

01.2020

The blue zones diet: Eat like a centenarian

Why women's health gets shortchanged

SPECIAL ISSUE THE FUTURE OF MEDICINE

# NATIONAL GEOGRAPHIC

# Pain

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mysteries of pain—  
and exploring new  
ways to treat it.





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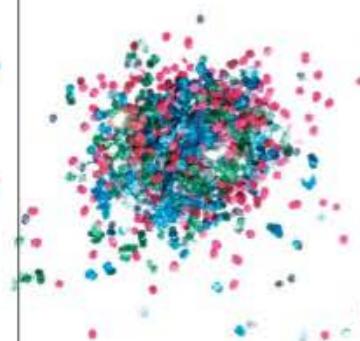
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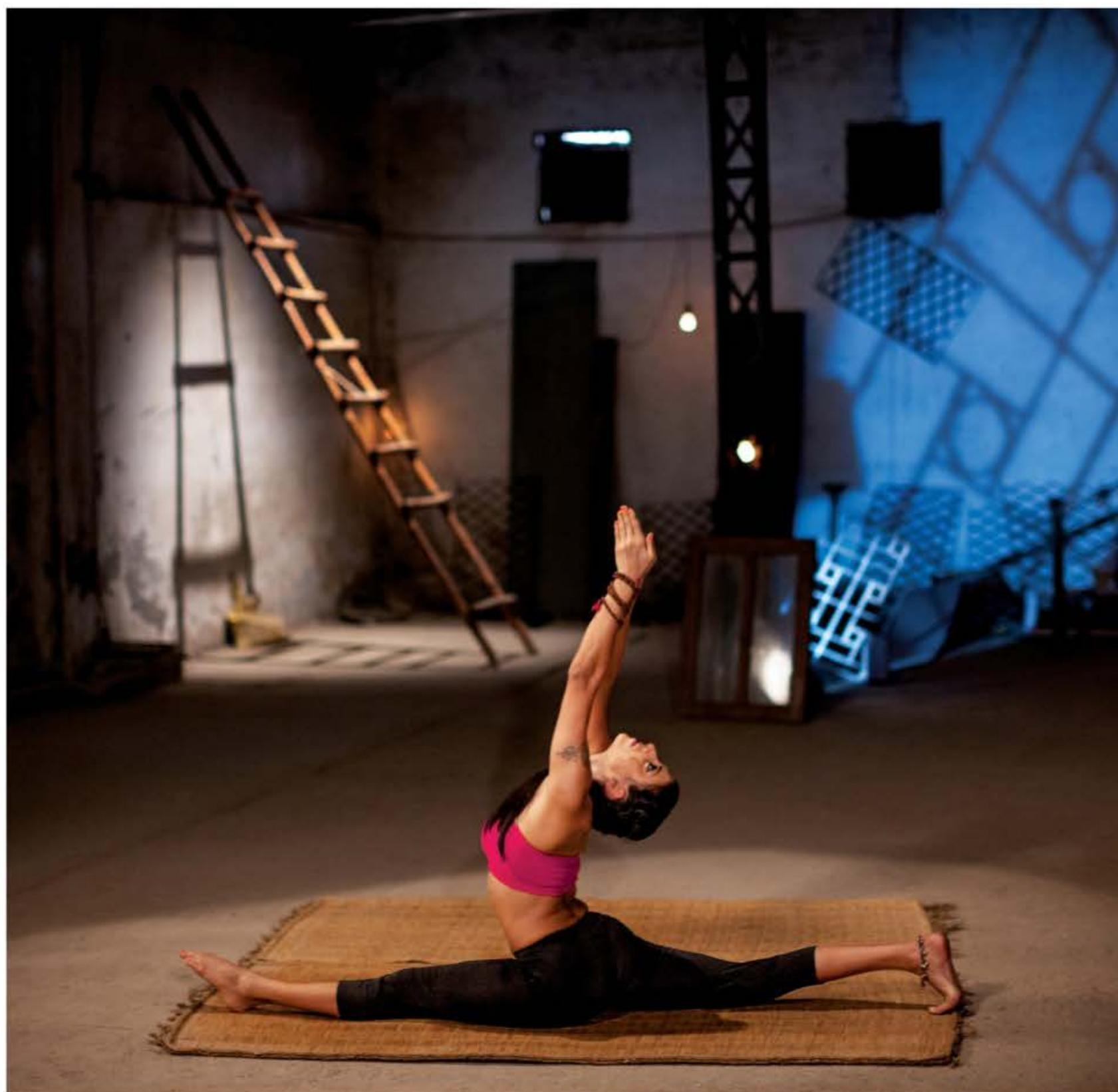
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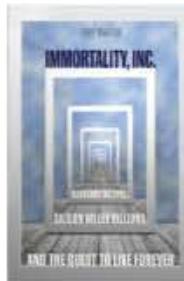
## Take your mind out to play with new *Brain Games*

Back with more mind-expanding illusions and experiments, *Brain Games* launches its eighth season by mixing brainpower and star power. Keegan-Michael Key (at left) hosts celebrity guests including Kristen Bell, Jack Black, Tiffany Haddish, and Ted Danson (at right). The two-hour premiere airs January 20 at 9/8c, followed by episodes on the next six Mondays at 9/8c on National Geographic. Previous seasons' episodes will be available in late January on Disney+.

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### BOOKS

#### ***Immortality, Inc.: Can we outsmart aging?***

In what *Publisher's Weekly* calls "a fascinating account," journalist Chip Walter follows a group of entrepreneurs determined to find a cure for aging. *Immortality, Inc.: Renegade Science, Silicon Valley Billions, and the Quest to Live Forever* is available where books are sold and at [shopng.com/books](http://shopng.com/books).

### NAT GEO WILD

#### ***In Tampa, Secrets of the Zoo revealed***

At Florida's Zoo Tampa, a stellar team cares for an exotic cast of animals and also rescues orphaned area wildlife. *Secrets of the Zoo: Tampa* premieres Sunday, January 5, at 9/8c on Nat Geo WILD.

### NAT GEO LIVE

#### ***Stalking panthers with Shannon Wild***

Attend Nat Geo Live events, coming to a venue near you. This month, hear about photographer Wild's journey to film a rare black panther in India. The Live schedule is at [nationalgeographic.com/events](http://nationalgeographic.com/events).



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LOOKING AHEAD  
TO A NEW YEAR

# Our Aim: To Illuminate and Protect

**THE NATIONAL GEOGRAPHIC SOCIETY** uses the power of science, exploration, education, and storytelling to illuminate and protect the wonder of our world. With this mission statement, we honor our legacy as a 131-year-old global nonprofit and the principles that will guide our work in the years ahead.

As we start 2020, I'd like to share our plans for what will truly be a consequential year. We will commemorate important milestones, such as the 50th anniversary of Earth Day. We'll celebrate the 60th anniversary of Jane Goodall's arrival in what is now Gombe National Park, with an immersive museum exhibit at our headquarters in Washington, D.C. And National Geographic will join world leaders at the Convention on Biological Diversity meeting in Kunming, China, to help inform a post-2020 framework for supporting global biodiversity.

In each instance, the Society's contributions will be driven by our unique approach. We illuminate the world's wonders by exploring a subject and bringing it to life with powerful storytelling. We protect what is wonderful by taking action to safeguard the planet's critical resources and inhabitants.

Our mission can take the form of photographer Joel Sartore's Photo Ark project: affecting wildlife portraits that connect us with at-risk species on an emotional level and inspire us to protect these remarkable animals.

Our mission also is exemplified by our recent work on Mount Everest, together with our partners at Rolex. Building on both organizations' histories of exploration, we used groundbreaking science to reveal how Earth's systems function and are changing over time. The expedition's achievements included installing the world's two highest-altitude automated



weather stations and collecting the highest ever ice core sample.

We work with the next generation of planetary stewards in mind. Young people increasingly identify as global citizens and unite around issues they care about. The Society is committed to growing their understanding of the world, and supporting their interest in geography and their empathy for the Earth.

Please know that your support makes the Society's work possible. Thank you for standing with us to illuminate and protect the wonder of our world.

Mike Ulica, President and COO  
National Geographic Society



**MIKE MCGILL**  
55-year-old  
skating legend

Advil

# UNBEATABLE STRENGTH

WHAT  
PAIN?

PROOF



NATIONAL GEOGRAPHIC

VOL. 237 NO. 1

# MAKING EYE CONTACT



---

PHOTOGRAPHS BY  
**REMUS TIPLEA**

A damselfly—one of photographer Tiplea's favorite summer subjects—obligingly pauses in front of a blue inflatable kiddie pool.

LOOKING  
AT THE  
EARTH  
FROM  
EVERY  
POSSIBLE  
ANGLE



When the weather is warm, Remus Tiplea spends hours in his garden in Romania, looking at damselflies. Occasionally he catches their eyes staring back.

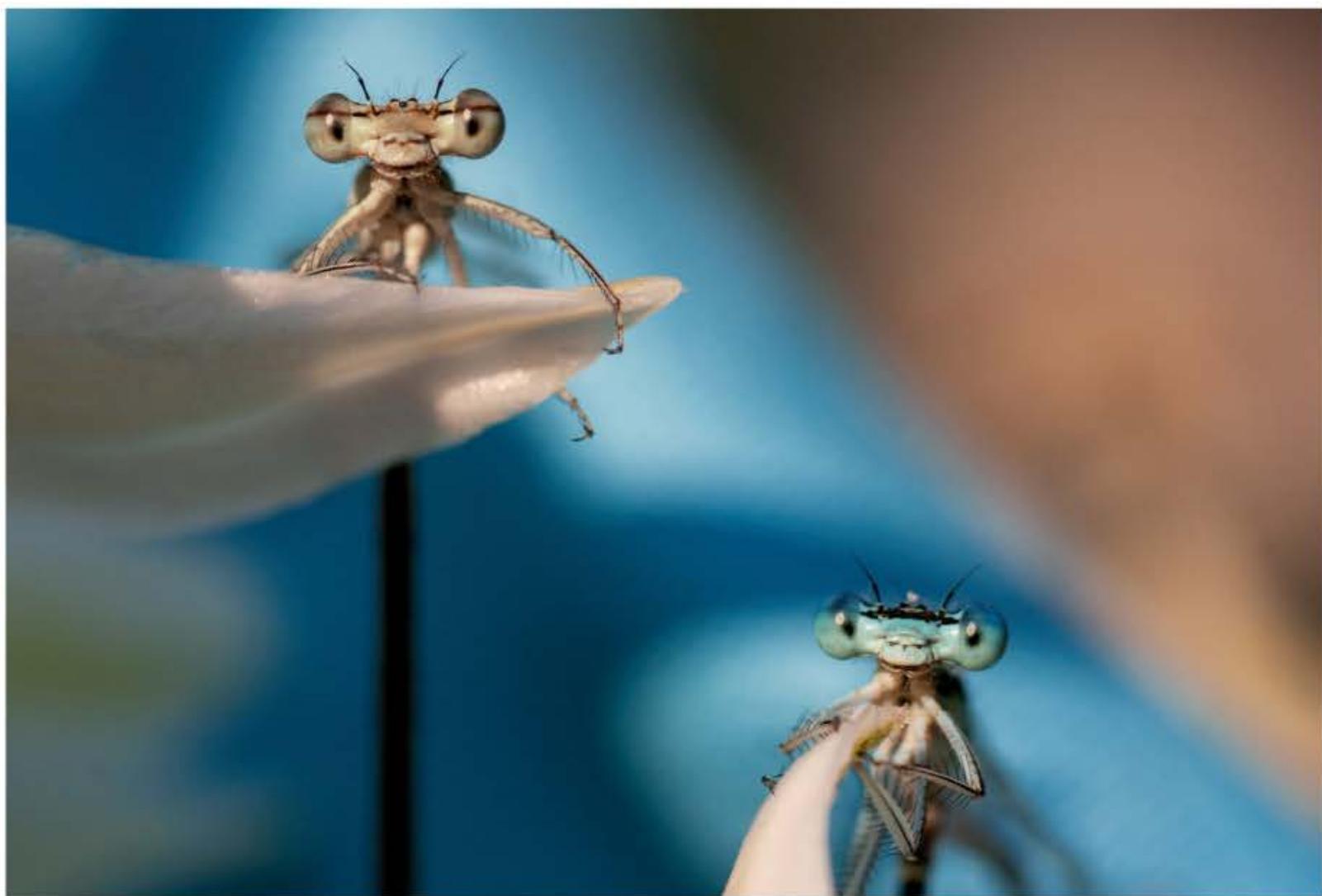




Often territorial, male damselflies will battle over the same leaf or flower. After extensive observation of the insects, Tiplea says he can tell when a battle is imminent.



Tiplea says photographing damselflies is often easier in the morning, when the light is soft and the air is usually still. In rain or bright sun, he shields the fragile insects with an umbrella.



Focusing a camera on small insects perched on vibrant leaves and flowers is a challenge, he says. It took him three seasons to find what he considers the ideal camera settings.

# THE BACKSTORY

A SUMMERTIME GARDEN TURNED OUT TO BE THE PERFECT INSECT PORTRAIT STUDIO.

