., but the pandemic intensified everything: Illness, loneliness, job loss, grief, and other stressors related to COVID induced a nationwide rise in anxiety and depression. As difficult as the pandemic has been, however, it hit some groups far harder than others. It exacerbated social and economic inequities already known to drive and sustain poor mental health among marginalized communities. Those in rural America, already less likely to receive mental health care than those in urban areas, were particularly hard hit. So were people of color, who are more likely to be hospitalized and die from COVID and are less likely to receive mental health care compared with white people. And for those who were unhoused or formerly incarcerated, the consequences have been profound.

Madhuri Jha, director of the Kennedy-Satcher Center for Mental Health Equity at the Morehouse School of Medicine, witnessed how COVID impacted unhoused people with serious mental illness when she led a mobile behavioral health unit in New York City early in the pandemic. “It wasn’t just death” that increased when the pandemic hit, she says. “It was accidental overdose, suicide, incarceration. It was people going missing and no way to account for it.”

Now experts in the mental health field are acknowledging that they must confront ugly truths in the American health-care system, including structural racism and classism. “The pandemic has caused universal harm to everybody’s mental health, but for people who are most vulnerable, for people who are most traditionally oppressed and marginalized, that harm becomes greater and more significant,” says Ruth Shim, who researches equitable approaches to mental health care as director of cultural psychiatry at the University of California, Davis.

The pandemic was an urgent wake-up call for providers, community stakeholders and politicians, prompting them to reimagine mental health care and delivery. Shim and others are looking at how they can improve equity. What they are finding is that, to succeed in underserved communities, they need solutions that foster a sense of belonging. These include expanding access to care, improving research on community mental health and empowering people to tackle their own problems.

Combining these efforts leads to the most robust and long-lasting response, says Helena Hansen, associate director of the Center for Social Medicine at U.C.L.A.’s David Geffen School of Medicine. All efforts, she says, must be built on the understanding that issues such as racism and classism drive social determinants of mental health, such as unstable housing or lack of insurance. “The way our system is set up now is deliberately crafted to exclude certain people,” Hansen says. “If we want to address social determinants that provide a sense of connection to others, which is really the heart of mental health recovery, we have to rethink what mental health care looks like.”

**“They have things I can’t medicate away.
They have things I can’t therapy away.”**

**—Michael Mensah, a psychiatrist
at the Yale School of Medicine**

GAINING ACCESS TO CARE

DURING HIS ADDICTION, Youins learned that just because mental health care services existed did not mean they were accessible. Although equal access to mental health care is broadly acknowledged as a civil right, many still struggle to get it. One major reason is cost: Not only is it expensive but many mental health practitioners do not accept insurance, let alone Medicaid, because insurance companies do not compensate them adequately. People who are most likely to be in therapy are those who can pay out of pocket.

The obvious solution to expanding access in the U.S., Shim says, is establishing universal health care, which would assure coverage regardless of someone’s ability to pay. Until that happens, however, mental health organizations that are designed by and serve marginalized communities can play a meaningful role in overcoming cost-related and social factors that reduce access to care. “We need to be at the table, making decisions,” Youins says.

Some groups have emerged to do exactly that. One of the mental health equity projects Youins works with is *Imani Breakthrough*, a free, New Haven–based recovery program designed to help Black and Latinx people overcome drug and alcohol use disorders within a church setting. Another group called the *Asian Mental Health Collective (AMHC)*, which formed partly in response to the rise in anti-Asian violence during the pandemic, connects 30 people per quarter to eight free sessions of therapy with an Asian American provider through its *subsidized therapy program*.

In addition to cost, another factor that might prevent people from seeking care is stigma around mental illness. By confronting and dismantling negative stereotypes about mental health, organizations such as the AMHC and another group, called *Rural Minds*, aim to expand access to care in their communities.

Jeff Winton founded *Rural Minds* after his 28-year-old nephew, who worked on the family dairy farm in upstate New York, died from suicide. Neighbors suggested Winton tell people that the death was the result of natural causes. In rural areas, Winton explains, “mental health is not considered an illness; it’s considered a character flaw.” Instead of covering up the suicide, he spoke about his nephew’s struggles in his eulogy. Afterward, people lined up to share their own experiences with mental illness.

In rural America, stigma is hardly the only issue: even when people want care, they often cannot find a therapist. As of March 2022, more than 35 million Americans in rural areas lacked access to a mental health provider.

One solution that has shown promise is telehealth, which ex-

ploded in popularity during the pandemic. *Pravesh Sharma*, a pediatric psychiatrist in Eau Claire, Wis., says the technology has enabled him to talk with patients who would otherwise have to travel for hours to reach his clinic. Now up to 40 percent of his practice is made up of telehealth appointments. Such a call allowed him to connect with a transgender patient in a rural area who needed support communicating with their conservative family. After their calls, Sharma says, the client was better able to have conversations with their family and community.

Telehealth’s primary drawback is, yet again, access. It’s useless when someone lacks an Internet connection, a private place from which to call, a computer or mobile phone, or the ability to navigate a digital environment—all common issues for people in poor communities and communities of color.

THE HEART OF THE PROBLEM

GROWING UP NEAR YALE, Youins noticed that a number of the university’s mental health studies were focused on the city’s Black population, but his community rarely saw any lasting impacts. “People come in and do a lot of research, but they don’t share that information. They use us as guinea pigs,” he says. Because the projects would come and go, “you can’t even measure if they really work.”

Researchers agree that to focus on the inequities of marginalized groups, it is critical to gather data on their experiences. “People in Congress do not see a problem when there [are] no data,” Jha says. But a data set is useless if it is not collected in a culturally sensitive way, and current research tools are not always sensitive enough to gather information about nonwhite populations. Non-English speakers, for example, are usually not represented in mental health data, because they do not understand survey questions, Jha says. Furthermore, because people self-identify in a number of ways, racial and ethnic demographics can be difficult to capture.

Historically biased systems also mean measurements of suffering among certain racial and ethnic minority groups can be inaccurate. Mental health stigma prevents people from seeking care and reporting symptoms in the first place. Even when they do, they are often misdiagnosed as a result of longtime racialized diagnostic biases, which the psychiatric community has only now begun to address. For instance, studies show that Black Americans are more likely to be misdiagnosed with schizophrenia than white Americans.

Another issue with data collection on disparities is that most efforts focus on measuring a community’s deficiencies rather than its strengths, Jha says, which leaves “no pathway to actually understanding what the solutions are.” For example, a study might focus on measuring how many people of color have a serious mental illness but not their ability to withstand and adapt to the challenges their condition poses.

Ultimately good data are useful only when applied effectively and appropriately. For research to translate into something that serves the people it is about, Shim says, it must involve them throughout the scientific process, from conceptualization of the

study to dissemination of the results. And a share of the funding, which often comes from government grants and may amount to millions of dollars, should go toward supporting the communities that the research is focused on. “The very communities that they’re studying don’t see any of that investment at all,” Shim says.

COMMUNITY HEALING

ALLOWING COMMUNITIES to be engaged in their own care may be the most important step toward achieving mental health equity. “When a community is empowered to solve their own problems, they’re often very effective,” Shim says.

Imani Breakthrough, where Youins is a peer coach, has been recognized as a successful model for community mental health support. Co-developed by psychiatry researchers Ayana Jordan of New York University and Chyrell Bellamy of Yale University, the program offers classes, provided in a church setting, to promote wellness and recovery. Sessions are led by people from the local Black and Latinx communities—usually a member of the church and a coach who has lived with substance use. “The person sitting on the other side of the table looks like me, knows about me and knows we have similar things in common,” Youins says. This familiarity helps people in the program overcome hesitancy in seeking care that often stems from discrimination they may face at traditional clinics. Holding classes in a church, which has cultural significance, fosters a comfortable and welcoming environment.

Another successful model is Crisis Assistance Helping Out On The Streets (CAHOOTS), a mobile mental health crisis intervention program in Eugene and Springfield, Ore., that is more than 30 years old. CAHOOTS diverts mental health–related crisis calls away from the police and toward its own team of trained specialists, who handle crises without weapons or law enforcement. Funded by the Eugene and Springfield police departments, it mostly serves people marginalized by racism, classism and ableism, people who are typically wary of police-led crisis responses, which often result in arrest or even death.

CAHOOTS is staffed largely by survivors of mental health crises like Daniel Felts, who has worked for the organization as an EMT and crisis worker for five years. When Felts attempted suicide at age 19, six police officers with guns showed up. He was a danger to himself, he says, “But then I became distinctly aware that these folks could take my life if I made the wrong move.”

Felts later joined CAHOOTS because it provided a nonviolent, unarmed response to mental health crisis calls, did not bill its patients and prioritized comprehensive care—everything from medical aid to connecting people to food and shelter. It aims to “meet people where they are and be sensitive to the intersectionality of our patient population,” Felts says.

PROVIDERS ALSO NEED SUPPORT

ADMINISTERING equitable mental health care comes with a cost: provider burnout. A survey of more than 20,000 health-care workers between May and October 2020 found that 49 percent had burned out and 43 percent suffered from work overload. Providers who are Black, Indigenous and people of color (BIPOC) caring

for their own disproportionately affected communities are among the hardest hit. During the pandemic, female, Black and Latinx workers have reported higher stress levels than their male and white counterparts.

“There’s a certain urgency in mental health care,” Hansen says. A growing number of psychiatrists and therapists are reporting burnout, and a record number are leaving clinical practice. Even at a community-led group like CAHOOTS, COVID-related setbacks made it difficult to retain burned-out staff, Felts says.

Jessica Dominguez, founder and lead clinician of La Clínica, a program offering culturally sensitive mental health therapy to Latinx patients at a Kaiser Permanente center in California, says she has seen more BIPOC clinicians leave the company during COVID than ever because they felt undervalued. With fewer Spanish-speaking and other bilingual clinicians available, non-English-speaking patients have wait times that are much longer compared with those of their English-speaking counterparts.

In October 2021 Dominguez and other mental health clinicians working for Kaiser Permanente in California and Hawaii voted to strike when the provider rejected their union’s proposals to increase staffing. Some locations are still without a contract. Kaiser, however, has spotlighted La Clínica as a diversity and inclusion success story to be replicated.

“My community has been decimated,” Dominguez says through tears. “My colleagues are devastated. They can’t work for a company who doesn’t value them and who wants to harm their community by depriving them of what they need.”

Giving communities what they need requires a rethinking. Youins, for his part, has seen that equitable, culturally competent mental health care is possible and can be life-changing. But even though individual organizations and providers have taken inspiring and meaningful steps toward mental health parity, they alone cannot fix the crisis of inequity. The fundamental problem is bigger than them, bigger than the health-care system in which they work. It is ingrained in the foundations of American society. This is why Hansen and others argue that improving access to traditional care is not enough.