**FIRST THEY WERE LOOKING** at him—and then he started looking back. Photographer Remus Tiplea noticed the damselflies perched on foliage in his garden in Negrești-Oaș, Romania. Staring with bulging eyes, the delicate insects looked inquisitive, Tiplea thought, and a little imposing. Long afternoons photographing damselflies became his summertime ritual.

Through hours of watching, Tiplea learned the behaviors of the damselflies, a close relative of dragonflies but with slimmer bodies and narrower wings. He observed when they got hungry, when they reproduced, and what caused them to suddenly

take flight. He saw how they behaved in rain and how they chose where to sleep. With time, he could tell their gender and the dominant qualities in mate selection. If he saw multiple damselflies in one frame, he'd have a few seconds to shoot before they'd show themselves as territorial rivals (by starting to fight) or lovers. "They would ignore me completely," he says.

As years have passed and summers have grown warmer, Tiplea has noticed fewer damselflies at his garden pond. "Their number is inconsistent," he says—but "the important thing is that we are together in the same backyard."

—DANIEL STONE



When his garden population is low, Tiplea captures damselflies at a neighboring pond.

# EXPLORE

## IN THIS SECTION

- Dirty Dirt Floors
- Lab of the Future
- Bootbuilding Tools
- How Many Passports?

ELIMINATING THE MYSTERIES—AND WONDERS—ALL AROUND US EVERY DAY

NATIONAL GEOGRAPHIC

VOL. 237 NO. 1

# The Science of Annoyance

LOUD CHEWING, PESKY FLIES, FLIGHT DELAYS, OR POP-UP ADS ... ARE YOU FEELING ANNOYED YET?

BY JOE PALCA

P

PICTURE YOURSELF AT A CROWDED airport departure gate. Your flight is 20 minutes late, although the illuminated sign still says On Time.

The woman on your left is noisily eating something that smells awful. The overhead TV is tuned to a celebrity gossip show, a relentless stream of Bieber after Gwyneth after Miley, plus countless Kardashians. The man to your right is *still* braying into his cell phone, and the traveler next to him is preparing to kill time with... wait, is that a toenail clipper?

Unless you are saintly or unconscious, a few things in that description—or many things, or all the things—are likely to really bug you. We know an annoyance when we experience it. But from a scientific perspective, just what makes something annoying? Are some things universally annoying, while others are specific to an individual? And does research offer any advice for preventing life's annoyances from making our heads explode?

The answers to those questions are: We don't know, we don't know, and no.

Annoyance may well be the most widely experienced and least studied of all human emotions. On what do I base that assertion? About a decade ago, fellow journalist Flora Lichtman and I made that claim in a book called *Annoying: The Science of What Bugs Us*—and in the intervening years, no one has challenged us.

After we noted the lack of studies on this topic, did scholars step up to the plate? Did even one university create a Department of Annoyance Science... endow a Distinguished Chair for Continuing Research Into Annoyance... or offer a major in annoying studies? No. Nothing. *Nada. Zilch.*

It's not as if the proliferation of things that drive us crazy has slowed in the past 10 years. Quite the opposite. Consider the explosive, ineluctable growth of Twitter: Once a seemingly benign social media platform, it now intrudes on every sphere of existence, tempting us to address matters we should rightly have no interest in. There's the pandemic of social media influencers, the unwelcome bounty of robocalls, and the invasive assault of personalized and pop-up ads. There's my personal favorite at the moment: electric scooters, threatening the well-being of pedestrians when the contraptions are moving and forming sidewalk stumbling hazards when they're parked. And the list goes on and on: See responses to *National Geographic*'s online survey about what annoys us, on this page and page 22.

**WHAT MAKES SOMETHING ANNOYING?** Our analysis came up with three qualities that seem essential.

First: It must be noxious without being physically harmful. A housefly buzzing around your head is unpleasant, but it won't kill you.

Second: It must be unpredictable and intermittent. The loud ticking of an alarm clock or the odor of a cat litter box may at first be annoying, but with constant exposure over time, it ceases to be noticeable. Psychologists' term for this gradual tolerance of a stimulus is habituation. Yet when an unpleasant noise or smell comes and goes, it becomes annoying each time it shows up.

The intermittent nature of annoyances makes them hard (if not impossible) to anticipate and thus to prepare a defense against. If you know you're going to be stuck in traffic, you might be able to take it in stride or bring along a distraction. But when the slowdown is unexpected, it gets to you before you can stop yourself.

Third and finally: To be truly annoying, something has to persist for an uncertain period of time. A flight that's delayed an hour is a bother, but tolerable, so long as it really is just an hour. A flight that's delayed and delayed and delayed, with no explanation and no end in sight, is excruciatingly annoying.

**Joe Palca** is a science correspondent with NPR. His ability to annoy others is legendary.

## Our annoying survey answers

In an online survey, *National Geographic* asked readers to name their most vexing annoyances by category. Here are some of their responses.

### The most annoying technology

Robocalls ... Pop-up ads ... Selfie sticks ... Other people's cell phones ... Electric scooters ... Captchas (typing symbols to prove you're not a robot) ... Virtual assistants like Alexa, Echo, Siri ... "Everything after the wheel."

### The most annoying noise

Buzzing insects ... Barking dogs ... Leaf blowers ... Open-mouthed chewing ... Car alarms ... People singing really badly ... Construction ... Entitled people screaming ... Knuckles cracking ... Loud neighbors ... "Being told no."

### The most annoying people

Fakers ... Telemarketers who don't stop at the first NO ... TSA agents ... Line cutters ... Narcissists ... Low talkers ... Celebrities ... Bigots.



SMARTPHONES



LOW TALKERS



Now it could be that you read that last paragraph and said to yourself, Wait a minute—a delayed flight isn't that annoying. If I have a good book to read, I don't mind waiting in an airport. That speaks to another key feature of annoyance: It's "highly context-specific," says Russell Shilling, the American Psychological Association's chief scientific officer. "There is a lot of variability between individuals and cultures." For example: The same kind of intermittent, unexplained delays that might exasperate airline passengers are just part of the job for a pilot.

As for an example of annoyances varying by culture: If a U.S. family visits a beach with only one other family present, they'll tend to throw down their towels a discreet distance away. In some Mediterranean countries, plopping down right next door is the norm, but that would cause many Americans to seethe.

Shilling says individual variability is one reason it's so hard to tease out the universal properties of annoyances. But that individuality may be useful in certain settings. A psychiatrist friend of mine notes that while her patients may be reluctant to talk about their private dark thoughts, they have no problem railing about the people and situations that annoy them. Encouraging people to share their annoyances could be an easier way to open a window into their psyches.

**AN INTRIGUING THING** about annoyances is how they appear to change over time. A decade ago, our research led us to conclude that one of the most annoying things in the world was listening to someone else's loud cell phone conversation. We hypothesized that the reason it was so annoying is that our brains are naturally predisposed to painting a complete picture of reality, but when you only hear half of a conversation, that's not possible.

Then, cell phone conversations seemed annoying only to the people not on the phone. Today it's the call recipients that seem to be getting annoyed. I'm not talking about receiving a robocall. I'm talking about the 20-something who recently told me that an unexpected call, even from a close friend, is annoying. The thinking seems to be, Why call when a text will do? Or even, You should have texted to ask if you could call...

If there are some things in life that are universally annoying, human physiology may provide clues to

ANNOYANCE IS CONTEXT-SPECIFIC. INTERMITTENT, UNEXPLAINED DELAYS THAT MIGHT EXASPERATE AIRLINE PASSENGERS ARE JUST PART OF THE JOB FOR A PILOT.

help us define them. We have a variety of reflexes that kick in to protect us from truly dangerous stimuli. Gagging could prevent us from ingesting something that's potentially poisonous. The blink reflex protects our eyeball if an object is heading toward it. There's even something called the middle-ear muscle reflex that protects our eardrums from damage from truly loud noises.

The reason someone with a cloying cologne is annoying may derive from the gag reflex. Likewise our response to a vuvuzela, that deafening plastic horn, may be a vestige of our natural protections from any loud noise.

Another place to look for clues to the fundamental nature of annoyance is to study people with conditions that make them particularly prone to annoyances. Just as studying people with hypercholesterolemia—dangerously high cholesterol—led to the first drugs for lowering cholesterol, so might studying people with the disorder misophonia lead to ways to help keep us from becoming annoyed.

According to the National Institutes of Health's Genetic and Rare Diseases Information Center, people with misophonia have an extreme emotional response to sounds that others find innocuous. Just hearing someone breathe or yawn or chew a potato chip can generate severe agitation in susceptible individuals. If researchers find more ways to calm those people, there may be some benefit for all of us.

**IN THE DECADE SINCE** the book came out, I've thought a lot about what makes people, things, and situations annoying, and what any of us might do to inoculate ourselves against becoming annoyed. The answer's actually surprisingly simple: All you have to do is

**Editor's Note:** The contract for this article set a strict word limit. The writer exceeded the limit; the magazine feels obliged to enforce it. We regret any annoyance this might cause, dear readers.



## Annoyances, Continued

### Popular expressions

LOL ... Cray cray ... Lean in ...  
Impactful ... Man up ...  
My bad ... Fake news ...  
Could care less ... Woke ...  
"It is what it is."

### Foods

Stinky cheese ... Okra  
... Pizza with pineapple  
... Lite beer ... Cilantro ...  
Black licorice ... "Pumpkin-spiced anything."



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INNOVATOR

# GAYATRI DATAR

BY MARC GUNTHER PHOTOGRAPH BY CHRIS SCHWAGGA

**She's helping Rwandans live cleaner by replacing unsanitary dirt floors.**

Days after graduating from business school at Stanford University in 2014, Gayatri Datar set off for Rwanda to pursue an unorthodox goal: to rid the world of dirt floors, which can make people sick.

"There are bugs all over the place. Termites. Jiggers. Worms," she explains. "Babies don't have diapers, so kids poop and pee on the floors. They're hard to clean. They don't look good. People hate them." Yet more than one billion people live on dirt because they can't afford anything better.

Datar's start-up nonprofit, EarthEnable, sells an earthen floor made of locally sourced clay, pebbles, and sand, sealed with a proprietary eco-friendly varnish. It costs about \$70 per home, far less than concrete.

EarthEnable struggled at first. Getting raw materials to rural villages proved costly. Masons had to be trained to install the floors. Quality was spotty. Datar, 34, says: "Everything that could go wrong did go wrong."

These days EarthEnable is faring better. More than 4,400 earthen floors have been installed, Datar reports, and customers love them. EarthEnable has raised money from foundations, the U.S. Agency for International Development, and a Dutch competition that supports green entrepreneurs. Best of all, Datar is working closely with Rwandan government officials who say they too want to eliminate dirt floors. □





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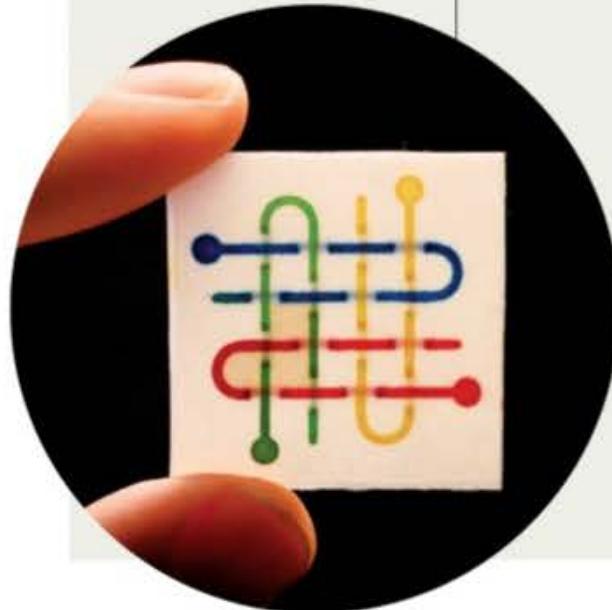
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OF SCIENCE  
AND INNOVATION**

MEDICAL SCIENCE

## A lab the size and cost of a stamp

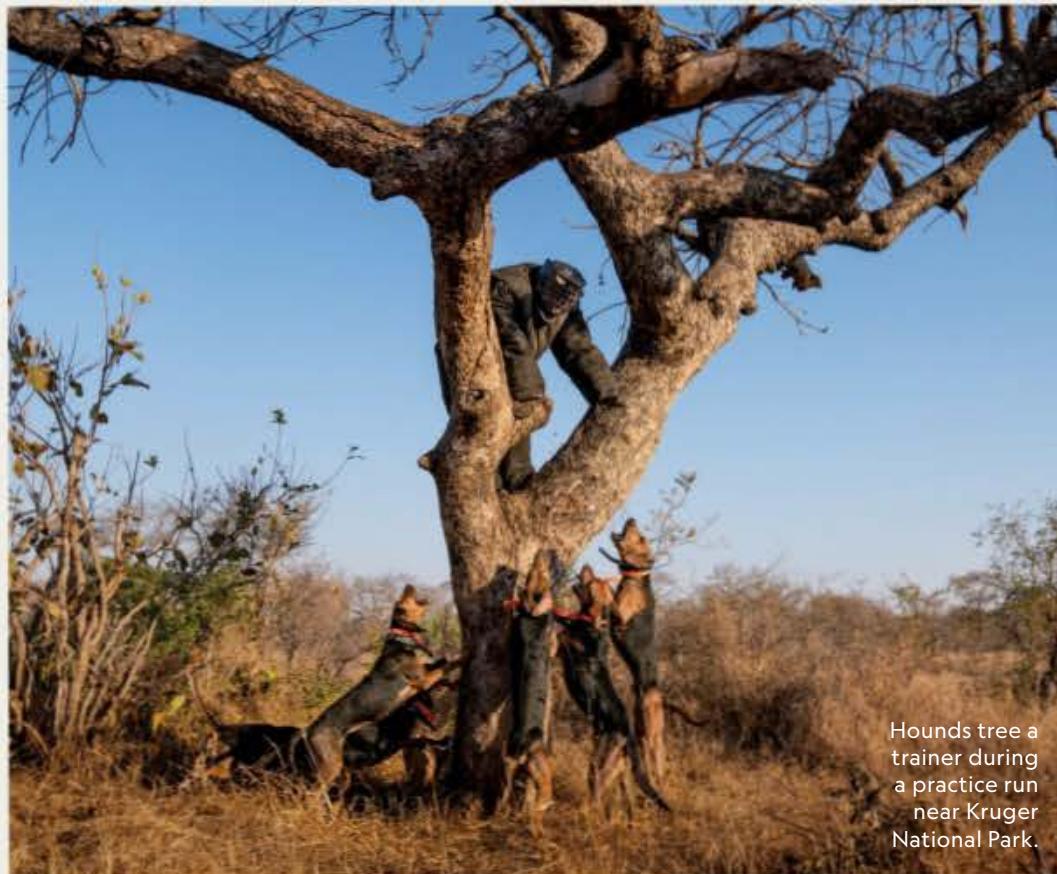
Diagnosing patients' ills often means sending samples to testing laboratories. For areas that lack such resources, Harvard's George Whitesides has spent years developing a "lab" on a stamp-size filter paper square. When this low-cost, easy-to-use device absorbs a drop of blood or urine, dots of chemical reagent change color to indicate various conditions, such as an abundance of protein. —AR



### A sparkling way to cut microplastics

All that glitters is not green: Most glitters are plastic based and take hundreds of years to break down. Enter Bioglitter, created with cellulose from eucalyptus trees. In nature, the glitter biodegrades into harmless specks, says the U.K. firm that makes it. —ANNIE ROTH

Learn more about plastic waste and take the pledge to reduce it at [natgeo.com/plasticpledge](http://natgeo.com/plasticpledge).



Hounds tree a trainer during a practice run near Kruger National Park.

WILDLIFE PROTECTION

## SNIFFING OUT POACHERS

### TEXAS FREE-RUNNING PACK HOUNDS JOIN SOUTH AFRICA'S EFFORT TO STOP WILDLIFE PLUNDERING

**TEXAS HOUNDS ARE REVOLUTIONIZING** anti-poaching work in South Africa. By some estimates, 4,000 rhinos were killed in the Kruger National Park area during the past decade; how many remain there is debated, with claims ranging from 5,000 to 9,000. Since May 2018, the hounds, raised by Texas rancher Joe Braman, have contributed to a 24 percent drop in rhino poaching in the park and a 54 percent increase in apprehensions of poachers, authorities say.

In the past, law enforcement teams that used individual lead dogs to track poachers on foot struggled to keep up. Staff at the Southern African Wildlife College, a training facility outside Kruger, were eager to test free-running dogs in the area. After visiting, Braman, a passionate houndman and part-time cop, offered to train a team of his own dogs back in Texas and ship them to South Africa. In live operations, the hounds, wearing GPS collars, track a poacher's scent, with helicopters and rangers close behind. By charging and biting en masse, the dogs keep their quarry at bay, Braman says: "If a dog starts attacking you, the first thing you're gonna do is throw the gun and climb a tree." —PAUL STEYN



## LINE OF SIGHT

PHOTOGRAPH BY  
**REBECCA HALE**

**Fine-Tuned Fish Sense**

Note the thin black stripe down this mackerel's side. That's the lateral line, part of a valuable system that reads water motion and pressure. Tiny sensors along the line, called neuromasts, allow fish to identify movement very precisely—helping them hunt prey, avoid obstacles, and swim in schools, even in the dark.

—THERESA MACHEMER

# the Workplace of the future

**A RISING TREND OF WELLNESS-FOCUSED ARCHITECTURE AND DESIGN IS MAKING INDOOR SPACES HEALTHIER AND TRANSFORMING THE WAY WE WORK.**



We spend 90 percent of our time indoors—much of that at work—and what we're exposed to impacts our health in ways we might not even be aware of. Lighting can disrupt sleep, air pollutants can

cause respiratory issues, and noise can increase stress hormone levels. But it doesn't have to be this way.

Architects, designers, and engineers are becoming more attuned to wellness in the workplace, and global rating systems that provide guidelines for creating healthier indoor spaces are at the heart of the movement. The WELL Building Standard™ rates spaces based on 11 design concepts including light, sound, and mind:

**A THIRD OF AMERICANS** aren't getting enough sleep, and electric light might be a culprit. It disrupts our natural circadian rhythm, as it's too dim for daylight and too bright for night. **Circadian lighting design is an innovative solution.**

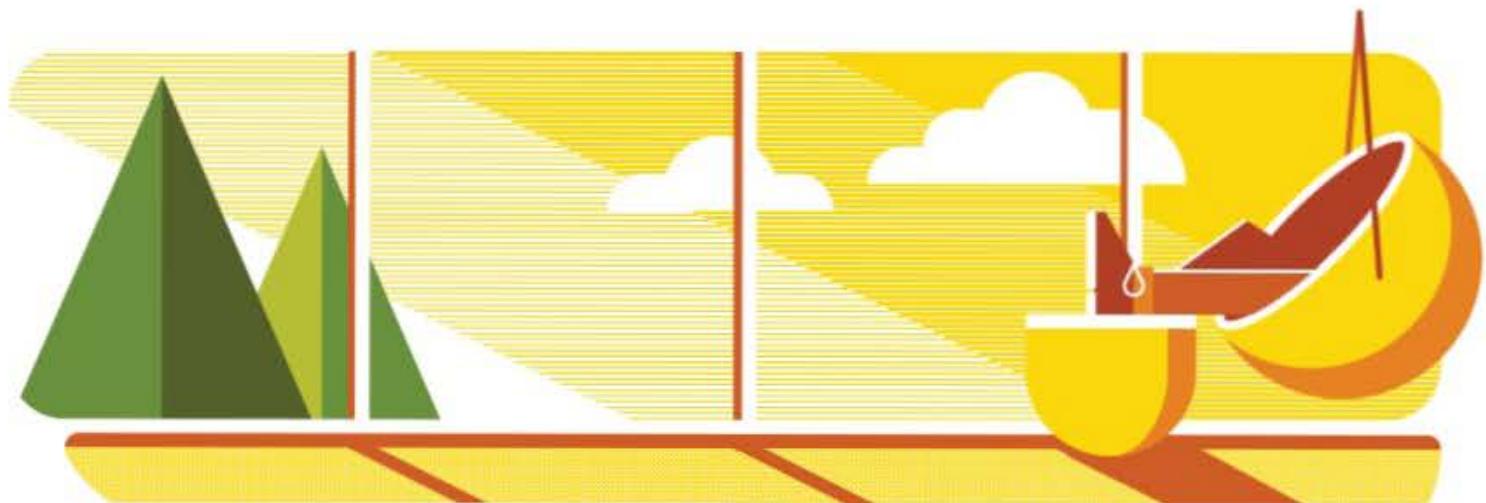
At the WELL Certified™ Gold Boston office of architectural firm Arup, the color of light inside changes throughout the day. In the morning, the light has a warm glow that slowly transitions to a cool temperature until the afternoon, when it begins transitioning back to warm.

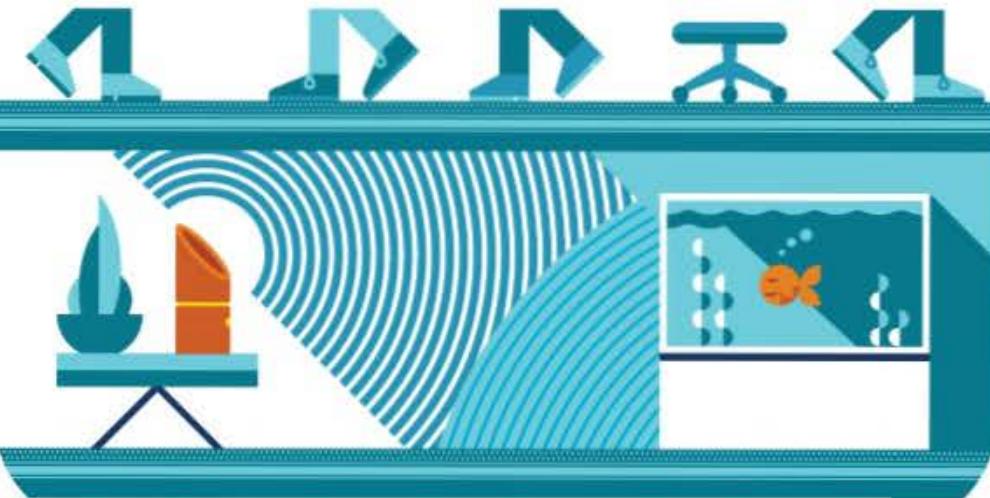
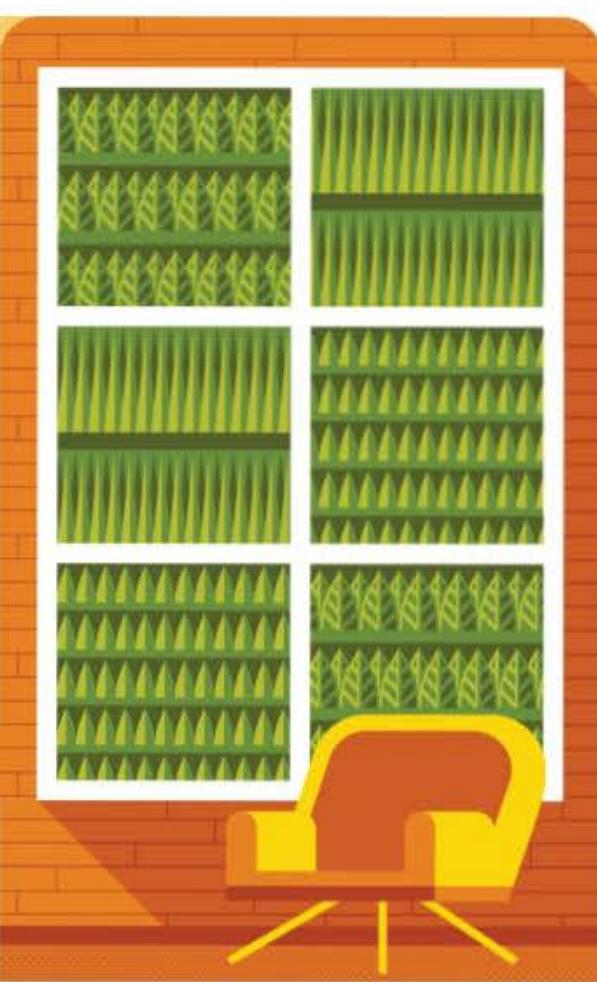
Natural daylight is still the truest form of circadian light, so designers strive to enhance it. Milliken & Company's WELL Certified Platinum Chicago showroom has semi-transparent blinds that block glare without reducing natural light, and workstations are placed near the windows to maximize daylight and views of the Chicago River.

**L** OUD SPACES TEND TO IMPACT concentration and productivity, but long-term exposure to even low-level

Light

Sound





background noise can raise stress hormone levels. Designers might create quiet spaces, install phone booths for private conversations, use white noise machines to provide an underlying hum, and integrate sound-absorbent materials.

**Carpet can act like a sponge for ambient sound,** and it can also prevent movement across the floor from creating excessive noise. In spaces with multiple floors, carpet also helps prevent the transmission of noise to the room below.

But not all carpet is equal. *Milliken* has developed an open-cell cushion backing with high-density foam for better acoustics. Product tests show that their cushion-backed carpet absorbs up to 60 percent more ambient noise than hardback carpet. Walking or moving a chair on cushion-backed carpet generates 25 percent less noise than on hardback carpet, and 90 percent less than on hard surfaces.

**M**ENTAL AND EMOTIONAL HEALTH are essential to employees' well-being. **Biophilic design—that is, design that connects people with nature**—is an innovative way to reduce stress and enhance creativity, clarity of thought, and happiness.

## Mind

Architectural firm CBRE's WELL Certified Gold office in Madrid was inspired by a cabin in the woods, and includes a green wall, furniture crafted in fluid shapes, and grass-like carpeting.

At real estate company JLL's WELL Certified Platinum headquarters in Shanghai, polished wood furniture evokes the feeling of walking in a forest. *Milliken*'s cartography-inspired carpet patterns contribute to the topography. The centerpiece is a fish tank with 360-degree views, where the smart design makes fish appear to fly freely in the air.