Equitable mental health care requires equity across all aspects of life. The foundational drivers of health—access to nutritious food, a clean environment, job security, freedom from racism and police brutality—are bound to structural inequities, namely, racism. “As a mental health provider, I see it in my patients all the time,” says Michael Mensah, a psychiatrist at the Yale School of Medicine. “They have things I can’t medicate away. They have things I can’t therapy away.”

Yet people have a remarkable ability to persevere, given the opportunity. Youins sees this resiliency when he meets with his Imani Breakthrough group, which gathers at one of the oldest Black churches in New Haven. There, he says, “people are finding miracles within themselves.”

“The traditional way has its place,” Youins says. “But I think we need to look at some things differently.”

Sarah Sloat is a writer and editor based in Brooklyn, N.Y.

The Oldest Pandemic

Tuberculosis is preventable and curable, yet it afflicts one quarter of the world's population—mostly because of poverty

By Sofia Moutinho

MEERA YADAV GAVE BIRTH to her first baby in 2013, when she was a 23-year-old living in a slum in Mumbai, India, with her husband's family. She was filled with joy and hopes for a bright future. But four months later she began having fevers and coughing up blood.

Yadav's husband took her to a private hospital, where a doctor prescribed blood tests, a chest x-ray and a sputum test.

She was diagnosed with tuberculosis, a disease at least 9,000 years old that has likely killed more people than any other plague—as many as one billion in the past 200 years. Although the illness may seem like a historical footnote in high-income countries, it continues devastating poorer nations, afflicting the most disadvantaged: poor people, prisoners and those who are HIV-positive.

TB is a bacterial infection caused by *Mycobacterium tuberculosis*. It spreads when someone coughs, pushing bacteria into the air. In most cases, the immune system stops the bacteria from growing. It can remain in the body, dormant but alive, for years without causing symptoms or spreading. These cases are difficult to detect because people have normal chest x-rays and negative sputum tests.

But for about 10 percent of infected people, like Yadav, the infection develops into a serious disease and becomes contagious. Nearly two billion people—one quarter of the world's population—are infected today. Roughly 10 million fall ill annually. Without treatment, most cases lead to prolonged illness that culminates in fatal respiratory failure; TB kills about 1.5 million people every year.

The World Health Organization estimates that more than 95 percent of these deaths are in low- and middle-income countries where malnutrition, lack of health care and crowded hous-



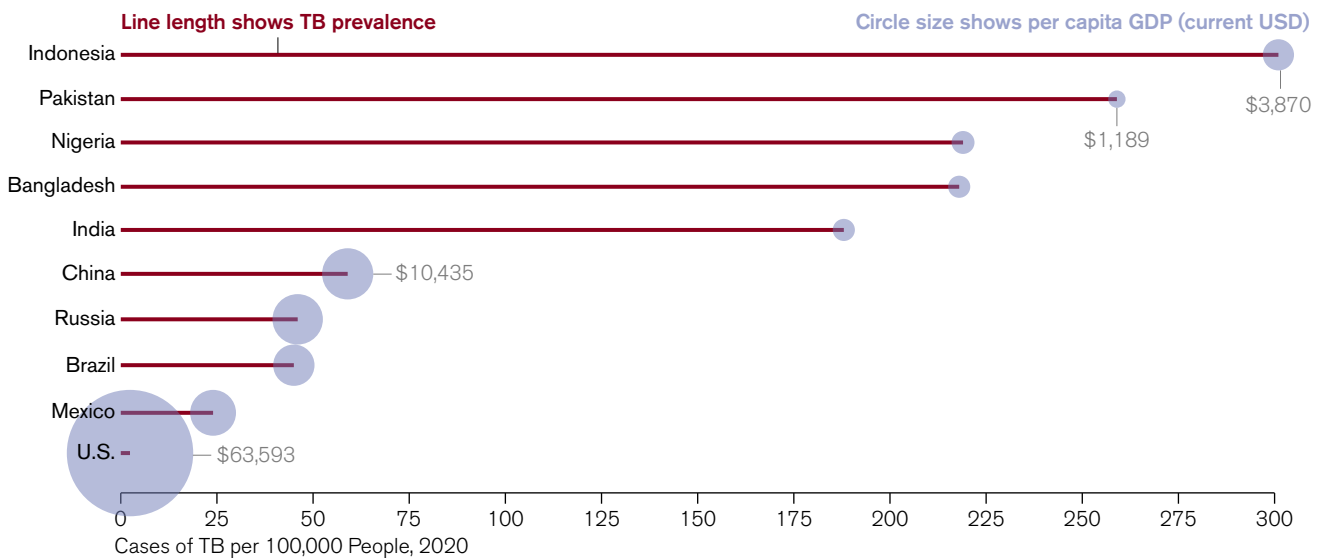
THE SITYAYA FAMILY in Khayelitsha, South Africa, all had tuberculosis, except for the baby, who received preventive treatment.



TB Strikes the Poor

These World Health Organization data show the pattern: Across the globe, poverty and tuberculosis go hand in hand. In wealthy countries, rapid detection prevents spread, and effective drugs cure most cases. But in poor and middle-income nations where crowded conditions foster disease and affordable treatment is hard to find, TB kills more than one million people every year.

TB Prevalence and Gross Domestic Product in the World's 10 Most Populous Countries



ing allow the disease to thrive and spread. In these places, inadequate public health systems fail to detect many cases, and effective treatment may be too expensive or unavailable. “Wherever there is poverty within a country, TB will find such people,” says epidemiologist Madhukar Pai, a TB expert at McGill University. “It’s mostly Black, brown, Indigenous and poor people who suffer from TB, and that’s why it doesn’t get much attention.”

It was easy for TB to find Yadav. She was living in poverty amid dilapidated houses stacked close together. Mumbai is one of the worst hotspots in India, a nation that accounts for one quarter of all diagnoses worldwide.

There is a desperate need for more research on TB. The one existing vaccine is ineffective in adults and almost a century old. Many strains of TB have developed resistance to antibiotics, and some are resistant to many or all drugs used to treat the disease. For years the WHO has been calling on nations to invest in developing better drugs and diagnostics. The agency estimates that an extra \$1.1 billion is needed every year.

In recent years, global TB cases declined about 2 percent annually, too slow to hit the United Nations goal, announced in 2015, of ending the pandemic by 2030. The COVID pandemic exacerbated TB, overwhelming national health systems, making it impossible for many patients to receive treatment and pushing more people into poverty. “Even before the pandemic, we were not making good progress,” Pai says. “But the past two years have been so bad that

we have lost something like 10 years of progress in TB.” In 2021, for the first time in more than a decade, TB mortality increased.

Despite this slide, there are reasons for hope. Across the globe, innovative initiatives focused on the most vulnerable patients are targeting prevention, detection and treatment. None of these efforts alone will vanquish TB. But they point the way forward to a future in which the disease is no longer neglected.

FIGHTING THE RESISTANCE

AFTER HER DIAGNOSIS, Yadav was hospitalized for a month, at a cost of 300,000 rupees (almost \$4,000), arduously paid by her husband’s family. Once home, she was separated from her newborn, and her relationship with her husband and in-laws soured. “They all discriminated against me because I had TB,” she remembers. Despite treatment, she did not improve.

Her husband took her to a second hospital, where they diagnosed her with MDR-TB (multidrug-resistant tuberculosis). Her treatment now involved 13 different medications, including injections of kanamycin, which can cause permanent hearing loss and kidney impairment. Instead of the six-month course that cures most TB, MDR-TB treatment can last as long as 48 months, with a success rate of only 59 percent. India estimates that about 130,000 people get sick with MDR-TB every year, but less than half of those cases are diagnosed, and even fewer are treated. Errors in diagnosis and treatment fuel the transmission of drug-resistant TB.

Sources: Global Tuberculosis Report, World Health Organization, 2021 (TB prevalence data); World Bank (GDP data)

“We [doctors] are somewhat responsible for the increase of MDR-TB,” says pulmonologist Vikas Oswal, who divides his time as a TB physician between public and private sectors in Mumbai. Medical errors and failure to follow up on patients are common, especially in the private system. In India, public-sector TB treatment is free, but patients often face long lines. Instead more than half seek private care, which is faster but not as prepared to deal with TB. Most private clinics don’t have access to medications to treat MDR-TB, and doctors see as many as 14 patients at the same time in an exam room, he says.

Seven months after her second round of treatment, Yadav’s fever came back, and she woke up early one morning coughing blood. A CT scan showed her right lung was collapsing and had to be removed. She spent another month in the hospital, at which point her husband’s family evicted her and took custody of her son. She moved back to her parents’ house, where her mother was already suffering from a case of untreated TB that would soon kill her. “I attempted suicide twice,” Yadav says. “I asked myself: Why me? I questioned why God had chosen me to bear all that.”

Three years after her initial diagnosis, a friend referred Yadav to a Doctors without Borders clinic in Mumbai. They offered to treat her for free, this time with newer drugs. With help from psychologists, she convinced herself to try again, mostly for the sake of her son. She got bedaquiline and delamanid, two potent and less toxic medicines for MDR-TB introduced in 2012. “These drugs saved my life,” Yadav says. In 2018, almost six years after her diagnosis, she was cured. The WHO now recommends both drugs as standard treatment for MDR-TB, but access is an issue in India.

Until 2019, the country relied on pharmaceutical company donations of these medicines. Today the government pays about \$350 for a six-month course of bedaquiline and \$1,200 for delamanid. The prices are too high for India to treat all who need it. In 2019 alone, 66,255 people were diagnosed with MDR-TB in India, but only 2.6 percent received the newer drugs.

In 2021 Yadav and another TB survivor filed a petition in the Bombay High Court requesting the national government invalidate the medications’ patents—which expire after 2023—allowing Indian drug companies to manufacture cheaper generic versions. The lawsuit, delayed because of COVID, is unlikely to succeed: India has issued this kind of license only once before, for a cancer drug in 2012.

Yadav remains hopeful about the case. She still gets breathless quickly and must regularly drain liquid from her lung. But she has found inspiration in fighting for other patients. “I want to make sure that no one has to suffer what I did,” she says.

DANGEROUS AIR

CHILDREN ARE ESPECIALLY vulnerable to developing severe TB; they account for 11 percent of cases and 13.8 percent of deaths worldwide. But prevention and treatment usually focus on adults, who are more likely to spread the disease, and children are often overlooked. Of the estimated 200,000 children who die of TB every year, 90 percent are never diagnosed or treated.

A South African program, led by national and municipal departments of health in partnership with Doctors without Borders,

protects members of this vulnerable group living in the shantytowns of Khayelitsha and Eshowe.

Nurse Ivy Apolisi wanders the unpaved alleys of Khayelitsha, searching for her patients among tiny shacks made of tin, wood and cardboard. Here most homes lack formal addresses, indoor toilets, running water or electricity. Families of 11 or more often share a single room with little or no ventilation. “If one is coughing, it is so easy to infect another,” she says. Khayelitsha has one of the highest burdens of TB in the country, with surging cases of drug-resistant strains.