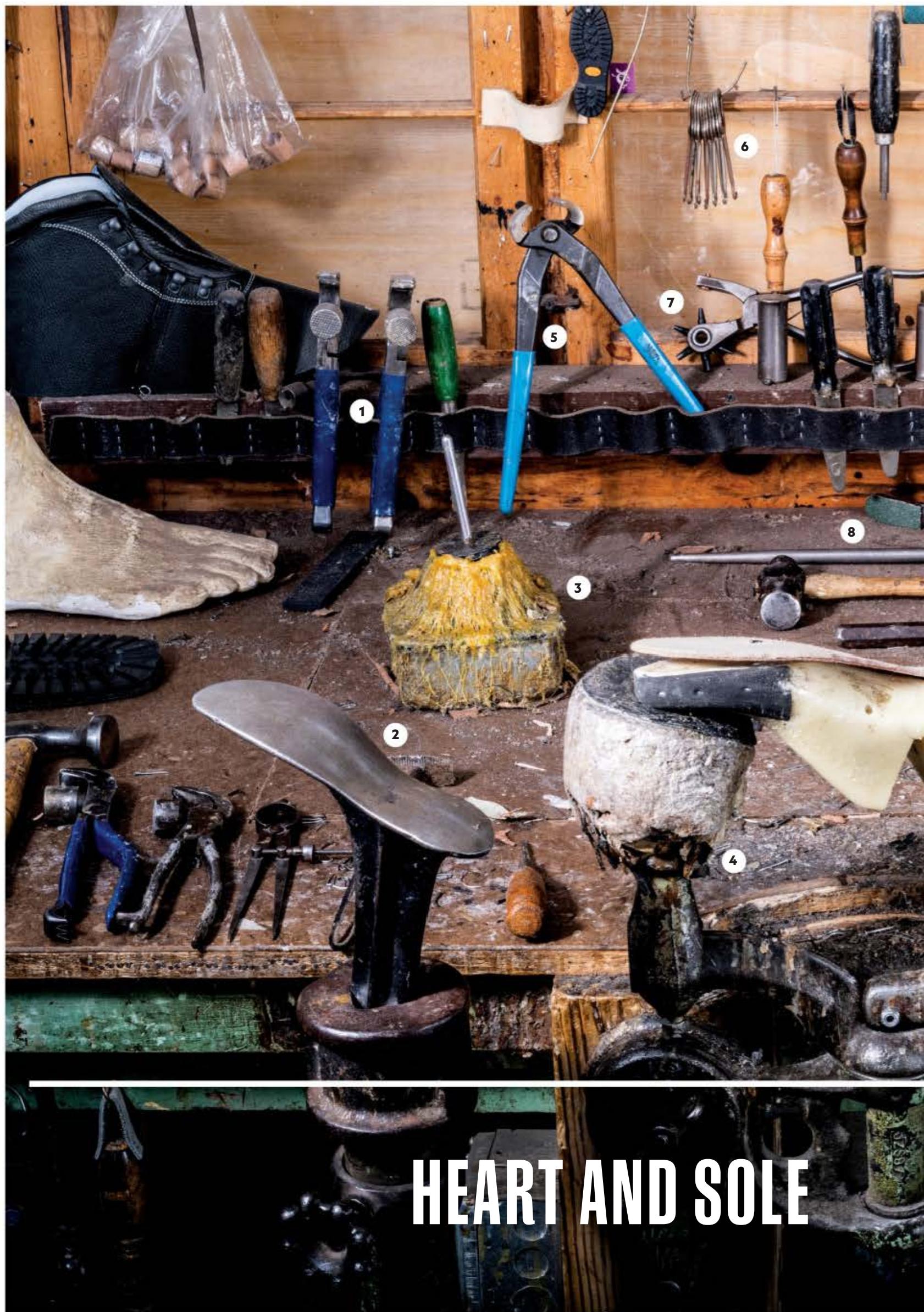
*Milliken*'s Chicago showroom features nature-inspired carpet patterns reminiscent of a meandering stream or woodland forest. The space is anchored by reclaimed tree stump tables. For fresh air, employees can stroll along the Riverwalk or relax on the rooftop garden.

As WELL and other rating systems expand globally, they have the potential to reach beyond office workspaces to transform schools, hospitals, manufacturing floors, and more. Designing the workplace of the future isn't just about the environment—it's about the experience.

- Architects, designers, and engineers
- are becoming more attuned to
- wellness in the workplace.

*Milliken*

LEARN MORE AT [MILLIKEN.COM](http://MILLIKEN.COM)





PHOTOGRAPH BY HANNAH WHITAKER

**IN 1939 A GERMAN-BORN SHOEMAKER** named Peter Limmer got the first U.S. patent for a “ski boot”—a stiff, square-toed leather shoe made to order. Today, gray-bearded Peter Limmer III hammers out about 200 pairs of hiking boots a year using his grandfather’s tools in the Intervale, New Hampshire, shop his grandfather opened. There’s a perpetual waiting list for the custom boots, priced at \$775 and up; loyalists come from as far away as Tasmania for final boot fittings. Limmer, 63, still loves his work. “The best part,” he says, “is seeing customers dance in the driveway with their new boots on.” —JENNIFER S. HOLLAND

**1. Lasting pincers**

These two blue-handled tools are part leather grabber, part hammer, used to stretch and form leather over a foot model (10).

**2. Jack stand**

This steel device holds a shoe upside down for relatively quick work on the sole or heel.

**3. Rubber cement pot**

Limmer has used his grandfather’s glue-crusted pot for 45 years. Cordwainers—another word for shoemakers—brush the adhesive on soles to attach them to shoes’ undersides.

**4. Jack stand with vise**

Used for custom work, it has a soft, leather-wrapped rest for the toe of a nylon (shown) or wooden foot model.

**5. Nail nippers**

For pulling out and cutting nails used in boots.

**6. Button hooks**

“Back when shoes had tiny buttons, they helped cobblers with fat fingers,” Limmer says of these 100-year-old hooks.

**7. Rotary hole punch**

This cuts the holes for bootlace hooks.

**8. Tools, back to front:**

Rasp, for sanding and shaping; knife sharpener; striker, for smoothing knife edges; and mandrel, for setting nails and smoothing rough spots inside the boot.

**9. Cordwainer’s hammers**

Hammers for tamping soles and tapping nails and tacks, such as those in the dish near the tools.

**10. Wooden foot model**

Limmer puts additions on standard-size models until they match the measurements of customers’ feet. Boots are built directly on the models; Limmer says “strong muscles and a beer belly help” when it’s time to pull the models out of the boots.

# THE FLU SUCKS EVERYTHING OUT OF YOU.



## Feel better in just over 2 days with XOFLUZA.\*

When the flu hits, the fever, aches and chills can flatten you fast. Over-the-counter medicines just treat symptoms, but prescription XOFLUZA works differently. It attacks the flu virus at its source with just one dose. But your window for prescription treatment is short, so you need to act fast.

**xofluza™**  
(baloxavir marboxil) tablets 20mg  
40mg  
**ONE DOSE CAN DO IT.™**

**Ask your doctor about XOFLUZA within 48 hours of your first symptoms.**

\*On average, patients felt better in 2.3 days versus 3.3 days with placebo.

### INDICATION AND IMPORTANT SAFETY INFORMATION

XOFLUZA is a prescription medicine used to treat the flu in people 12 years of age and older who have had flu symptoms for no more than 48 hours.

Do not take XOFLUZA if you are allergic to baloxavir marboxil or any of the ingredients in XOFLUZA. If you develop an allergic reaction, call your doctor immediately.

XOFLUZA is not effective in treating infections other than influenza.

Please see the following page for brief summary.

## Brief Summary

XOFLUZA™ (zoh-FLEW-zuh) (baloxavir marboxil) tablets

### What is XOFLUZA?

XOFLUZA is a prescription medicine used to treat the flu (influenza) in people 12 years of age and older who have had flu symptoms for no more than 48 hours. It is not known if XOFLUZA is safe and effective in children less than 12 years of age or weighing less than 88 pounds (40 kg).

Do not take XOFLUZA if you are allergic to baloxavir marboxil or any of the ingredients in XOFLUZA.

Before you take XOFLUZA, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. It is not known if XOFLUZA can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if XOFLUZA passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Talk to your healthcare provider before you receive a live flu vaccine after taking XOFLUZA.

### How should I take XOFLUZA?

- Take XOFLUZA exactly as your healthcare provider tells you to.
- Your healthcare provider will prescribe 2 tablets of XOFLUZA you will take at the same time as a single dose.
- Take XOFLUZA with or without food.
- Do not take XOFLUZA with dairy products, calcium-fortified beverages, laxatives, antacids or oral supplements containing iron, zinc, selenium, calcium or magnesium.

If you take too much XOFLUZA, go to the nearest emergency room right away.

### What are the possible side effects of XOFLUZA?

XOFLUZA may cause serious side effects, including:

Allergic reactions. Get emergency medical help right away if you develop any of these signs and symptoms of an allergic reaction:

- |                                |  |
|--------------------------------|--|
| • trouble breathing            | • swelling of your face, throat or mouth |
| • skin rash, hives or blisters | • dizziness or lightheadedness           |

The most common side effects of XOFLUZA in adults and adolescents include:

- |              |          |            |             |            |
|--------------|----------|------------|-------------|------------|
| • bronchitis | • nausea | • diarrhea | • sinusitis | • headache |
|--------------|----------|------------|-------------|------------|

XOFLUZA is not effective in treating infections other than influenza. Other kinds of infections can appear like flu or occur along with flu and may need different kinds of treatment. Tell your healthcare provider if you feel worse or develop new symptoms during or after treatment with XOFLUZA or if your flu symptoms do not start to get better.

These are not all the possible side effects of XOFLUZA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. Keep XOFLUZA and all medicines out of the reach of children.

### General information about the safe and effective use of XOFLUZA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use XOFLUZA for a condition for which it was not prescribed. Do not give XOFLUZA to other people, even if they have the same symptoms that you have. It may harm them. You can ask for information about XOFLUZA that is written for health professionals.

You are encouraged to report side effects to Genentech by calling 1-888-835-2555 or to the FDA by visiting [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or calling 1-800-FDA-1088.

For more information, go to [www.xofluza.com](http://www.xofluza.com)

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# NINE PATHS TO MULTIPLE CITIZENSHIP

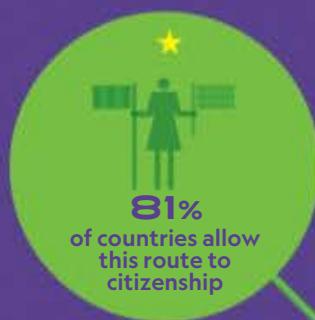
**HALF A CENTURY AGO**, most countries revoked the citizenship of a person who became a national of another country. Today some 75 percent let their people hold foreign passports, dramatically increasing citizenship options for children. There are more paths to citizenship in European countries, fewer in the Americas (although birthright citizenship is more common), and limited routes in non-democratic countries, says Maarten Vink, of Maastricht University. Having nine passports is rare; here's how it could happen.

BY MANUEL CANALES AND KELSEY NOWAKOWSKI

## MATERNAL DUAL CITIZENSHIP

Children can become citizens of the country where their mother was born and holds citizenship.

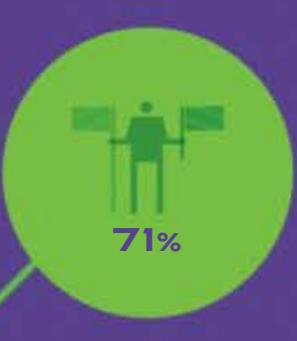
Children can pick up their mother's second citizenship, even if she wasn't born in that country.



## PATERNAL DUAL CITIZENSHIP

Children can become citizens of the country where their father was born.

Children can inherit their father's dual citizenship regardless of where he was born.



*In 47 countries, it's easier for men than women to pass citizenship to their children.*

## MARRIAGE

Nearly two-thirds of all countries grant citizenship through marriage after three years.



## HISTORY

Citizenship is granted because of ethnic, historical, or cultural ties to a country.



FAMILY TIES

OTHER BONDS

## MIGRATION

A person can get citizenship within five years of immigrating in nearly half the world's countries.



## BIRTH

Citizenship is automatic at birth, a law that's rare globally but is more common in the Western Hemisphere.

18%

## INVESTMENT

A large investment in a country can come with full citizenship, often without habitual residence.



★ Applicable to the U.S.



## NO CITIZENSHIP

The exact number of stateless people isn't known, but many millions around the world aren't recognized as a citizen by any country.



## ANTI-TERRORISM TACTIC

Countries are increasingly stripping away citizenship from people who've engaged in terrorist activities at home or abroad.

# PLANNING FOR YOUR FUTURE CAN HELP SAVE HERs

For many of us, creating or updating our will is one of those tasks that always seems to fall to the bottom of the pile. In fact, the average person takes more time to plan their vacation than to plan for their future. You owe it to yourself and your family to be prepared. When you leave a gift to the National Geographic Society in your will or trust, or by beneficiary designation, you can protect critical animal species for generations to come.