Apolisi, together with a physician colleague, ensures that children in close contact with her TB patients take the daily preventive medication isoniazid for at least six months, as recommended by the WHO. The practice is routine in wealthy nations but not poorer ones.

In Khayelitsha, COVID brought a spike in TB transmission and mortality. Children stayed indoors, sharing air with their sick relatives. So the team began making house calls rather than asking adults diagnosed with TB to bring their children to clinics. Apolisi checks any children in the household for signs of TB. Children with symptoms head to the clinic for tests. Those who are not ill get preventive treatment. Some are as young as six weeks old. For children up to three years old who can eat solid food, the team dissolves the medicine in mango yogurt, an exciting treat for them. “Preventing TB in children is much better than watching and waiting to see if they will get sick,” Apolisi says.

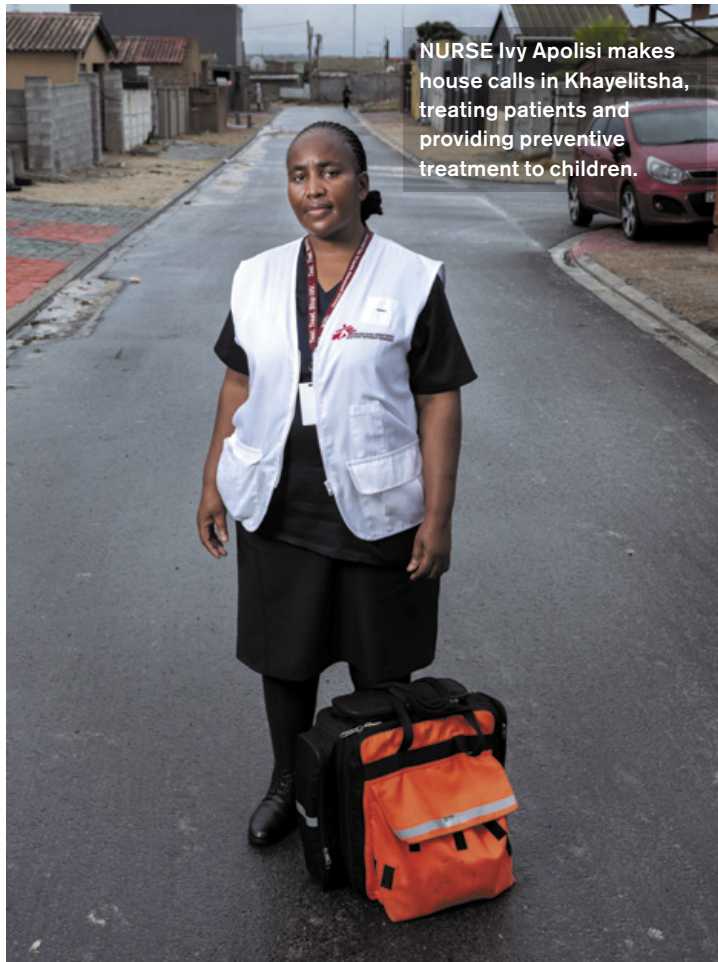
Only 2.8 million people worldwide received preventive medication in 2020, a 21 percent slide from 2019. “We are not doing nearly enough to prevent TB and drug-resistant TB in children,” says Jennifer Furin, an infectious diseases clinician at Harvard Medical School who has been working with TB in developing nations for more than two decades.

So far the South African program has enrolled more than 300 families and provided preventive treatment to 200 children, none of whom developed the disease. The project can serve as an example, Furin says. “We have to focus on prevention in households if we want to make a dent in the TB epidemic.”

TB BEHIND BARS

PRISONERS ARE ANOTHER neglected group in the TB pandemic, and they often face an unintended sentence. Conditions such as overcrowding, poor ventilation and poor nutrition make them susceptible to the disease. And because most convicts enter prison with prior risk factors such as malnutrition and substance use, they are even more vulnerable.

Last August, Eduardo da Silva, a 22-year-old inmate in a prison in the state of Mato Grosso do Sul in southwestern Brazil, had the misfortune to face all these conditions at once. Locked behind a thick steel door, a tiny hole his only window, da Silva was wracked with fever, cough, chest pain and night sweats. Other convicts forced him to sleep in a corner on the cold floor, thinking he had COVID. Isolating was impossible because da Silva shared a cell twice the size of a king-size bed with more than 50 people. “I couldn’t do anything but lie down,” da Silva recalls, but space in



NURSE Ivy Apolisi makes house calls in Khayelitsha, treating patients and providing preventive treatment to children.

the cell was so tight that people often slept in a sitting position or on top of one another.

He had no energy to walk or eat, and in two months his weight plummeted to 89 pounds. It was TB, not COVID.

It has become a common story in South America. While TB has declined across the world, here it has surged along with incarceration. The incarcerated population grew by 200 percent in the past two decades. Among that group, TB cases more than doubled from 2011 to 2017, according to a *Lancet* study. Brazil accounts for almost half of that increase. Those entering prison in Brazil have roughly average infection rates, but their risk increases 25 percent each year of incarceration, according to a study co-authored by Julio Croda, an epidemiologist at the Federal University of Mato Grosso do Sul. “Prisons are TB amplifiers,” Croda says. “But unfortunately, most people in society don’t care about what happens in prisons.”

They may not care, but prison walls are not strong enough to keep TB inside. The disease spreads among inmates, visitors and workers alike. To trace the path of infection, Croda and his colleagues compared the genomes of TB bacteria sampled from prisoners and recently released convicts. In Mato Grosso do Sul, they identified at least 18 chains of contagion by which prisoners and

ex-convicts transmitted TB to others. In one sample of 320 cases of people never incarcerated, half were directly connected to prisoners. Because TB can remain dormant, researchers have found inmates may become ill and infectious up to seven years after release.

Croda and his colleagues are developing a strategy to stop this spread, conducting mass screenings in three major Brazilian penitentiaries in Mato Grosso do Sul. Since 2017 they have tested more than 7,000 inmates for TB every nine months using the standard sputum test plus artificial-intelligence software that assesses chest x-rays.

When da Silva was diagnosed with advanced TB, he was scared. His father had had TB in prison and was never properly treated, so he did not realize the disease was curable. After counseling and treatment, his confidence grew. “I felt the health team cared about me, and they told me I would be cured,” da Silva says. “So I took the medicines.”

TB spreads quickly in prisons, but it also can be better controlled there because prison staff ensure treatment adherence. “Everyone in the cell helps each other to keep the treatment going,” says Andrea Santos, a nurse with the project. The intervention cut TB cases by half in one prison in Mato Grosso do Sul. Predictive models designed by Croda and his collaborators suggest that mass screening in prisons can reduce TB prevalence in surrounding communities by nearly 20 percent.

After six months of treatment, da Silva is cured. He is back to his normal weight and says he feels good. But he is an exception. Mass-screening programs for TB in prisons are rare because there is a general failure to recognize the role of prisons in the disease. The WHO does not keep any official record of TB cases among prisoners or list them as a risk group. “We won’t reduce TB incidence, especially in South America, if we don’t address this population,” Croda says.

FIGHTING A SOCIAL DISEASE

THE COVID PANDEMIC amplified an important lesson in public health: conquering a disease requires multiple combined efforts. “We learned with COVID that masks were good, but not enough. Isolation was good, but not enough. Vaccines were good, but also not enough,” Pai says. “Now is the time to do the same with TB.”

A comprehensive approach to TB requires investment in screening, preventive therapy and better drugs but most of all in fighting poverty. Universal health care and increased income correlate directly with a drop in TB rates. To make real progress, Pai notes, governments and public health organizations must tackle social aspects of the disease, such as stigma, crowded living conditions, malnutrition and the economic burden of treatment. “If we focus on only the biomedical aspects of TB, we can make an improvement, but we will never control the epidemic,” he adds. “There is no way to really solve TB without tackling inequality.”

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Sofia Moutinho is an award-winning Brazilian journalist covering health and the environment, appearing in *Science*, *Nature*, NPR, and elsewhere.

Profiles in Health Equity

Four innovators are finding new solutions for the problem of injustice

By Julia Hotz

THE WORLD HAS NEVER HAD better medicine, more knowledgeable doctors or stronger data on disease. But these benefits are not equally shared. To take one conspicuous example: two years of data from the Centers for Disease Control and Prevention show that Black, Hispanic and Native American people are significantly more likely to be hospitalized and die from COVID than white people in the U.S.

Health inequity includes the lack of access to appropriate care, the failure to address social factors that influence health, and the dangerous conditions that people in some neighborhoods endure. Achieving equity requires campaigns on all these fronts. These four health-care champions—a data-digging epidemiologist, an activist midwife, a doctor who traded clinic work for community activism and a pollution-tracking entrepreneur—embody that effort. —J.H.

THE SOCIAL RULES OF HEALTH

MICHAEL MARMOT

Michael Marmot has spent his entire life working with data—finding, analyzing and applying them. When he was 12, his focus was cricket statistics. When he was a student, it was branches of medicine; he mastered biochemistry, physiology and epidemiology. And when he was a physician in the 1960s in Sydney, it was his patients. Marmot was fascinated by what united or differentiated them, as if they, too, were a data set.

Marmot's mindset would eventually influence millions of other physicians by inspiring tools to identify the social determinants of health. Back then there was no such framework. "There was this idea that the social conditions that so clearly affected patients' health were out of the reach of doctors," he says. When he thought about an immigrant mother who was abused by her husband and struggled with chronic pain or about a young woman who had had a difficult childhood and now experienced depression, he wondered: Why treat people and then send them back into the situation that made them sick?

In 1971 Marmot pivoted to research, pursuing a Ph.D. at the University of California, Berkeley, to study coronary heart disease

(CHD). Textbooks at the time blamed it on behavioral factors such as diet and smoking, but Marmot suspected stress and social factors contributed, too. His 1976 analysis of medical records from Japanese American men confirmed it—the men with the most Westernized lifestyles had rates of CHD three to five times higher than those of men with more traditional Japanese lifestyles, a difference not explained by food or tobacco.

His Whitehall studies in the late 1970s and 1980s similarly revealed that the health of British civil servants was related to factors such as income and job satisfaction. Marmot found that the lower employees were in their workplace hierarchy, the higher their risk of dying from heart disease.

Over the next 30 years Marmot amassed more insights and data. In 2012, for instance, he found that the strongest predictors of health for adolescents are national wealth, income inequality and access to education. His work established and legitimized the phrase "social determinants of health" in health policy and medical circles.

Marmot's approach changed how physicians, public health experts and governments think about health inequity. In 2008 the U.K. secretary of state for health asked him to investigate health gaps. The resulting "Marmot Review" revealed that injustice degrades the health of nearly all U.K. citizens and is preventable.

Because of Marmot's influence, physi-



cians today have ways both to talk about social conditions and to address them through community partnerships—a practice called social prescribing. "Understanding the social determinants of health ensures you focus on what matters to patients rather than just what the matter is with them," says Sam Everington, a general practitioner at the Bromley by Bow Center in London, who pioneered social prescribing and cites Marmot's work as crucial for training doctors.

Today Marmot directs the University College London Institute of Health Equity. His work has been cited more than 250,000 times. His Review has spread, from the eastern Mediterranean in 2019 to Manchester in 2021. His focus is still on data: "Health equity comes from greater equity in society," he says.



DELIVERING EQUITY AT BIRTH

SHAFIA MONROE

As a teenager in Boston in the 1970s, Shafia Monroe learned a startling fact: Black infants were more likely to die than babies of any other race. And there seemed to be no urgency in the scientific community to address the disparity. “We’ve got Harvard [and] Tufts, and nobody’s doing anything,” she remembers thinking.

This early knowledge sparked a lifetime’s work in expanding Black mothers’ access to doulas and midwives—caregivers who help mothers with practical and emotional support during labor and delivery. For this work, Monroe has come to be recognized as the mother of the Black midwives’ movement.

Because Black women are frequently misdiagnosed, mistreated and racially stigmatized in health care, they and their babies are more likely to die in childbirth. Inspired by Black women known as “granny” midwives who helped mothers like them in the postemancipation South, Monroe trained as a midwife herself and realized something important: if more Black mothers could get one-on-one birth support from other Black women, they and their babies might be healthier.

She did not yet have empirical proof, but she knew Black women wanted support from other women of color—either midwives, for at-home births, or doulas, for hospital births. In 1978 Monroe

formed the nonprofit Traditional Childbearing Group, and she soon began working with similar professionals from Ghana, Uganda, Pakistan and Alabama. Together they trained midwives, taught \$5 birthing classes, provided breastfeeding information and supported at-home births. In 1988 the Massachusetts Department of Public Health started funding their work. “Doctors were calling us up because people were having better birth outcomes,” Monroe recounts.

Since then, research has affirmed her observations. In 2007 a comparative analysis of birth outcomes among more than 11,000 women found that second-time mothers with doula support had lower rates of cesarean deliveries. A smaller study in 2017 found that women with doulas had lower rates of preterm birth and of low-birthweight infants.

In 1991 Monroe launched the International Center for Traditional Childbearing (ICTC), which has trained more than 2,000 doulas. In 2011 she helped Oregon pass legislation that reimbursed doulas through Medicaid. Other states are following suit.

“Community-competent and culturally and structurally competent doulas can help make the labor room safer for a birthing woman,” says Arline Geronimus, a research professor at the University of Michigan Population Studies Center, whose work has demonstrated the health burden of racial discrimination on Black mothers. She praises the ICTC for training doulas who are more likely to be trustworthy to women of color, as well as its policy work to allow those with low incomes to access doula services.

Inequity persists, however; compared with their white counterparts, Black infants are 2.3 times more likely to die, and Black women are 3.5 times more likely to die of pregnancy-related causes. So Monroe’s work continues through actions such as advocating for an Alabama bill to expand access to traditional midwife care, as well as mentoring others fighting for birth justice. “I was alone for many years, but the movement has birthed itself into the next generation,” she says.

Julia Hotz is a journalist reporting on systemic solutions to loneliness, anxiety, depression and disease. Follow her on Twitter at @hotzthoughts

TREATING INEQUITY AS DISEASE

VERA CORDEIRO

Vera Cordeiro founded one of the world’s most influential health programs, but as a child she never wanted to go near medicine. She loved art and literature, spending her days writing poetry in her treehouse and reflecting on the ways she, born into a wealthy family outside Rio de Janeiro, experienced life differently from her neighbors—many of them sick and poor.

Following family pressure, Cordeiro went to medical school, where she met a professor equally interested in people. If someone died of a heart attack, that professor would encourage his students to consider how circumstances such as the patient’s marriage or job affected their illness. In 1988, while working in the pediatric ward of Rio’s Hospital da Lagoa,

THE AIR WE BREATHE

DAVIDA HERZL

Growing up in southern California, Davida Herzl used to look out to the Port of Long Beach with her parents, who ran a supply-chain business, to watch the container ships come in. She wondered how those ships’ emissions affected people living nearby. “You see the underbelly of what it takes to live our lives with convenience,” she says now.

As an adult, Herzl created a powerful sensor-based pollution-measurement system to prove what many people suspected: poor neighborhoods have poor air.

The social justice component of her work took root long ago, she says, when she was growing up as a multiracial Jewish girl with a belief that everyone is entitled to clean air. But it was not until 2008 that she found a way to act. A landmark study published that year

Cordeiro saw for herself how life and medicine intertwine.

"We'd treat a child for pneumonia, but then we'd send her back to a house where she could not eat well or where her father was jobless, and then she'd come back again with a different infection," Cordeiro says. Other doctors faced the same frustrations, so she started asking her patients nonmedical questions such as whether they had food or clean water or jobs, and she called on other medical professionals and friends to help them.

In 1991 she turned that informal practice into a formal organization by founding Associação Saúde Criança Renascer at the hospital. Through the association, doctors can screen for poverty, unemployment, housing issues and other root causes of disease, and volunteers help to fulfill those needs with money, food and other resources. The teams also help the parents develop Family Action Plans, setting long-term goals around things such as access to nutritious food and training for a stable job.

"Saúde Criança is a pioneer in the de-



sign and delivery of comprehensive antipov-
erty programs," says James Habyarimana
of Georgetown University, a public policy
professor specializing in health outcomes.
He praises the organization for recognizing
how one dimension of poverty, such as in-
come, affects other dimensions, such as
housing, which together determine a child's
health. He says it could be replicated in all
but the poorest parts of the world.

Children who were enrolled in the pro-

gram were significantly less likely to need
surgery or clinical treatment, according to
Habyarimana's 2013 study. If they were
hospitalized, their stays were 86 percent
shorter than other children's. At the start
of the program 56 percent of families
identified their well-being as bad or very
bad, but by the end 51 percent reported
it was good or very good.

That success might explain why the
organization, now called the Dara Institute,
has grown rapidly. It has served 75,000 peo-
ple across Brazil and inspired some 20 pro-
grams in Africa, Asia and Latin America.
It has even reached Baltimore, where, since
2017, the University of Maryland has been
adapting Dara's methods to its local context.

Now 71, Cordeiro is president of the
Dara Institute and is still fighting for the per-
son behind the disease. She shows before-
and-after photographs of patients' houses—
bathrooms once dilapidated and doors once
cracked now renovated, allowing families
to live with more dignity in their homes—and
says their stories keep her going: "People
move my heart."

linked air pollution with premature mortality
and a range of illnesses, including asthma,
respiratory infections, lung cancer and
heart disease. Those consequences dis-
proportionately affect communities of color,
subsequent research found.

The entrepreneur in Herzl emerged
shortly after. Despite pressure to reduce
emissions, most stakeholders did not know
how to address the problem. "We were
completely missing the data and measure-
ment infrastructure to understand two very
critical things: Where are emissions coming
from, and who are they impacting?" she
says. In 2010 Herzl launched Aclima, a
technology company that uses sensors to
measure air pollution and greenhouse gas-
es at the hyperlocal level. Aclima creates
high-resolution air-quality maps by aggre-
gating data points over time, showing
where, for instance, carbon dioxide or car-
bon monoxide is concentrated.

Aclima has teamed up with governments
and local organizers that use the resulting
data maps to catalyze action. In 2015 a pro-
ject with NASA, the U.S. Environmental Pro-
tection Agency and Google used Aclima

sensors on Google Street View vehicles to
carry out a comprehensive air-quality analy-
sis in [Denver](#). In 2019 a similar effort in [San
Diego](#) revealed high concentrations of fine
particulate matter and black carbon in Otay
Mesa and San Ysidro, communities with
busy border ports. Those [two pollutants](#) are
associated with lung and heart dysfunction
and poor cognitive function. That same
year a block-by-block analysis of West
Oakland measured especially high levels
of nitrogen dioxide in Marcus Garvey Com-
mons and near the Mandela Parkway,
[where](#) some of the highest poverty rates
in the Bay Area are found.

"The work being done by Herzl with local
organizations is so important because it helps
to identify which communities should be
prioritized when creating policies to reduce
pollution exposure," says David Reichmuth,
senior engineer at the Union of Concerned
Scientists. His 2019 report demonstrated
that in California, Latinos, African Americans
and Asian Americans are exposed to more
vehicular pollution than are white people.

Reichmuth points to West Oakland,
where Aclima's [air-quality analysis](#) was

used by community groups such as the
West Oakland Environmental Indicators
Project to generate a plan designed to re-
duce emissions.

With these and other initiatives, data
lead the conversation, Herzl says: "It's less
about finger-pointing and more about say-
ing, 'Here's the science. What are we col-
lectively going to do about it?'"



Gatekeepers of Health

HIV care has improved dramatically—but not for everyone

By David Malebranche

ON A SWELTERING JUNE DAY IN 2021, Nicole, whose real name has been changed to protect her privacy, walked into an HIV treatment clinic in Atlanta, Ga., expecting something different. She had shouldered a lifetime of discrimination for being both Black and transgender while also dealing with HIV, diabetes and hypertension. She worked as a manager of a fast-food restaurant while parenting several LGBTQ youths. Accessing consistent health care was a daily battle, and Nicole's past interactions with providers had left her feeling discouraged. But she and I had hit it off during a previous telemedicine appointment, so she scheduled a face-to-face visit at the clinic where I worked. As a Black, same-gender-loving physician, I wanted to do better by her.

Despite the [amazing scientific advances](#) in HIV care that have taken place since the epidemic began 40 years ago, many people in racially and sexually minoritized communities still fall through the cracks. Some can't afford care, and others can't access it because of job or family demands, lack of transportation or documentation, or other barriers. Many face stigma and discrimination from medical providers themselves. I was determined to do everything I could to change the narrative of Nicole's health-care experiences that day.

She obtained HIV medications through the AIDS Drug Assistance Program, which provides antiretroviral therapy (ART) for the uninsured. To remain eligible for the state-sponsored program, she endured cum-

bersome bureaucratic paperwork, drove 45 minutes each way to the clinic for regular visits and attended required meetings with a benefits counselor every six months. To save money, she filled prescriptions for some of her other conditions at several different local pharmacies. She got her hormones off the street because a previous clinician had refused to prescribe them unless she sought mental health counseling first.