PHOTO: JOEL SARTORE, A FEDERALLY ENDANGERED FLORIDA PANTHER.  
NATIONAL GEOGRAPHIC PHOTO ARK



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# TRAVEL

## IN THIS SECTION

Costa Rica's Frogs  
Going Mudlarking  
Secluded Samoa  
New Trails in Wales



WHERE TO GO, WHAT TO KNOW, AND HOW TO SEE THE WORLD

NATIONAL GEOGRAPHIC

VOL. 237 NO. 1

# SKY-HIGH SCIENCE

**FOR ONE YEAR** Konsta Punkka traveled throughout Europe photographing Integrated Carbon Observation System research stations, which measure greenhouse gases. The stations tend to be in remote areas of the continent, but no others are as high as Jungfraujoch in Switzerland—or as accessible to tourists.

### ARRIVAL

#### RIDE UP A MOUNTAIN

The Jungfraujoch research station looks rugged and isolated—and it is—but beneath its windswept stones lie an ice palace, a chocolate shop, and the highest train station in Europe. Like the travelers, Punkka rode a cogwheel train from Kleine Scheidegg through a tunnel under the mountain to get there. After he disembarked, he stepped into a high-speed elevator. It shot him up to the research station on top of the peak where he, unlike the tourists, was allowed to bunk with the scientists for four days.

### PACKING LIST

#### BUNDLING UP

Punkka dressed for early spring in the Alps—in down, fleece, and multiple layers.

- Boots for deep snow
- Camera with three lenses
- Snow pants (warm enough to let him lie on the ground while photographing wildlife)
- A drone with three extra batteries (batteries die quickly in these harsh conditions)
- Winter mittens, with room for hand warmers (Punkka piloted the drone barehanded, so he needed to be able to warm his hands quickly)

### LAUNCH

#### 'A VERY MAGICAL MORNING'

Just before a spring storm hit after two days of "bad sunrises," Punkka went out on the upper deck with his drone. "I wanted to highlight the station, to watch the mountain with the sunrise light." He sent the drone soaring away from the peak. When it reached a good vantage point, Punkka flung his arms up in the air: "I don't often shoot myself in pictures, but I wanted to show the scale." It was so cold that after he got the shot, he hurried inside to pilot the drone from the relative comfort of the research station.



'THERE WERE EARLIER VIDEO PROJECTS THAT LOST SEVERAL DRONES. I MANAGED TO KEEP MY DRONE IN THE AIR.'  
—Konsta Punkka

GETTING THERE

BY THE NUMBERS

11,745  
FEET ABOVE SEA LEVEL

1931  
YEAR RESEARCH STATION WAS BUILT

18° F  
AVERAGE TEMPERATURE



The Jungfraujoch research station is in the Swiss Alps.

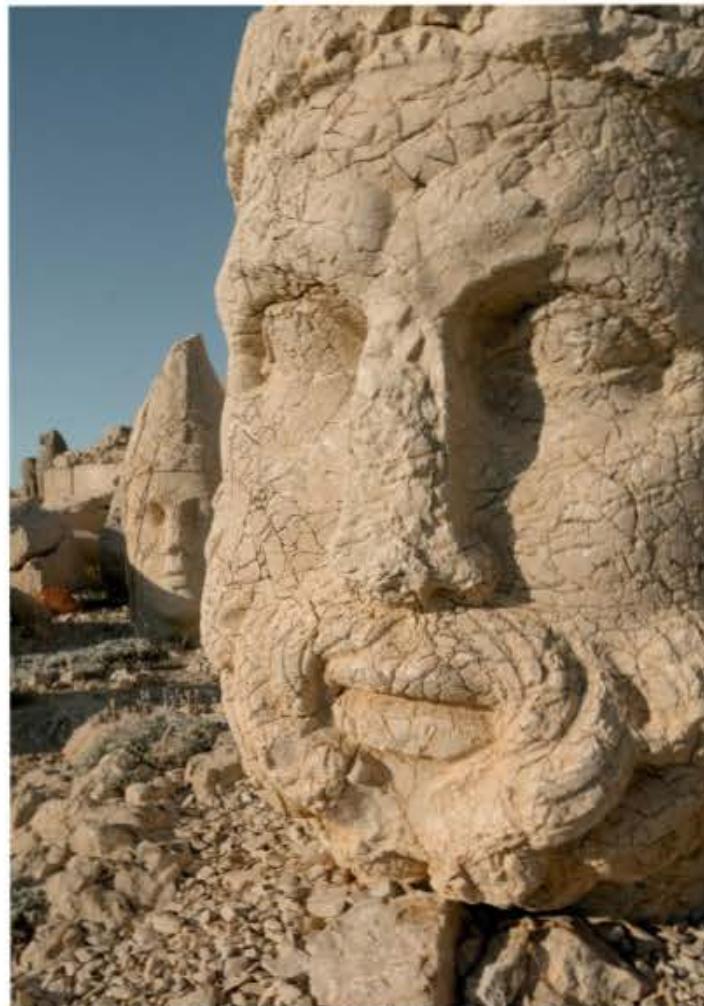
BY RACHEL HARTIGAN SHEA PHOTOGRAPH BY KONSTA PUNKKA

# A LAND CALLED SUNRISE

From the fertile plains of Mesopotamia to the twinkling metropolis of Istanbul, Anatolia has always stood at the forefront of human civilization. Poised at the crossroads of continents, Turkey is a wonderland, rich with history

Words by Andrew Evans  
Photographs by Matthieu Paley

**FROM LEFT:** Mount Nemrut, tomb  
sanctuary of King Antiochus I



Anatolia means ‘the land of the sunrise’, and each day I witness the warm light that passes from the far edge of Asia and shines onwards to Europe. Time is part of the landscape in Turkey, where humans have witnessed this same daybreak since time was first recorded. The rhythmic play of shadow and sun details every stone fragment, lights up engravings etched in ancient script, spelling out the elaborate chapters in Turkey’s long and layered history.

From the eastern border to Istanbul, I follow the time-trodden grooves in the stone streets, polished by Greek and Roman soldiers, Silk Road merchants, Christian pilgrims, Byzantine monks, Catholic crusaders and Ottoman sultans. At every site I wonder, is it Bronze or Iron Age, Paleolithic or Neolithic, and is it Greek, Roman, Byzantine, Ottoman — or all of the above? Exploring Anatolia has changed my concept of time. Indeed, Turkey redefines old.

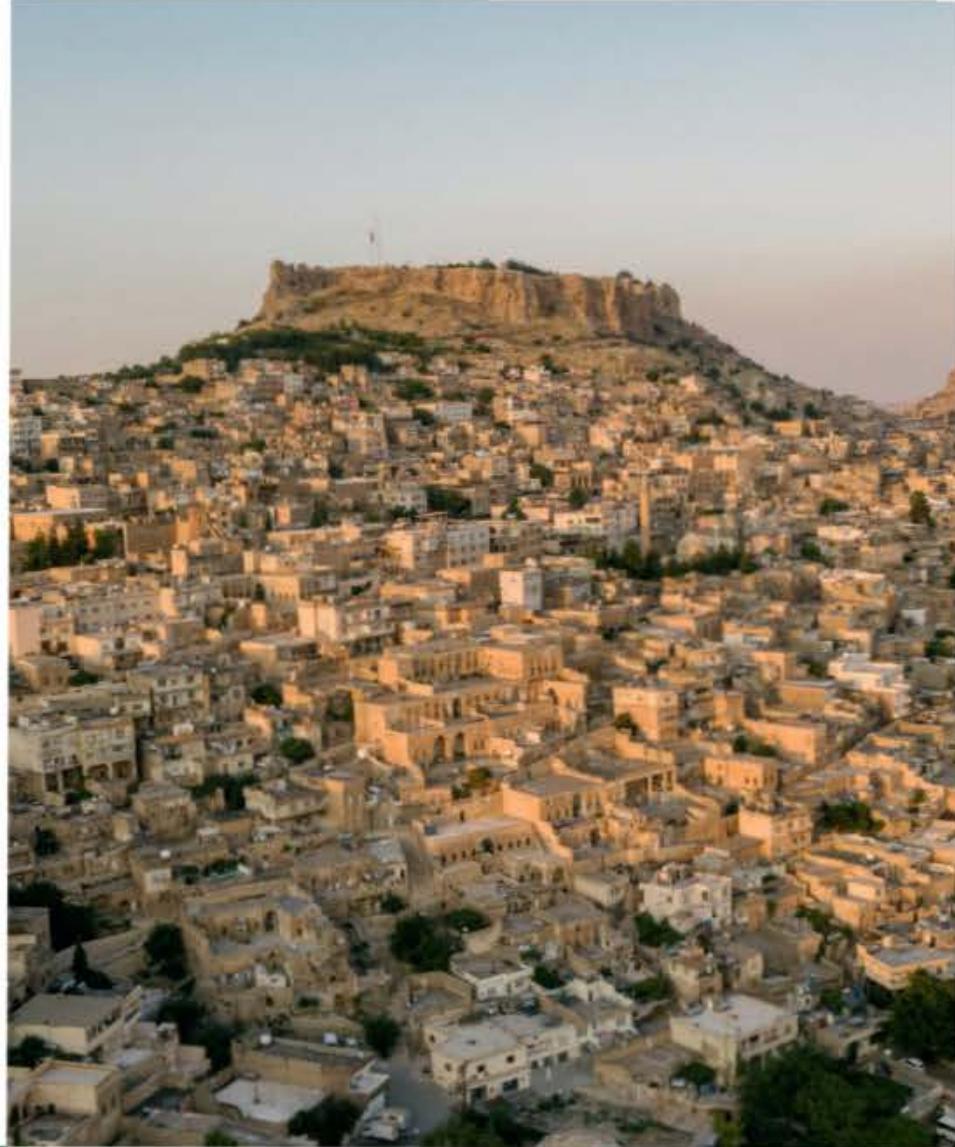
### **Mount Nemrut**

On a morning hike up Mount Nemrut, the peach-pink dawn reflects off the silent stone figures that guard the ancient summit tomb of King Antiochus I. The view is immortal — stretching out for miles and miles over the deep and furrowed valleys of the Taurus Mountains. Up here, the hills have eyes; gigantic statues of gods and creatures straight out of Greek mythology all stare blankly at the glowing horizon.



## Cappadocia

Some of Turkey's best-kept secrets are underground, like the churches of Göreme, carved from the volcanic stone that defines the region's landscape. I'm amazed by the frescoes of the 'dark church' before descending into Derinkuyu, a subterranean city that housed more than 20,000 people. Join one of the daily hot air balloon flights that float above the fairy chimney formations.



## Pool of Hierapolis and Pamukkale

A spa since the second century BC, Cleopatra's Pool offers an unforgettable swim among the ruins of Hierapolis. Paddling through the clear water, I tiptoe over marble columns and stone steps, surrounded by Mediterranean gardens. Then at dusk, I walk the white ledges of the 'cotton castle' — the calcite slopes of Pamukkale rising like a staircase to the sky.

## Göbeklitepe

This 12,000-year-old monument is more than twice as old as Stonehenge. Stepping down into Göbeklitepe is haunting — as if I'm unlocking the secrets of my own being by staring at mankind's first ritual space. The carved animal figures look ready to leap from the stone, each one carved from the limestone cliffs placed upright by human hands that lived so long ago.

## Mardin

This historic city, set upon a high ledge, is known for its diverse architecture. From the rooftop restaurants I peer across the wide-open span of the Fertile Crescent, wedged between the Tigris and Euphrates rivers. This is the place where humans first domesticated animals, where they learned to cultivate wheat and invented the wheel, and where they developed the first written language. Shop for handmade silver treasures on the winding streets, or go out late to experience the lively nightlife in this historical Silk Road outpost.





## Istanbul

A city at the centre of the world, Istanbul boasts a skyline of domes and minarets, skyscrapers and elegant bridges. Istanbul is a flurry of motion, art, and good food. Draped over hills and shorelines, the city pulsates with the urgency of today and the momentum of tomorrow. Yet despite the twinkling modernity of this global metropolis, Istanbul loves tradition — Turkish coffee in Beyoğlu, Friday prayer, a visit to the hammam (Turkish bath), or hunting for bargains in Çukurcuma's antique shops. Every day feels new because each street offers an unexpected reminder of the past — a block from a Roman temple laid into the foundation of a mosque, a fragmented Byzantine mosaic peeking out from the stucco, or a kitten napping in the window of a grand Ottoman facade. And beyond that, a glittering skyline of TV towers and glasshouses. Each new layer is built on the one before, now home to millions who share the history of these stones, and who live in a land named after the ever-rising sun.

## Lake Van and Akdamar Island

The city of Van is truly ancient. Some of the oldest stories in the world point back to Anatolia, telling me this fascinating country is even older than Noah, whose ark is said to have landed upon the snow-topped peak of Mount Ararat. While the archeological evidence is disputed, the legend remains, along with some remarkable alleged descendants — the strange and beautiful white cats of Lake Van. Said to be 'touched by Allah', the snow-white cats stand out due to their affinity for water and their alluring mismatched eyes: one blue, one yellow. Across Lake Van is the sacred outpost of Akdamar Island. Over a thousand years old, the Cathedral of the Holy Cross dates back to the time of Armenian kings. Striking carvings cover the outer facade, recounting the Biblical tales of David and Goliath, and Adam and Eve.