Nicole arrived 30 minutes late for our appointment after a long commute into the city during rush-hour traffic. As we discussed her gender identity, sexual health and romantic partners, I saw a surprised look on her face, suggesting to me that few clinicians had asked her these questions before. Her physical exam was mostly normal,

except for extensive anal warts. "They've been there a long time," she said. "No one knows what to do with them." I imagined some medical providers being so uncomfortable with her being transgender that they bypassed the genital exam altogether.

As we sat together in that sterile exam room, I realized that the medical community had failed her, and it wasn't because of a lack of advances in HIV treatment and prevention. ART has evolved from toxic medications taken multiple times a day to single-tablet regimens with few side effects. We now have bimonthly injections that can maintain full viral suppression. First approved in 2012, preexposure prophylaxis, or PrEP, given as a daily oral pill or bimonthly injection can reduce one's chances of contracting HIV by 90 to 100 percent. Despite these great scientific strides, Nicole wasn't reaping the benefits of this progress.

What's to blame? Many social, institutional and [interpersonal medical barriers](#) are. Inequities in housing and food insecurity, access to insurance, and bias and stigma in medical care contribute to [persistent racial and ethnic disparities](#) in HIV incidence rates, engagement in care and viral suppression. For Nicole, HIV is just one of many circumstances that make everyday life challenging. America's fragmented and dysfunctional health-care system only makes things worse.

These disparate HIV health outcomes are complicated by a labyrinth of bureaucracy within medical spaces that make it nearly impossible for many to access medications that should be within their reach. This includes cumbersome paperwork to obtain ART if one is uninsured, underresourced clinics and medical staff burnt out from COVID, and institutional policies that prioritize visit numbers and copay billing over patient-centered care. For people living with HIV, these issues within our nation's clinics can make getting and staying on ART a climb that feels insurmountable.

After her exam, Nicole asked, "So, can I get my lab work done?" Unfortunately, because our appointment started late, the technicians had already left for the day. She would have to make another trip. Even our clinic, which worked hard to help those who needed it most, wasn't flexible enough to help her on this occasion. As I watched her



face cloud with disappointment, I feared we would lose her again. I feared that I was failing her, like so many clinicians before me.

Despite my concerns, Nicole told me she left that day feeling encouraged because she felt heard for the first time in eons. We planned to restart her ART, refer her to colorectal surgery to evaluate her warts, explore insurance options with her employer and consolidate all her medications at a single pharmacy. I sent in her hormone prescriptions, confirming what she already knew: there is no universal policy requiring a mental health specialist to approve them.

The burden of improving HIV prevention and treatment is now on the should-

ers of our medical systems. As we seek to provide more equitable care, statewide and national policy improvements must be accompanied by changes within health-care systems and clinics: We must enhance case management staff to ensure patients can get to their appointments and understand the processes required to access treatment. We must make sure patients can have necessary blood work done on the day of their checkup appointment. We must develop sensible patient-flow protocols to ensure that people are seen in a timely and efficient manner. Offering patients a diverse range of appointments, such as telehealth, walk-ins and house

calls, can accommodate the fluidity of life. Clinics need to hire staff and providers who reflect the communities served, and they should invest in cultural humility training to reduce bias and stigma in treatment. Modifications at the clinic level, though relatively small compared with sweeping national policies, can have an enormous impact on whether someone living with HIV decides to continue accessing care there or not.

Medical approaches to HIV prevention and treatment have come a long way. These revolutionary breakthroughs can help tackle the current HIV health inequities in the U.S. and ultimately lead to a cure. But this will all be for naught if the medical systems and personnel who are the gatekeepers to these advances act more like health-care barriers than facilitators.

I'd like to tell you that the work we did that day helped Nicole feel more optimistic about trusting medical systems and providers. I'd like to tell you that her future clinic appointments went smoothly and didn't require repeat visits. I'd like to tell you that she found her voice with her employer, obtained private insurance through her job and is now receiving care for all her medical issues. I'd like to tell you she is being treated by other medical staff with the dignity and respect she deserves.

But I can't. She missed our next appointment, and by the time the clinic was able to reschedule her, I had stopped working there. Truth is, patients fall out of care more often than we like to admit, sometimes because of a revolving door of clinical providers entering and leaving these settings. I took solace in knowing that we had connected that day and that I did my best to give her the medical care she deserved. Perhaps our interaction restored her faith in human connectedness—a dynamic that may alleviate some of the harm inflicted by broken and discriminatory health-care systems. Nicole came to our appointment expecting something different. I hope she now realizes that something different is possible.

David Malebranche is an internal medicine physician with 20 years of clinical and public health expertise in sexual health and HIV/STI treatment and prevention. He resides in Atlanta, Ga.

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Men Aren't from Mars, nor Are Women from Venus

Most personalities blend characteristics associated with both traditional genders

By Spencer Greenberg and Holly Muir

How different are men and women *really*? About 30 years ago, if dating guides are any indication, some people assumed vast differences in personality, with *Men Are from Mars, Women Are from Venus* relationship advice. Today, in contrast, certain communities are pushing back against the idea of binary gender, which presents men and women as separate categories. (A quick reminder: gender—described in terms such as “man,” “woman” and “nonbinary person”—has strong cultural and social components. But sex—sometimes described with adjectives such as “male,” “female” and “intersex”—refers to a combination of biological features.)

Scientists are also taking harder looks at gender, sex and personality. For one, researchers are debating how big the personality differences between cisgender men and women truly are. (These are people who describe themselves as either a man or a woman and say that this gender identity aligns with their sex assigned at birth.) The answer depends on how psychologists measure an individual's characteristics.

For example, a study involving more than 300,000 people in the U.S. who self-identified as either male or female looked both at broad personality traits, such as extraversion and agreeableness, and at more specific aspects of these traits, such as a warm communication style or a tendency to act altruistically. In this sample, researchers found moderate differences between male and female participants in the broad traits but, in most cases, larger differences at the more specific level. Overall, for instance, both male and female people in the study were similarly extraverted (a broad trait). When the scientists looked at specific aspects of extraversion, however, they found that male participants, on average, sought out exciting situations more often than female ones did. And female participants demonstrated higher activity levels than male ones.

To test the most comprehensive set of personality traits to date, our project, [ClearerThinking.org](https://clearerthinking.org), ran a series of 15 studies and conducted analyses on more than 15,000 people. Our analyses are limited to cisgender men and women: 98 percent of the participants in our research identified themselves this way, so we did not have enough data to shed light on the per-

sonality traits of nonbinary and transgender people. From the data, we discovered 18 specific self-reported traits that varied between these men and women. Next, we built an algorithm designed to predict a person's gender based on their self-reported scores on those traits, which was accurate 78 percent of the time. That accuracy is high but far from perfect, revealing the challenge of predicting an individual's gender from their combination of traits. Finally, we adapted our study questionnaire—in which people rated how much they agree with statements such as “I laugh aloud” and “I frequently worry”—into an online interactive assessment.

To create the questions for our studies, we cast a very wide net, looking at large personality projects, reviewing the academic literature and crowdsourcing ideas. We ended up testing more than 600 personality questions for gender differences before identifying the 18 traits with the greatest variation between the self-identified men and women in our sample. These traits included not only the broad characteristics that are widely used in psychological research (such as extraversion and agreeableness) but also more specific patterns of thought and behavior, such as how frequently an individual takes risks or their degree of focus on aesthetics. We also double-checked our conclusions by running a final study to replicate the major findings. Ultimately we found no large differences in personality between cisgender men and women on any traits. But we did find small and moderate differences in the 18 personality traits.

The most sizable of these differences was the degree to which cisgender people thought about sex, assessed by asking people to rate how much they agreed with the statement “I often have sexual thoughts when I meet an attractive-looking person” and disagreed with the statement “I do not frequently think about sex.” (This “sex-focused” characteristic, while not linked to major personality traits commonly studied in psychology, nonetheless fits the conception of a personality trait as a pattern in thought, emotion or behavior. It also relates to a concept called sexual preoccupation.) We found that gender could explain about 18 percent of the variation in the extent to which people are sex-focused. Men had a higher average score on this trait than women. There were still plenty of women who had a higher score than most men, however. In other words, individual men and women were highly varied, even though at the group level, men tended to differ from women.

On every trait, there was a substantial overlap between men and women. Yet at the tail ends—where people either strongly agreed or disagreed with the questions we asked them—larger differences emerged. For example, very low compassion was rare in both men and women, but the few people who identified as very uncompassionate were much more likely to be men. This result is consistent with the finding that antisocial personality disorder, which often involves a lack of remorse or empathy, is more common among men than women.

So is there a “man's personality” and a “woman's personality”? Fascinatingly, almost everyone in our study was a mix of “more often seen in men” and “more often seen in women”



traits. For any given trait, an individual woman was closer to the overall average for women than the overall average for men just 61 percent of the time. And a man was closer to the average for men than the average for women only 57 percent of the time. Only about 1 percent of men and 1 percent of women had almost entirely “more often seen in men” or “more often seen in women” personality traits.

To test how accurately gender can be predicted from personality, we developed a simple machine-learning algorithm (a computer program that looked for patterns in data regarding which personality traits are associated with being a cis man or a cis woman). We trained our algorithm using results from past study participants, then presented the algorithm with the personality traits of new participants to see how well it could predict their gender. Using just the most predictive trait—being sex-focused—the algorithm could predict a person’s gender correctly 69 percent of the time. This result may be impressive to some. But the prediction is far from perfect because some women are much more sex-focused than the average man.

The algorithm’s accuracy rose to 78 percent when we allowed it to incorporate all the personality differences at once. That’s a big improvement—but for the other 22 percent of people, the algorithm was predicting incorrectly. When we released our quiz to the public, accuracy slipped a bit further to 74 percent. That’s still much better than the average human, though: We gave another group of study participants sets of personality traits that, we explained, belonged to particular individuals. Then we asked the participants to predict the gender of those

other people using the personality traits. They were correct only 58 percent of the time, hardly better than a coin flip. The quiz is called the Gender Continuum Test, and you can [try it yourself](#) on our Web site to see whether the algorithm predicts your gender.

We believe our results shed new light on the size of gender differences in personality. There are, however, some important caveats. First, all our study participants were from the U.S., and given that factors such as culture [influence personality and gender](#), we would be hesitant to extend our conclusions to other communities. Second, our study cannot provide insight into the *causes* of personality differences—for instance, how much these differences can be explained by environment and culture as opposed to biology. Third, as we noted earlier, we do not have enough data to comment on transgender, intersex or nonbinary individuals. We hope that future research explores these and other dimensions of the personality, sex and gender debate.

Right now our study is a reminder that, on average, cisgender men and women do have some small to moderate differences in how they report their personality, but almost everyone is a mix of traits seen more often in men *and* seen more often in women. If you try to guess someone’s personality from their gender, you’ll very often be wrong. ■

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NONFICTION

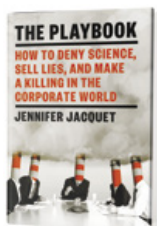
Selling Denial

What's it like to ignore science?