**CLOCKWISE FROM TOP LEFT:** Church interior, Göreme Open Air Museum; view over Mardin; Life on shore opposite Maiden's tower; Akdamar Island; Göbeklitepe; the antique Pool of Hierapolis.

IMAGES: MATTIEU PALEY



### Essentials

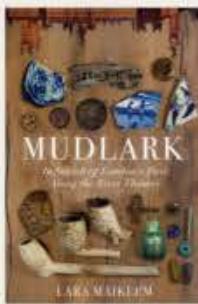
**Getting there:** Istanbul (IST) offers direct flights to and from hundreds of destinations.

**Getting around:** Internal flights link Istanbul with all major tourist destinations in Turkey, or step onto the vast rail network, which includes the famed *Orient Express*. The Metro is the quickest way to move around Istanbul.

**When to go:** Spring and autumn offer clear skies and mild temperatures, while sunshine makes summer a popular season on the coast. Istanbul is good to visit year-round.



JANUARY



1

## NEW BOOK TO READ

**What Lies Beneath the Thames**

Mudlarking is more than simply scavenging for historic objects on a river's fore-shore. It can be a meditative act in which looking is as enjoyable as finding, writes Lara Maiklem in *Mudlark*. Travelers can try London mudlarking with tours led by Thames Explorer Trust and others.

3



## WILDLIFE SIGHTING

**IT'S NESTING TIME** for Magellanic penguins. The monogamous pairs and their chicks can be seen in colonies along the coasts of the Falkland Islands (pictured), as well as Argentina and southern Chile.



**From treasure hunting to penguin spotting, here's how to see the world this month.**

## BIG EVENT

**GO FLY A KITE?** **DON'T MIND IF WE DO—AT THE INTERNATIONAL KITE FESTIVAL, JANUARY 6-14, IN AHMEDABAD, INDIA.** FANCY FLYERS, FROM LONG-TAILED DRAGONS TO EERIE ALIENS, DRAW GLOBAL KITE EXPERTS AND SUPERFANS.

4



## NATIONAL PARK FINDER

**The Tropical Island Escape That Isn't Hawaii**

Lush rainforests, soft sand beaches, and tiny thimble jellyfish (left) are just some of the treasures in the National Park of American Samoa, the only U.S. national park south of the Equator. Its far-flung location, about 2,600 miles southwest of Hawaii, means that travelers hike, snorkel, scuba dive, and explore Samoan culture with few crowds.



## KICKING IT WITH FROGS

BY LISA KRIEGER

**FROG-SPOTTING**, like bird-watching, takes patience and perseverance. Like birders, we have lists and our own jargon. We keep odd hours, swat mosquitoes, and wear closed-toe shoes to prevent snakebite. In a world that is rapidly losing frogs, our group of amphibian-focused travelers set out for Costa Rica to find them.

Organized by the nonprofit organization Save the Frogs, these ecotours help to support the growing number of parks and lodges in places such as Belize, Peru, and Ghana that protect the vital habitats for these vulnerable creatures.

Costa Rica is home to 149 frog species. (The one perched on this heliconia flower is a blue-sided tree frog.) At the peak of the soggy season, we identified 23 species, but kept hoping for more. It's an addictive game full of disappointment and discovery, chasing eyes that glow like jewels in the dark.



In Snowdonia National Park, summer dusk bathes a slope above Lake Idwal, in the Ogwen Valley.

# EPIC WALES

JUMP INTO COASTAL ADVENTURES,  
THEN HIKE TRAILS AT THE SPEED OF SHEEP.

BY AMY ALIPIO

**THE SIMPLE WORDS** painted on a billboard-size wall overlooking a parking lot in Swansea, Wales, read: “More poetry is needed.”

A plea to locals? More likely an exhortation to the rest of the world—because poetry isn’t something I find Wales lacks. A short drive beyond any Welsh city leads to landscapes of imagination: hillsides embroidered with bluebells, lonely castle ruins on windswept crags, rocky coastlines noisy with seal song, valleys that are an encyclopedia of green.

The industrial port city of Swansea is the gateway to the Gower Peninsula, the first Area of Outstanding Natural Beauty (AONB) designated by the British

government, in 1956. The recognition singles out for conservation exceptional landscapes of “distinctive character.” Wales now has five AONBs, in addition to three national parks.

Three new touring routes, collectively called the Wales Way, showcase the best of this ancient land—and they appear on National Geographic Travel’s annual Best Trips 2020 list, which heralds them as essential experiences for travelers. At 185 miles, the Cambrian Way is the longest of the three, snaking north to south along the backbone of Wales. Sandwiched between peaks and sea, the Coastal Way is a sweeping 180-mile journey around Cardigan Bay

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AND KNOCK YOUR SYMPTOMS OUT COLD.



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Built on decades of research, the authentic regional dishes featured in the latest book from best-selling author Dan Buettner use ingredients and cooking methods proven to increase longevity and improve wellness and mental health. Complemented by mouth-watering photography and an insider's look at each Blue Zone, these recipes can improve your health, extend your life, and fill your kitchen with happiness.

ALSO AVAILABLE BY DAN BUETTNER

AVAILABLE WHEREVER BOOKS ARE SOLD



The hiking trail around Carmarthen Fans, in Brecon Beacons National Park, takes in windy escarpments and glacial lakes.

on the country's west coast. The castle-rich North Wales Way follows a centuries-old trading route 75 miles from northeastern Queensferry to the cliffs at Holyhead on the Isle of Anglesey.

Each route is a gateway to wider outdoor adventure. On the western Pembrokeshire coast, surfers ride the swells at Freshwater West, site of the Welsh national surfing championships. Climbers can follow in the footsteps of Sir Edmund Hillary, who trained on 3,560-foot Mount Snowdon before his 1953 Everest ascent. Elsewhere in Snowdonia National Park, the River Tryweryn is the top destination for white-water kayaking and rafting in Britain. This is poetry to get the blood pumping.

In the 1980s the Welsh pioneered a new adrenaline rush called coasteering. This increasingly popular adventure sport may include rock climbing, cliff jumping, cave exploring, swimming—experiencing with all senses the impact zone where water meets land.

The speed is slower on Wales's hundreds of miles of walking trails, including the 870-mile Wales Coast Path, which follows the country's entire shoreline, from Chepstow in the south to Queensferry in the north. Once I spent a sunny afternoon unexpectedly walking a very short section of the path from Port Eynon Bay to Oxwich Bay, in the Gower Peninsula, where I've been visiting relatives since I was 14 years old. I'd thought only to stroll out to one end of the bay and back, but the desire to see what was beyond the headland kept me walking. At Oxwich Bay, I



found families out enjoying the unseasonably warm weather on broad golden sands. The bay flows out to the Bristol Channel, which has one of the highest tidal ranges in the world. In Wales it always pays to see what wonders lie around the bend.

Or what surprises. At Devil's Bridge, in the northern Cambrian Mountains, a steep trail leads down a wooded gorge to Devil's Bridge Falls. I arrived one spring at dusk and had the trail nearly to myself. I heard the rumble of the falls before I saw them. They plunge 298 feet in several cascades, the water sometimes gathering in potholes, where the bedrock has eroded. The trail wound down closer to the base of the falls, and each view seemed different, as if I were looking at a multitude of waterfalls, rather than the same one from various vantages.

Its prismatic beauty attested to why this has been a tourist attraction since Victorian times. Nature's green generosity was on display, brightened by bursts of pink and purple rhododendrons. The lushness reminded me of Hawaii. "Can such force / Of waters issue from a British source ..." wondered William Wordsworth in his poem "To the Torrent at the Devil's Bridge, North Wales, 1824." As I made my way back up out of the valley, I couldn't help but smile. If this is devil's territory, then let all hell break loose.

Beyond lyrical landscapes, there's the torrent of actual poetry Wales has produced. Its poetic tradition reaches back to the late fourth century and forward to the annual National Eisteddfod, a full-blown festival of poetry and music that is Wales's biggest gathering.

Some of the earliest written sources of the Arthurian tale, dating from the ninth century, have connections to Wales or were written in Welsh. Travelers search for connections to the legendary ruler and his knights at towns such as Caerleon, a supposed site of Camelot, and Carmarthen, said by some to be Merlin's hometown.

Dylan Thomas, perhaps Wales's most famous poet, was born in Swansea and still influences artists and writers today. That parking lot billboard? It's a work by artist Jeremy Deller, who was commissioned as part of the city festivities around Thomas's 100th birthday in 2014. Deller was right: Even in Wales, you can never have enough of words and wonder. □

**Amy Alipio** is senior editor at National Geographic Travel.

## Castles of Wales

Wales is said to be home to more castles per square mile than any other country in Europe. Why the density? Blame it partly on Wales's history as a contested territory among native Welsh, Normans, and English, who all erected epic fortresses. Here are four of the best. —RAPHAEL KADUSHIN

### Chepstow Castle

Has the oldest castle doors in Europe

### Castell y Bere

Rates as one of Wales's most photogenic ruins

### Kidwelly Castle

Starred as a backdrop in *Monty Python and the Holy Grail*

### Powis Castle

Renowned for terraced, Italian Renaissance-style gardens

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'HERE'S  
THE REALLY  
AMAZING  
THING:  
EVERY ONE  
OF US HAS A  
PARTICULAR  
MIX OF  
MICROBES  
THAT'S  
DIFFERENT  
FROM  
EVERYONE  
ELSE'S.'



Vitaly Napadow,  
a neuroscientist at  
Harvard Medical School  
and Massachusetts  
General Hospital, studies  
how the brain perceives  
pain. To do that, he uses  
electroencephalography  
to track the brain wave  
patterns of patients with  
chronic lower back pain.

ROBERT CLARK

JANUARY 2020

WELLNESS  
ISSUE

Scientists are  
unraveling the  
mysteries of pain—

# A WORLD OF PAIN

BY  
**YUDHIJIT  
BHATTACHARJEE**

PHOTOGRAPHS BY  
DAVID GUTTENFELDER,  
ROBERT CLARK,  
ROBIN HAMMOND,  
CRAIG CUTLER,  
AND MARK THIESSEN

and exploring  
new ways to treat it.





During surgery, Brent Bauer eases his pain by playing a virtual reality game called SnowWorld. Orthopedic trauma surgeon Reza Firoozabadi at UW Medicine's Harborview Medical Center in Seattle was testing the effectiveness of the game, developed by the University of Washington's Hunter Hoffman, a pioneer in VR for pain relief. Bauer fell three stories and broke numerous bones, including his pelvis. He had one stabilizing pin removed from his pelvis without VR. "That got very intense," he said. The other was removed with VR. "It was a very pleasant distraction," he noted, "and the pain was a lot less." Bauer was participating in a study that suggests VR could decrease the need for general anesthesia, reducing the risks and cost.

CRAIG CUTLER

In Chu Yang Sin National Park in Vietnam, Zoltan Takacs, a biomedical scientist and National Geographic explorer, finds a venomous scorpion, which glows blue in ultraviolet light. Collecting venom from around the world, Takacs hopes to identify novel pain medications because there are currently few good alternatives to opioids. Venom has already led to one notable success. Scientists derived a drug for chronic pain from one of the world's deadliest animals: the cone snail.

DAVID GUTTENFELDER





# M

**O**RE THAN THREE DECADES AGO, when Tom Norris was fighting cancer, he underwent radiation therapy on his groin and his left hip. His cancer disappeared and hasn't come back. But Norris was left with a piercing ache that burned from his hip up his spine to his neck.

Since then, Norris, now 70, has never had a single day free from pain. It cut short his career as an aircraft maintenance officer in the

U.S. Air Force. It's been his constant companion, like the cane he uses to walk. On bad days, the pain is so excruciating, he's bedridden. Even on the best days, it severely limits his ability to move about, preventing him from doing the simplest chores, like taking out the garbage. Sometimes the pain is so overpowering, Norris says, that his breathing becomes labored. "It's like I'm drowning."

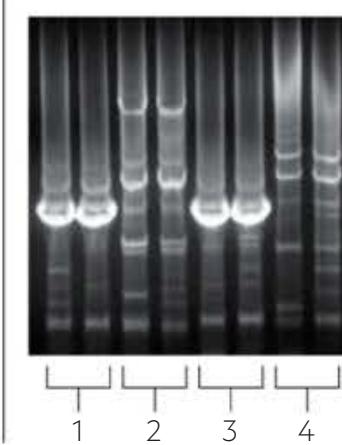
Norris, who lives in a Los Angeles suburb, spoke to me from a long, cushioned bench, which allowed him to go from sitting to lying flat on his back. A tall and genial man, he's become adept at wearing a mask of serenity to hide his pain. I never saw him wince. When his agony is especially intense, his wife of 31 years, Marianne, says she can tell by a certain stillness she sees in his eyes.

When the pain began to take over his life, Norris sought solace in speaking out. He became an advocate for chronic pain sufferers and started a support group. And for 30 years he has searched for relief. For many of those years he was on fentanyl, a powerful opioid that he says covered his pain "like a thick blanket" but kept him "basically horizontal and zoned out." He has tried acupuncture, which was somewhat helpful, as well as bee stings, magnet therapy, and faith healing, which weren't. Norris now manages his pain with physical therapy, which improves his mobility, and steroids injected into his spine, which quiet his inflamed nerves.