Trusting the scientific process is undeniably the right thing to do when trying to make good decisions in a complicated world. But it can also be no fun. Many of the truths science reveals—that burning fossil fuels harms the environment, that smoking cigarettes causes cancer—are real bummers. Wouldn't it be fun to side against the scientific consensus for once?

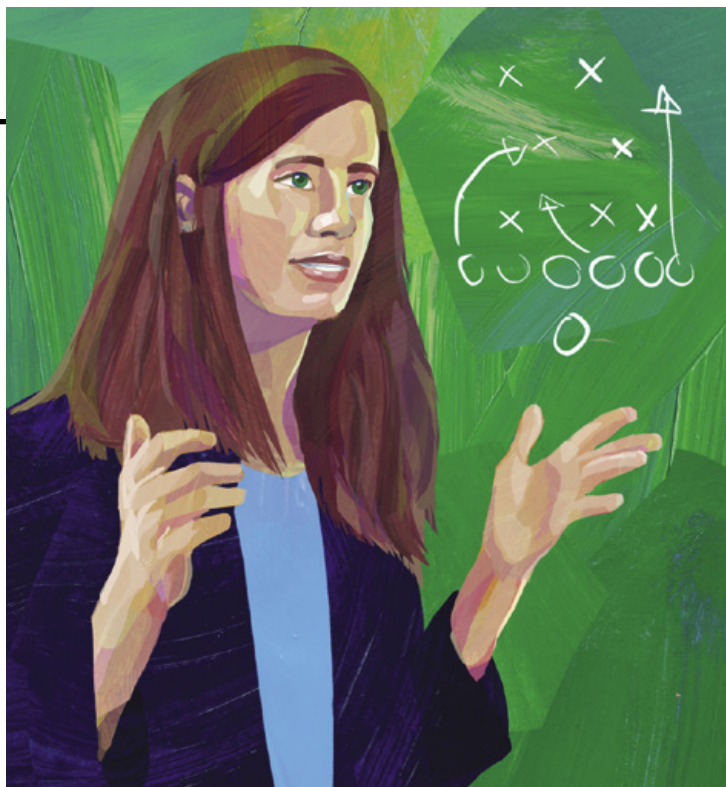
If you feel exhausted from constantly taking the high road, *The Playbook* offers an enticing alternative. Author Jennifer Jacquet, an associate professor of environmental studies at New York University, indulges a reader's fantasy of acting as a company executive for whom science is simply another facet of corporate propaganda. Presented as a how-to guide for co-opting or covering up science in the name of Business, the narration never breaks character.

I wondered more than once if a bad actor could take the book at its word and thrive in the corporate world by, for instance, conducting industry-sponsored studies and burying undesirable results or pointing fingers at others when legitimate issues with a company's practices arise. *The Playbook* is loaded with "success" stories of spun science, from retro classics



The Playbook: How to Deny Science, Sell Lies, and Make a Killing in the Corporate World

by Jennifer Jacquet
Pantheon, 2022 (\$28)



of oil, cigarette and Big Pharma giants to modern-day malfeasance by technology and vaping companies.

Without Jacquet's dry humor suffusing each chapter, the book would have made for a depressing, exhaustive history of corporations duping consumers, bypassing regulators and silencing critics. But her tone is gleeful, mimicking the rhetoric of a motivational speaker turned corporate consultant, advising retired professors to "put your emeritus title to work" shilling for companies. When a conflict arises be-

tween science and your company's products, she advises deflection: "DDT might kill birds, but malaria, which DDT helps prevent, kills people."

One effect of the book's tongue-in-cheek format is a chilling realization that the villains in *The Playbook* are extraordinarily banal. The tactics that enable their misconduct have been recycled across decades. Perhaps a powerful first step to stopping the misuse of science, then, is noticing these hackneyed themes—and calling them out. —Maddie Bender

IN BRIEF

Bitch: On the Female of the Species

by Lucy Cooke. Basic Books, 2022 (\$30)

In this effervescent exposé, British zoologist Lucy Cooke documents the "scientific phallocracy" that has warped our perceptions of biological sex in the animal kingdom. Cooke reveals how sexist cultural and historical influences, particularly those of the Victorian era, led scientists to misinterpret, undervalue and ignore the female of the species. Her playful, enlightening tour of the vanguard of evolutionary biology not only highlights animals that disrupt our assumptions about biological sex and its "natural" behaviors (lesbian albatrosses, jezebel bluebirds, infanticidal meerkat matriarchs, orgasmic female macaques), it also celebrates the underappreciated scholars whose research is shifting this reductive paradigm. —Dana Dunham



Lapvona: A Novel

by Ottessa Moshfegh. Penguin Press, 2022 (\$27)

Ottessa Moshfegh brings her trademark brutality to the Middle Ages in this allegorical pandemic novel. In the fictional Eastern European village of Lapvona, a boy named Marek befriends a proto-scientist named Ina, whose experimental tinctures with herbs and flowers bring relief to a community suffering through plagues, droughts and famines. Meanwhile Lord Villiam stays isolated in his luxurious home, weaponizing religious faith to keep the dying masses angry with one another instead of him. Moshfegh puts Marek and Ina on a thrilling collision course with Villiam to take over the village, while interrogating the role faith plays in social and environmental abuses of power. —Adam Morgan

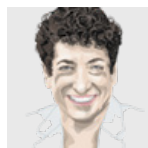


What Your Food Ate: How to Heal Our Land and Reclaim Our Health

by David R. Montgomery and Anne Biklé. W. W. Norton, 2022 (\$30)

Seeking to improve our health through nutrition, we might count carbs, go keto or become vegan. But other drivers of nourishment go deeper. In this timely investigation, geologist David R. Montgomery and biologist Anne Biklé dig into the earth to determine how we are not just what we eat but also the land our food comes from. They call out agricultural challenges, such as microbial deficiencies in soil, which affect both crops and livestock. And they detail transformative farming tactics, both functional and economic, because "we still have time to choose the regenerative path for our soils, our planet, and ourselves." —Mandana Chaffa





Naomi Oreskes is a professor of the history of science at Harvard University. She is author of *Why Trust Science?* (Princeton University Press, 2019) and co-author of *Discerning Experts* (University of Chicago, 2019).

Paper Predators

Journals that print shoddy research put people's lives at risk

By Naomi Oreskes

In the past year there's been a lot of talk about the lack of trust in science and the need to distinguish legitimate research from misinformation, disinformation, and other forms of fallaciousness. But how? Many commentators have pointed to the importance of peer review—the process through which scientific claims are scrutinized for validity by other researchers with expertise in relevant fields, before the papers are published. Those observers have insisted that a study's appearance in a peer-reviewed journal is a hallmark of legitimacy. Although that type of publication does not guarantee that a study is correct, it does indicate that its methods and conclusions have been vetted by appropriate experts. At least, that is the theory.

A recent development, however, threatens to undermine this criterion for distinguishing scientific sense from nonsense. It is the rise of “predatory journals.” These journals pretend to uphold scientific standards but do not. Typically they offer authors rapid publication, in part because they do not take the time to do high-quality peer reviews. Nor do they vet papers for plagiarism, faulty methods, conflicts of interest or missing ethics board approvals. Still, these journals make plenty of profits, collecting millions of dollars in fees from authors.

This is a big problem for society, not just for science. One study concluded that 8,000 predatory journals collectively publish 420,000 papers every year, nearly a fifth of the scientific community's annual output of 2.5 million papers. A medical news story on *Medscape* noted that dubious research funded by commercial interests can bypass proper vetting via publication in a predatory journal. These papers are listed in scientific databases alongside legitimate journals, making it difficult for researchers and policy makers to discern the difference.

At best, this is a giant waste of resources. At worst, it may put people's lives at risk because doctors and patients may wrongly accept spurious claims about medical treatments, supplements and inadequately tested drugs—and invalid studies wrongly influence public policy. And the danger is getting bigger: more of these predators are cropping up every year.

Why do scientists publish in these journals? One answer is money (or rather the lack of it). Prestigious scientific journals charge their authors for publishing, stating the costs cover careful editing and review. These “page” fees can amount to thousands of dollars. Well-funded academics charge these fees to outside grants, or wealthy institutions may cover a researcher's costs. In contrast, the typical fee in a predatory journal is less than \$200, which helps to explain why the authors of papers in these journals are disproportionately located in less wealthy countries and institutions.

Another reason is visibility: predatory journals offer more



opportunities for scholars to get their work published and cited, which helps them get jobs and grants. This reflects the perverse incentives of the “publish or perish” practices of science. It's no secret that researchers are often judged more by the quantity of their output than its quality. Universities place emphasis on metrics such as the numbers of published papers and citations when they make hiring, tenure and promotion decisions.

To warn scholars away from predatory journals, librarian Jeffrey Beall developed a list of them in 2008. But his approach was criticized as subjective and even defamatory. Other lists have also been subject to dispute, in part because there was no agreement on precisely how to define predation.

Recently, after much debate, some researchers have reached a consensus definition; it includes presenting false and misleading information, among other features. As a result, scientists may now be able to make more useful lists. That is well and good, but it addresses the symptoms more than the disease.

To put an end to predatory practices, universities and other research institutions need to find ways to correct the incentives that lead scholars to prioritize publication quantity in the first place. Setting a maximum limit on the number of articles that hiring or funding committees can consider might help, for instance, as could placing less importance on the number of citations an author gets. After all, the purpose of science is not merely to produce papers. It is to produce papers that tell us something truthful and meaningful about the world. ■

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It is time to rethink how we advance health equity



The private sector, including pharmaceutical companies like Takeda, can play a pivotal role in advancing health equity in the United States and around the world. Addressing health inequities will require taking a step back and broadening the lens through which we view and approach the problem of health inequities – as industry professionals and as fellow members of a global community that is united behind a set of shared goals for a sustainable future.

Imagine instructing a patient to follow strict dietary guidelines because their recovery depends on it but it's not clear how their preferred food fits the categories. Where does hummus fall on this food pyramid? What about cassava, edamame or refried beans? And what if their refrigerator is empty and their pantry is bare?

Imagine a patient whose emergency surgery kept her in hospital for days, who missed too many shifts at work and lost her job as a result. A patient who missed appointments because he had no one to look after his children, or someone who couldn't make it to the clinic because he lacks the cash to pay for parking or the bus or who has to choose between medicine and paying next month's rent. Imagine a patient who ends up in the emergency room – repeatedly – because she's not able to get the routine care she needs.

These are examples of situations that lead to big differences in people's health in

the United States and globally, independent of whether they receive good (or bad) medical care. These are the realities that patients face and fight every day that healthcare providers may or may not realize are happening and that contribute to poor health outcomes.

“The pandemic was a stark reminder of just how much work there is still to be done – starting with how we tackle the social determinants of health.”