Like Norris, nearly 50 million people in the United States and millions more around the world live with chronic pain. The causes are diverse, from cancer to diabetes to neurological illnesses and other ailments. But they share a common source of suffering: physical agony that disrupts their lives, intermittently or all the time. It's not uncommon for cancer patients experiencing severe, unrelenting pain after chemotherapy to opt out of treatment in favor of the ultimate salve of dying.

When Jo Cameron had surgery for arthritis in her hand, her anesthesiologist found she felt no pain and referred the Scottish woman to a geneticist, who discovered she has two rare mutations. Researchers are investigating mutations that deaden or heighten the sensation of pain to learn how it's transmitted. The electrophoresis results below show the pain insensitivity mutation in Cameron's DNA (1) and her son's (3), but not in her mother's (2) and daughter's (4).

RIGHT: ROBIN HAMMOND  
BELOW: JAMES COX, UNIVERSITY COLLEGE LONDON





The toll exacted by chronic pain has become increasingly visible in recent years. After doctors in the late 1990s began prescribing opioid medications such as oxycodone to alleviate persistent pain, hundreds of thousands of Americans developed an addiction to these drugs, which sometimes produce feelings of pleasure in addition to easing pain. Even after the risks became evident, the reliance on opioids continued, in part because there were few alternatives. No novel blockbuster painkillers have been developed in the past couple of decades.

The misuse of opioid pain relievers—which are ideally suited for short-term management of acute pain—has become rampant across the United States. In 2017, an estimated 1.7 million Americans had a substance abuse disorder stemming from having been prescribed opioids, according to the National Survey on Drug Use and Health. Every day in the U.S., about 130 people die from opioid overdoses—a grim statistic that includes deaths from prescription painkillers as well as narcotics like heroin.

The quest to understand the biology of pain and find more effective ways to manage chronic pain has taken on fresh urgency. Researchers are making significant strides in detailing how pain signals are communicated from sensory nerves to the brain and how the brain perceives the sensation of pain. Scientists also are uncovering the roles that specific genes play in regulating pain, which is helping to explain why the perception and tolerance of pain vary so widely.

These advances are radically altering how clinicians and scientists view pain—specifically chronic pain, defined as pain that lasts more than three months. Medical science traditionally regarded pain as a consequence of injury or disease, secondary to its root cause. In many patients, it turns out, pain originating from an injury or ailment persists long after the underlying cause has been resolved. Pain—in such cases—becomes the disease.

The hope is that this insight, coupled with the steadily advancing understanding of pain, will lead to new therapies for chronic pain, including nonaddictive alternatives to opioids. Norris and other patients are keen to see those breakthroughs happen. Researchers, meanwhile, are testing promising alternative strategies, such as stimulating the brain with mild electric shocks to alter its pain perception and harnessing the body's intrinsic capacity to soothe its own pain.

Clifford Woolf, a neurobiologist at Children's Hospital in Boston who's studied pain for more than four decades, says it's tragic it has taken a "societal catastrophe" for pain to get the attention it deserves from scientists and physicians, but the impetus this has given to pain research is a silver lining. "I think we have the potential in the next few years of really making an enormous impact in our understanding of pain," he says, "and that will definitely contribute to new treatment options."

**THE CAPACITY TO FEEL PAIN** is one of nature's gifts to humankind and the rest of the animal kingdom. Without it, we wouldn't reflexively recoil our hand upon touching a hot stove or know to avoid walking barefoot over broken glass. Those actions, motivated by an immediate or remembered experience of pain, help us minimize the risk of bodily injury. We evolved to feel pain because the sensation serves as an alarm system that is key to self-preservation.

The sentries in this system are a special class of sensory neurons called nociceptors, which sit close to the spine, with their fibers extending into the skin, the lungs, the gut, and other parts of the body. They're equipped to sense different kinds of harmful stimuli: a knife's cut, the heat of molten wax, the burn of acid. When nociceptors detect any of these threats, they send electrical signals to the spinal cord, which transmits them via other neurons to the brain. Higher order neurons in the cortex—the final destination of this ascending pain pathway—translate this input into the perception of pain.

Upon registering the pain, the brain attempts to counteract it. Neural networks in the brain send electrical signals down the spinal cord along what's known as the descending pain pathway, triggering the release of endorphins and other natural opioids. These biochemicals inhibit ascending pain signals, effectively reducing the amount of pain perceived.

Scientists had sketched out this basic schematic of ascending and descending pain pathways when Woolf began working in the field in the 1980s. A soft-spoken man with eyes that seem to brim with kindness, Woolf was struck by the plight of patients he saw in the surgery ward when he was pursuing his medical degree.

"It was clear that all were suffering from severe pain," he says. Woolf felt the senior resident surgeon seemed almost resentful that they were

complaining. “I said to the surgeon, ‘Why aren’t you doing anything?’” Woolf recalls. “And the surgeon said, ‘Well, what do you expect? They just had an operation. They’ll get better.’”

“Pain was a problem the medical profession downplayed—to a substantial extent because there were no safe and effective interventions,” Woolf says. This realization kindled his desire to understand the nature of pain.

Using rats as a model, he set out to learn more about how pain is transmitted. In his experiments, Woolf recorded the activity of neurons in the animals’ spinal cords in response to a brief application of heat to their skin. As he expected, he observed these neurons firing excitedly when signals arrived from the nociceptive neurons. But Woolf made an unexpected finding. After a patch of skin subjected to heat a few times became inflamed, the neurons in the spinal cord attained a heightened state of sensitivity. Merely stroking the area surrounding the previously injured patch caused them to fire.

and certain other conditions. Their pain is not a symptom; it’s a disease—one caused by a malfunctioning nervous system.

With advances in growing human stem cells in the lab, Woolf and his colleagues are now creating different types of human neurons, including nociceptors. This breakthrough is allowing them to study neurons in greater detail than was previously possible to determine the circumstances where they become “pathologically excitable,” Woolf says, and fire spontaneously.

Woolf and his colleagues have used lab-grown nociceptors to investigate why chemotherapy drugs cause neuropathic pain. When the nociceptors are exposed to these drugs, they become more easily triggered and begin to degenerate. This likely contributes to the neuropathies that 40 percent of chemotherapy patients endure.

While scientists like Woolf are advancing the understanding of how pain is transmitted, other scientists have discovered that these signals are just one factor in how the brain perceives

## **'Pain was a problem the medical profession downplayed—to a substantial extent because there were no safe and effective interventions.'**

Neurobiologist Clifford Woolf, Children’s Hospital, Boston

This showed that the injury to the skin had sensitized the central nervous system, causing neurons in the spinal cord to transmit pain signals to the brain even when the input from peripheral nerves was innocuous. Other researchers have since demonstrated this phenomenon—called central sensitization—in humans and shown that it drives various types of pain, such as when the area around a cut or a burn hurts at the slightest touch.

A startling conclusion from Woolf’s work and subsequent research was that pain could be generated in the absence of a triggering injury. This challenged the view held by some doctors that patients who complained of pain that couldn’t be explained by any obvious pathology were likely lying for one reason or another—to get painkillers they didn’t need, perhaps, or to gain sympathy. The pain transmission system can become hypersensitive in the wake of an injury—which is what happened in the rats—but it also can go haywire on its own or stay in a sensitized state well after an injury has healed. This is what happens in patients with neuropathic pain, fibromyalgia, irritable bowel syndrome,

pain. Pain, it turns out, is a complex, subjective phenomenon that is shaped by the particular brain that’s experiencing it. How pain signals are ultimately translated into painful sensations can be influenced by a person’s emotional state. The context in which the pain is being perceived also can alter how it feels, as evidenced by the pleasantness of the aches that follow a strenuous workout or the desire for a second helping of a spicy dish despite the punishing sting it delivers to the tongue.

“You’ve got this incredible capability of altering how those signals are processed when they do arrive,” says Irene Tracey, a neuroscientist at the University of Oxford.

A skilled communicator who speaks in rapid-fire sentences, Tracey has spent much of her career trying to bridge the mysterious link between injury and pain. “This is a highly non-linear relationship, and many things can make it worse or can make it better or could make it very different,” she says.

In experiments, Tracey and her colleagues have imaged the brains of human volunteers while subjecting their skin to pinpricks or bursts

# HOW THE BRAIN FIGHTS PAIN

Pain has a purpose: self-preservation. It signals to the brain that the body is in danger and needs to react. Pharmaceuticals can suppress those signals and ease pain, but new research offers the hope that the body's own systems—made up of an ascending pathway and a descending one—can be amplified to reduce pain organically and with minimal side effects.

## A MESSAGE TO THE BRAIN

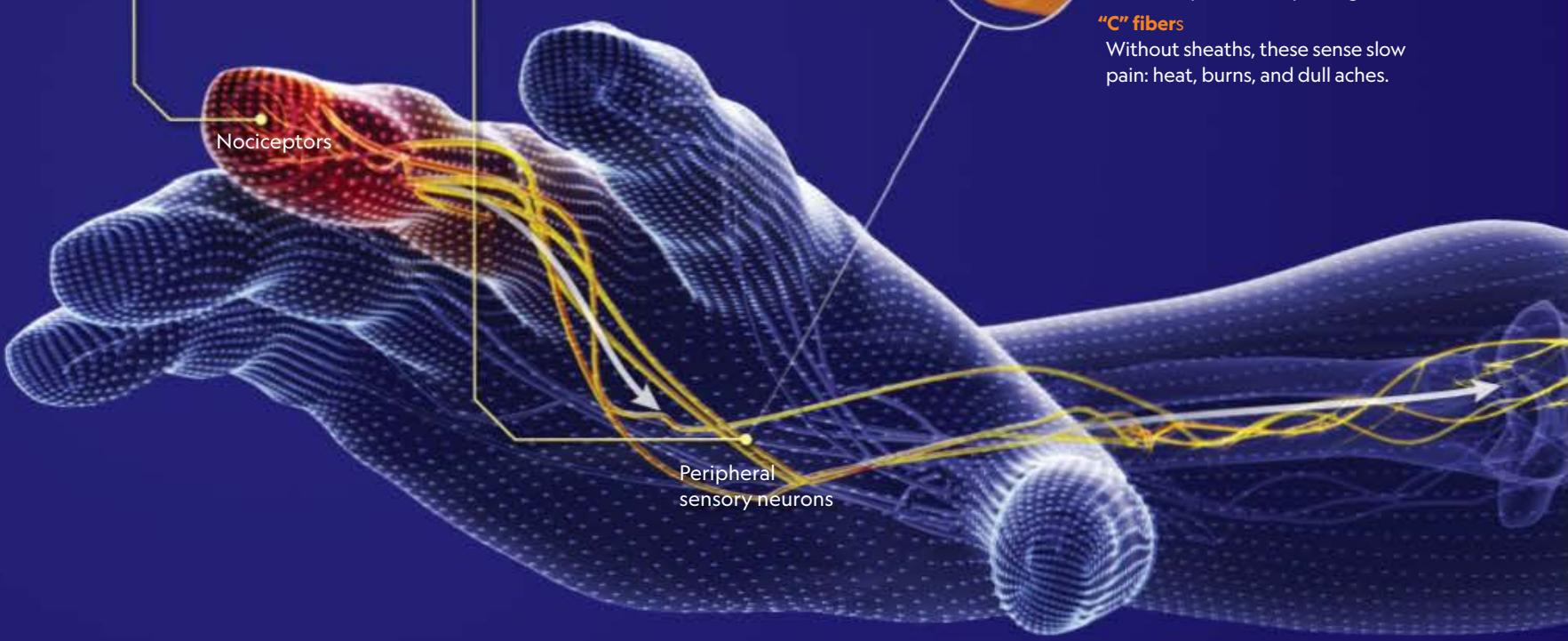
Acute pain calls attention to actual or potential tissue damage. Signals to the brain travel an ascending pathway to motivate the body to respond quickly.

### 1 Sensing pain

Neurons called nociceptors respond to external stimuli, such as sharp objects, fire, or chemical reactions.

### 2 Transmitting pain

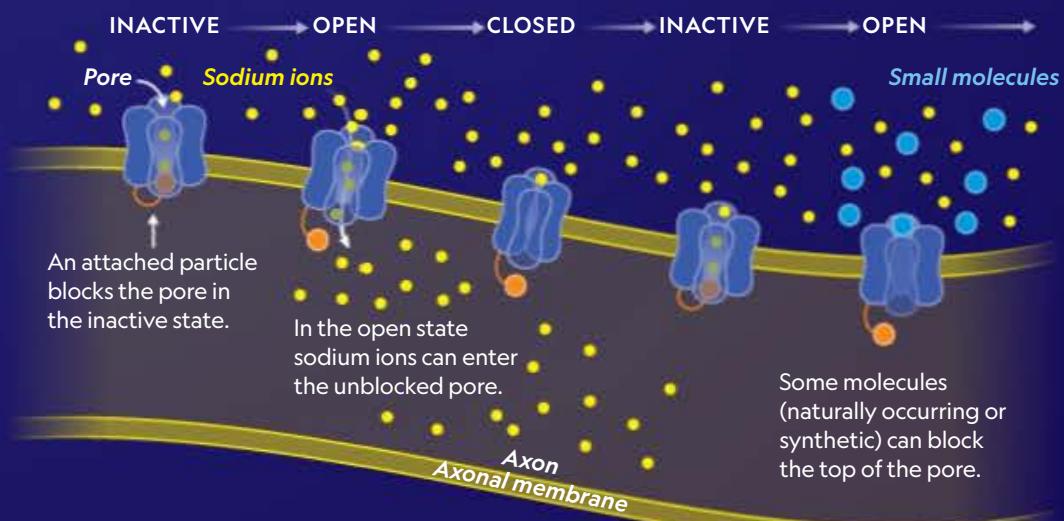
Electrical signals are routed from the nociceptors to axons, nerve fibers that relay the signal to the spinal cord.