The difficulties of COVID-19, its devastating and disproportionate impacts on communities of colour, on low-income families and on other disadvantaged groups, stoked new levels of frustration and fury with the lack of fairness that persists within health systems around the world. The pandemic was a stark reminder of just how much work there is still to be done, starting with how we tackle the social determinants of health.

ADDRESSING THE ROOT CAUSES OF HEALTH INEQUITIES

When there is health equity, every person has a fair and just opportunity to attain their full health potential, regardless

of social position or socially determined circumstances. This isn't always the case, and today's striking and persistent health inequities stem from the many ways those opportunities are compromised or crushed outright by factors and circumstances that have little or nothing to do with the physical body or genetic makeup. A person's health and life expectancy are heavily influenced by the social, environmental and financial conditions in which they are born, grow up, work, play and age^{1,2}.

Working towards the health equity ideal will require addressing the social determinants of health, their effects and their underlying causes (**Fig. 1**). As Bishop Desmond Tutu said, “there comes a point where we need to stop just pulling people out of the river; we need to go upstream and find out why they're falling in.”

We recognize that meaningful change can start at the corporate level and that we have more responsibility now than ever to create the world we want to leave for the generations to come. Takeda is a healthcare company dedicated to building trust in the

“We need to make equity core to the entire business. Health equity is not just an outcome, it is a process.”

communities we serve, and we insist on maintaining a holistic view of people's lives as we make good on our commitment to bring better health and a brighter future to patients. These are the values that drive us to advance health equity.

We believe that companies like ours need to take a similarly holistic approach in how we interact within the global ecosystem. We need to make equity core to the entire business. Health equity is not just an outcome, it is a process – what Camara Jones called “an ongoing process of assurance”. Advancing and improving the process to achieve health equity will involve many sectors – public, private and civil society – working together. The question is how.

GLOBAL PARTNERSHIPS THAT EMBOLDEN LOCAL LEADERSHIP

Through our own professional experiences as physicians, and through Takeda's collaborations, we have come to see that an important way forward is to encourage and support communities to lead the charge. We've learned that when communities themselves redesign or strengthen systems from the ground up, with our partnership, it can effectively and sustainably reduce the inequities they're facing.

Structured collaborations among corporations, government, nonprofit organizations or academia have been around for decades with mixed results. The most successful partnerships



This illustration is based on the original 2017 Robert Wood Johnson Foundation's "What is Health Equity" graphic.

Figure 1. The health equity challenge. Health equity is achieved when everyone has a fair and just opportunity to attain their full health potential regardless of social position or other socially determined circumstances, which means addressing social determinants of health, such as income and education levels, food insecurity, housing stability, racism and gender discrimination. Achieving health equity requires multi-sector collaborations between industry, health research and care delivery systems, government and community partners working together to address health disparities and inequities that disproportionately impact disadvantaged and underserved communities and patients. *Source: The illustration above is based on the original 2017 Robert Wood Johnson Foundation's "What is Health Equity" graphic.*

are those that are structured and governed in ways that leverage each partner's particular resources and strengths. For collaborations seeking community-level impact, that means putting community leaders in the driver's seat, making decisions based on local needs and priorities. It means 'decolonizing' global health efforts and instead co-creating solutions that empower communities to meet their own immediate needs while also developing solutions that narrow existing inequities and prevent future ones over the long term.

Achieving community-level impact is what we've sought to do through our own health equity partnerships. Since 2016, Takeda has been teaming up with non-governmental organizations (NGOs) to help doctors and researchers in low- and middle-income countries to build their capacities to address health inequities in their communities.

"For collaborations seeking community-level impact, that means putting community leaders in the driver's seat, making decisions based on local needs and priorities. It means 'decolonizing' global health efforts."

Projects include helping to build cancer care programmes in Kenya and Tanzania and establishing a community-based mental health program in Haiti³. The projects in which Takeda partners with NGOs focus on sharing scientific

and technical knowledge that is critical to building health research and care delivery systems in underserved communities.

Takeda employees contribute their scientific and technical expertise virtually and on-site through project teams composed of NGOs, academic partners and local medics, scientists and healthcare workers. Hundreds of Takeda experts have participated in these knowledge sharing programmes and we currently have approximately 150 community partners in 30 countries.

We learn a lot from these partnerships. We gain valuable insights into what it takes to identify and address local health inequities and how the private sector can be most effective helping communities tackle local issues, empowering communities and improving patient health now and for the next generation. Takeda's employees bring back innovative

ideas, new energy and a sense of urgency to activate change, within Takeda and across the industry. These partnerships inform what we do as a company and help us integrate health equity principles and priorities into our business activities.

EMBRACE AND ENACT THE 'MEGACOMMUNITY'

Partnerships that leverage private sector resources, civil society and governmental expertise and deliver reciprocal impact are needed now more than ever. Health inequities are a multifactorial problem that can manifest in each and every part of a person's health journey, anywhere, and at any time. While we can understand the social determinants of health, addressing and even solving any of them singularly will not move the needle when it comes to enabling health equity across communities globally. No one entity can do this alone, and

Partnering to achieve community-level impact



Dominican Republic: Strengthening the local COVID-19 response and pandemic preparedness to protect public health.

Dr Robert Paulino-Ramirez in the Dominican Republic has been involved in the creation of a world-class research hub, the country's first and only such facility dedicated to the study of global health and infectious diseases. When the COVID-19 pandemic struck the country, Paulino-Ramirez and his team were able to accelerate testing thanks to the specialized equipment and training they had received from Takeda in partnership with the NGO Seeding Labs. As a result, the Institute of Global Medicine and Tropical Health at Universidad Iberoamericana is now able to process more than 1,000 COVID-19 tests daily. And once the acute phase of the health crisis passes, the Institute's expanded research capacity will set them up for success in mitigating the impact of future health emergencies and protecting public health.

look at our researchers and where we conduct our research to create opportunities for providers and patients outside of the usual geographies. We can set up trial sites in more communities including those who are underserved. We can hire staff who are based in the same areas as the patients we want to recruit – strengthening local economies as an added benefit. We can provide training on how to engage more effectively with participants from different backgrounds. We can create mechanisms that enable patients from different communities to help define our research priorities. We need to ask ourselves: How are we engaging, empowering and elevating patients – from both underserved and more advantaged communities – to guide our work?

We also need to:

- Commit to continuously deepening our presence and understanding of global communities and our community-level engagement;
- Foster closer and long-standing relationships with community leaders and patient groups;
- Focus on improving patient outreach and communication to enhance awareness of trial opportunities;
- Take to heart the regulatory guidance on broadening eligibility criteria wherever possible to maximize inclusivity⁵;
- Remain aware of the many social and environmental barriers to trial participation and work proactively to clear those barriers; and
- Consider and address issues related to housing and transportation challenges and food insecurities, and revise scheduling to accommodate inflexible work schedules or issues with childcare.

everyone must do their part.

Progress towards many global health goals has been threatened, halted and, in some cases, even reversed by service disruptions and other pandemic-related burdens on health systems. To get back on track, we need to increase investment in upstream programmes led by organizations that are already gaining traction on addressing

“We need to increase investment in upstream programmes led by organizations that are already gaining traction on addressing the social determinants of health and the root causes of health inequities. We can be catalytic.”

the social determinants of health and the root causes of health inequities. We can be catalytic. We can be one of many doing their part for ‘megacommunities’, a problem-solving partnership dynamic that sheds what the authors of a book by the same name described as the traditional top-down, command-and-control, reductionist management methods in favour of innovative, integrative and holistic approaches. We can support partnerships that focus on understanding the complexities of an issue as much as on finding solutions⁴.

Building local capacities to meet local needs is the first part of the equation. Helping patients to achieve their best possible health can't be ensured without also clearing the deep-seated hurdles of poverty: food deserts, water scarcity, unstable housing and low education and employment levels. Whether you're a first-year obstetrics and gynecology resident in Detroit, United States, or a practising cardiologist in Erlangen, Germany, as we were, the lesson is the same, and often learned the hard way: a positive patient outcome, today and in the future, depends on evaluating

and understanding the whole person, their life situation and life experience. We can't just think about the science and the medicine. We can help a clinic in an underserved community build capacity to treat more patients but those patients and their families still need food, transportation and jobs to survive and thrive past the initial treatment.

We are still learning how to address the social determinants of health but know that our partnerships to build local capacity within communities have put us on the right path towards health equity.

INCREASE DIVERSITY IN CLINICAL TRIALS

Takeda believes that diversity in clinical trials is critical. Trials should represent the patients who will ultimately benefit from using the product. With diverse trials, we gain the clinical knowledge to effectively reach broad patient populations and create shared learnings for everyone.

But how can we achieve a meaningful representation of diverse participants and providers as we strive to bring innovative new therapies to the world? To start, we can

Lessening a clinical trial's reliance on in-person visits may be improved with remote trial modalities, but these require access to technology that some patients may not have. Digital solutions are one possible approach to managing a trial, and during the COVID-19 pandemic, technology played a pivotal role in healthcare. But we also witnessed how that digital shift exacerbated inequities among those who lack Internet access at home, or a smartphone, or a good data plan. Technology has become a new determinant of health.

Takeda is committed to continuing to enhance the ability for patients and communities to inform clinical trials, their design and their execution. Patients and communities have the answers for how to overcome the burdens of participation, by meeting patients where they are in their lives and building trust. Building confidence is also key to recruiting a diverse cohort of patients for clinical trials and helping them stay committed for the duration of the trial.

Takeda's efforts to understand and engage patients don't stop when a trial is over. We have to be vigilant about looking at health outcomes and how pharmaceutical innovation is contributing to improving patients' health and quality of life. This type of assessment of medicines, diagnostics and devices is challenging, but even more so for underserved populations who are too often left out of the picture.

SHIFTING MINDSETS FOR AN INCLUSIVE WAY FORWARD

We know we are not the first or only company in our industry – or any industry – that is already hard at work thinking about how to achieve health equity. We believe that the solution is to take an inclusive approach, one that recognizes the expertise of each person, each community and each entity, incorporating

Partnering to address local inequities



Vietnam: Improving treatment for a rare disease that is prevalent in developing countries.

Dr Anh-Hoa Pham Nguyen in Vietnam was able to expand her work and career path as a principal research investigator through a programme established by Takeda and the NGO Cures Within Reach. She is now leading clinical trials at three hospitals studying the use of inexpensive and readily available cancer medicines to improve outcomes for children with biliary atresia (BA), a rare congenital liver disease that causes bile duct inflammation and destruction that has a high disease burden in developing countries.

expertise shaped by individual lives and personal experiences.

At Takeda we are learning to find our way towards tackling the issues surrounding healthcare equity and contributing to global health goals in meaningful ways. To help us achieve our aims and to build on our corporate philosophy which puts patients first followed by building trust within society, we created a centre of excellence called the Center for Health Equity and Patient Affairs. The centre is composed of a dedicated multidisciplinary team working internally and externally globally to address health inequities, and build structural and knowledge capacity in communities. The centre also provides eligible patients with early access to Takeda medicines, brings together stakeholders from multiple sectors to solve problems that are too large for one entity to solve, and which engages patients throughout the development process.

One of our goals is to inspire and motivate others, mindful that we are still at a critical early stage of action. We know that achieving health equity

requires everyone from across our global organization to have an internalized health equity mindset. We know that this work should continue to 'live' inside the heart of our organization and be the driving force as both a business priority and a moral imperative.

We are clear-eyed about the role that we can play. By forging and nurturing partnerships that include the community, government and other businesses – within and outside of health – we can effect change that makes an impact and fortifies communities around the world today, tomorrow and for generations to come.

It's on all of us to close the gaps that persist, reduce disparities and provide equitable access to care. We invite you to join us on this collective journey to provide the best possible healthcare and to make the best possible health outcomes a reality for everyone.

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JUNE

1972 Neutrino Trap

“It is believed that the sun’s radiant energy originates with thermonuclear reactions deep in the interior. One product should be a flood of neutrinos: massless, uncharged particles that interact so little with other particles that solid bodies such as the earth are virtually transparent to them. Raymond Davis, Jr., of the Brookhaven National Laboratory has devised a detector to test the theory. It is buried a mile under solid rock in the Homestake Gold Mine in Lead, S.D., a huge tank containing 100,000 gallons of the dry-cleaning solvent tetrachloroethylene, 85 percent chlorine. When a neutrino is absorbed by an atom of chlorine, an atom of the radioactive isotope argon 37 is formed. At intervals of about 100 days the tank is swept with helium gas to remove the argon 37. Theory predicts that neutrinos are produced at such a rate that Davis’s detector should capture two neutrinos per day. Results over the past two years show that the capture rate is less than 0.2 neutrino per day. Explanations of the discrepancy are varied, but none is very satisfactory. The problem is certain to receive intense study in the near future.”



1972



1922



1872

on which the map is based. The big map is located in the hippodrome, or racetrack, at Guatemala City, and it has passed through two earthquakes without harm.”
The map still exists, albeit as a tourist attraction.

We Ought to Be in Pictures

“*Scientific American* has entered the motion picture field, as producers of *Scientific American* films, in collaboration with the Coronet Films Corporation of Providence, R.I. The films, which will appear once a month, will be shown in theaters throughout the country. Subjects will be taken from our columns and transplanted to the screen. We also have inaugurated a special radio-phone broadcasting talk in order that we might report and comment on the scientific news of the day. We are using the WJZ station of the Radio Corporation-Westinghouse organizations, located at Newark, N.J., covering a range of several hundred miles. In the very near future we

shall make arrangements to cover more or less the entire country.”

1872 Solar System Causes Cholera

“B. G. Jenkins recently read, before the Historical Society of London, a remarkable paper, in which he maintained that cholera is intimately connected with [the cycle of sun spots, which has a period of 11.11 years]. He said, ‘Cholera epidemics have, I believe, a period equal to a period and a half of sun spots. The date 1816.66 was shortly before the great Indian outbreak; another period and a half gives 1833.33, a year in which there was a maximum of cholera; another, 1849.99, that is, 1850, a year having a maximum of cholera; another, 1866.66, a year having a maximum of cholera; in 1883.33 there will be a maximum. I am not prepared to say that sun spots originate cholera; for they may both be the effects of some other cause. My own opinion is that planets, in coming to and going from perihelion—more especially about the time of the equinoxes—produce a violent action upon the sun [producing] a maximum of sun spots, and in connection with it a maximum of cholera on the earth.’”

1922 Guatemala in Two Acres

“The republic of Guatemala, to make it easy for visiting capitalists to decide on proposed investments, has built what seems by all odds the most extraordinary relief map in the world. This map is two acres in extent, and shows every contour, every town and every stream or lake in Guatemala and the neighboring territory of British Honduras. The giant topographical map is of concrete, assembled in sections. Almost two years were spent making the molds, and checking them up. The ultimate cost was \$100,000, and another like sum was spent in gathering the data



1972: The map shows the “range of submarine-launched ballistic missiles that could hit strategically important targets in the U.S.S.R., assumed to include population centers and industrial complexes, within 200 miles of the border (gray areas). Contours are concentric with the border. The solid (blue) contour shows the range of the Polaris A-3 and Poseidon C-3 missiles (2,500 nautical miles). The two inner broken contours show the ranges of older missiles. The two outer broken contours show the estimated ranges of the Navy’s proposed undersea long-range missiles (4,500 and 6,000 nautical miles). Black dots denote home ports and forward bases of the U.S. missile-submarine fleet.”

Sanitary Lead Pipes

“Several citizens of Sacramento, Calif., having been poisoned by the use of what is known as the ‘sanitary composite’ water pipe. The Board of Health has ordered its use to be discontinued. Water flowing through this pipe was found, on chemical analysis, to contain lead and arsenic. The pipe in question is believed to be composed of a species of brass.”

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Skin Cancer around the World

This leading cancer affects some populations and regions much more than others

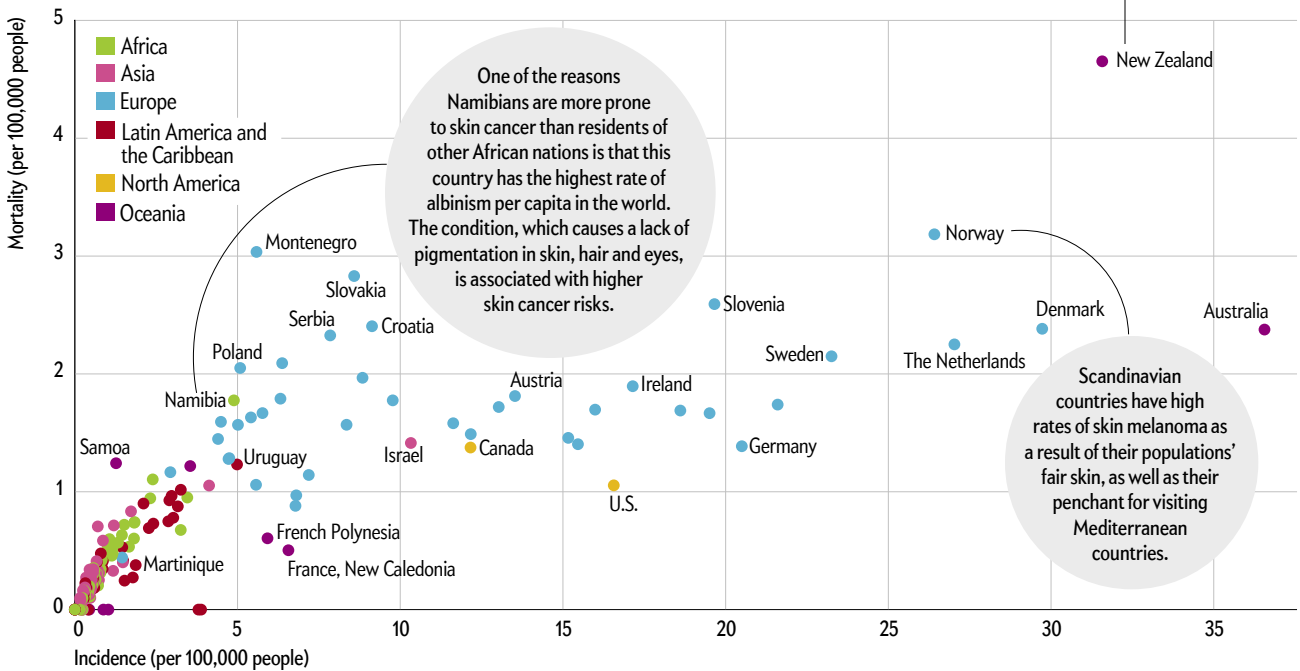
Skin cancer is the most common form of cancer, and because older people make up a greater share of the population in many places, including the U.S., it is on the rise. The main cause of skin cancer is exposure to the sun's ultraviolet rays, but the risk varies greatly across the globe because of differences in skin pigmentation—which protects against skin cancer—and the amount of direct sunlight that regions receive. “Skin melanoma is nearly 30 times higher in whites than in Blacks,” says Ahmedin Jemal, a cancer epide-

miologist at the American Cancer Society. “And even in white populations there is a difference in susceptibility—those with fairer skin, blue eyes and blond hair are more susceptible.”

Yet there are reasons for optimism. New treatments for skin cancer, including immunotherapy, have helped raise survival rates, which are now around 93 percent after five years for people diagnosed with melanoma relative to the general population.

UV radiation is about 40 percent stronger in New Zealand than it is at corresponding latitudes in the Northern Hemisphere. Because of Earth's tilt, the Southern Hemisphere is closer to the sun during its summer than the north is during its own summer.

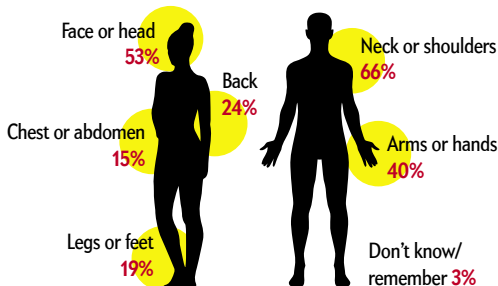
Skin Melanoma: Country-Level Mortality and Incidence Rates in 2020 (age-standardized)



The Where and When of Sunburns in the U.S.

A May 2021 study in the *American Journal of Preventive Medicine* analyzed a survey of more than 4,000 U.S. adults to find out what people were doing when they got sunburned and where burns occurred. Although sunburns are a major risk factor for skin cancer, exposure that doesn't lead to a burn can still be harmful, Jemal says. “It's important not to think you're safe just because you're not getting sunburned.”

Locations on the Body Where the Most Recent Sunburn Occurred
(percent of more than 3,000 survey respondents that ticked each box)



Activities Adults Were Engaged in When They Experienced Their Most Recent Sunburn



- Swimming or spending time in water **33%**
- Working outside own/family/friend's home **26%**
- Traveling or vacationing for leisure **21%**
- Engaging in nonswimming physical activity **14%**
- Attending an outdoor event **13%**
- Relaxing (e.g., reading, napping) **11%**
- Trying to get a tan **6%**
- Working at job **5%**
- Drinking alcohol **3%**

Sources: GLOBOCAN 2020; Global Cancer Observatory; International Agency for Research on Cancer 2022 (incidence and mortality rates); “The Context of Sunburn among U.S. Adults: Common Activities and Sun Protection Behaviors,” by Dawn M. Holman et al., in *American Journal of Preventive Medicine*, Vol. 60, May 2021 (survey results)

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