## THE PROMISE OF PAIN GATES

Multiple "pain gates," including the sodium channel Nav1.7, regulate the passage of sodium ions into axons, which can cause pain. Obstructing the gates with molecules via drugs or gene therapy may help doctors tailor pain treatment to individual patients.

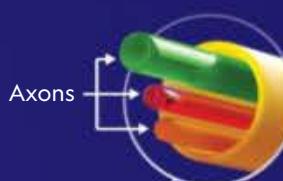
As a neuron fires, electricity-sensitive pores along its surface cycle through three states: inactive, open, and closed.



## Anatomy of a nerve

Nerves include bundles of axons. These fibers, reaching from nerve cells called neurons, conduct electrical activity. Different sensations travel on separate axonal fibers.

### Nerve bundle



### "A beta" fibers

With thick sheaths, these transmit touch, pressure, and vibrations.

### "A delta" fibers

With thin sheaths, these are first to sense quick, acute pain signals.

### "C" fibers

Without sheaths, these sense slow pain: heat, burns, and dull aches.

## THE BRAIN RESPONDS

After the signals are received by the brain, the descending pathway is engaged. It cues the entire central nervous system to modulate and respond to the painful stimulus.

**5 Emotional reaction**

The pain signals are registered in the anterior cortex, which can trigger anxiety, fear, and depression.

**4 Perceiving pain**

The signals travel to the somatosensory cortex and other areas that identify the location and intensity of pain.

**3 Ascending pain**

The spinal cord receives the signals and relays them up to the brain.

**5**

**6 Reacting to pain**

These areas send neurochemical signals down to start blunting the pain.

**4**

**3**

**5**

**7 Pain reduction**

The neurochemicals intercept and act as a brake on the ascending signal in the dorsal horn and periaqueductal gray.

**3**

## THE OPIOID PROBLEM

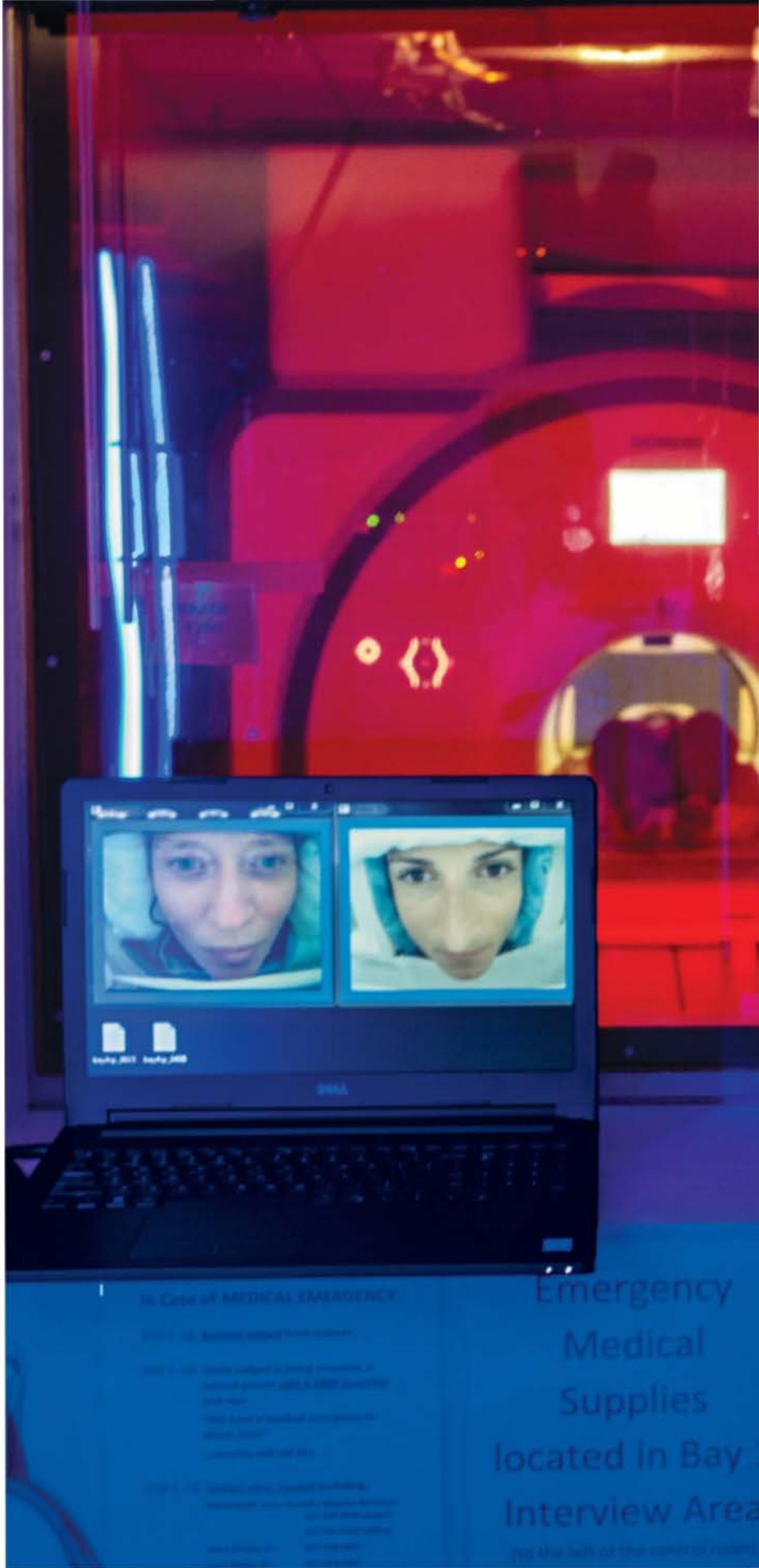
Opioids reduce pain by numbing indiscriminately, dampening signals from the ascending pathway of pain as well as the body's beneficial descending response. The drugs do provide relief from pain—but can also elicit a sense of euphoria that can lead to addiction.

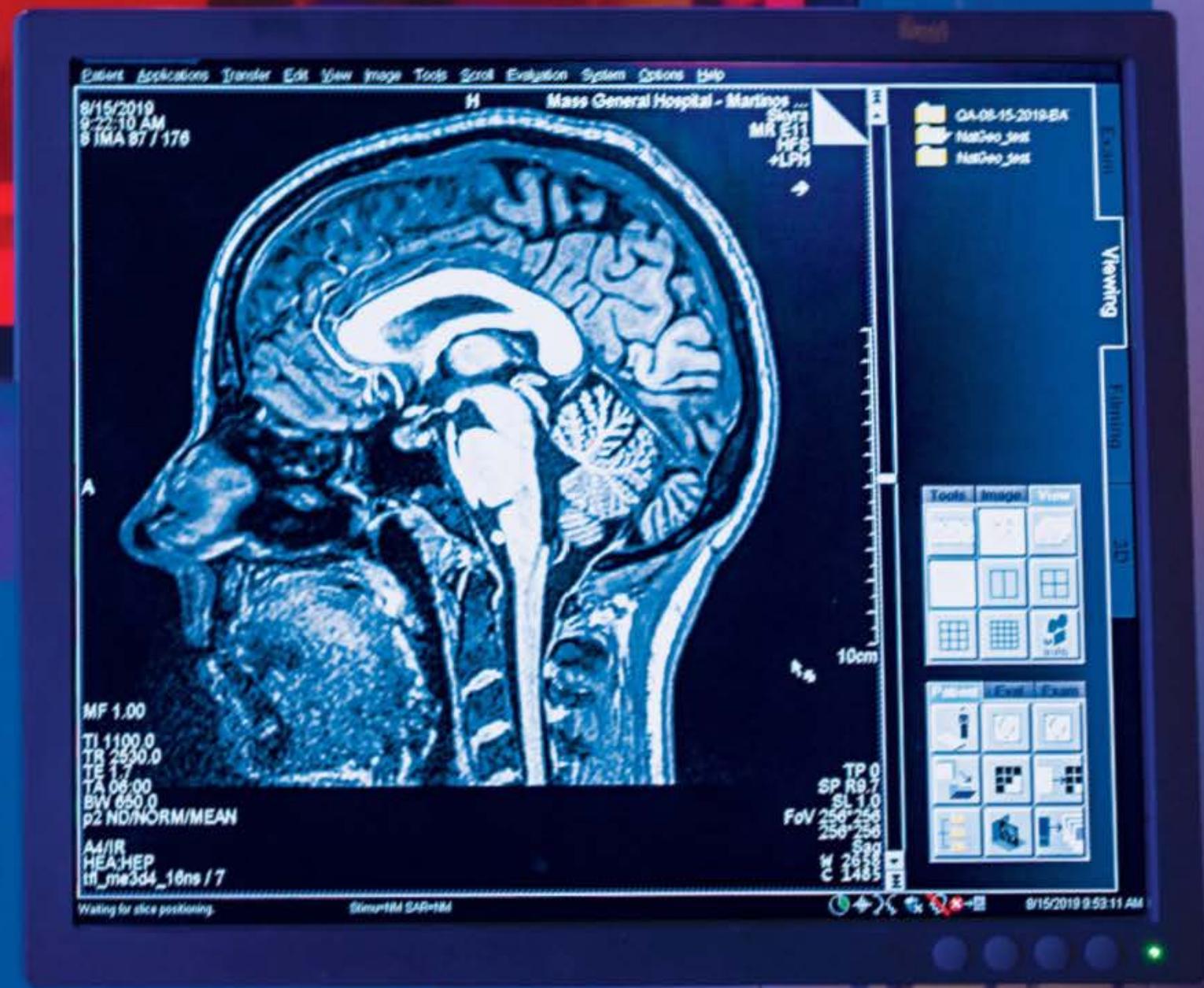
## ACUTE VS. CHRONIC

While acute pain signals follow ascending pathways to the brain, chronic pain, such as persistent back pain, is due to damaged neurons or axons. Its pathways aren't well understood.

The relationship a patient has with a doctor can affect how much pain the patient feels, Napadow said, "but we don't know why that is." To explore this phenomenon, Napadow simultaneously records the brain activity of an acupuncturist and a patient in separate functional magnetic resonance imaging machines. They communicate through a video feed (left monitor) while the patient is treated for experimentally applied pain. To relieve the discomfort, the clinician remotely triggers an electro-acupuncture device attached to the leg of the patient. The monitor at right shows a scan used to map activity in the patient's brain.

ROBERT CLARK







Hanna LeBuhn, who suffers from pain in her jaw joints, watches the mesmerizing motion of jellyfish on a virtual reality headset in Luana Colloca's lab. The scene, one of a series of relaxing marine images, is projected on the wall. Colloca, who studies the neurobiology of pain at the University of Maryland, has established that VR that entertains patients eases their pain. "VR has the unique capability," she said, "of regulating body responses to pain, improving mood, and reducing anxiety."

MARK THIESSEN



of heat or smears of cream laced with capsaicin, the chemical compound that makes chili peppers spicy. What the researchers have found has led them to discover a much more complex picture of pain perception than had been previously envisioned. There's no single pain center in the brain. Instead, multiple regions are activated in response to painful stimuli, including networks that also are involved in emotion, cognition, memory, and decision-making.

They also learned that the same stimulus doesn't produce the same activation pattern every time, indicating that a person's experience of pain can vary even when the injuries are similar. This flexibility serves us well, raising our pain tolerance in situations that demand it—for instance, when carrying a scorching bowl of soup from the microwave to the kitchen counter. The mind knows that dropping the bowl midway would result in greater misery than the brief anguish caused by holding the bowl, so it tolerates the momentary suffering.

Tracey and her colleagues have shown that fear, anxiety, and sadness can make pain feel worse. In one of their experiments, healthy student volunteers listened to Prokofiev's deeply melancholic "Russia Under the Mongolian Yoke," slowed to half speed, and read negative statements such as "My life is a failure." At the same time, they received a burst of heat on a patch on their left forearm, which had been rubbed with capsaicin. Later the students received the same stimulus as they listened to happier music and read neutral statements such as "Cherries are fruits." In the sad condition, they reported finding the pain "more unpleasant."

Comparing scans of the students' brains in the two moods, the researchers found that sadness influenced more than just the emotion-regulation circuitry. It led to increased activation in other brain regions, indicating that sadness was physiologically dialing up the pain. "We've made people anxious and threatened and fearful," Tracey says, "and we've shown that that makes the actual processing of those signals amplified."

**STRONG MEDICATION** would be needed to dull the pain after surgery for arthritis in her hand, Jo Cameron was informed by her anesthesiologist. But the 66-year-old Scottish woman doubted it. "I bet you any money I will not take any painkillers," she told him.

The anesthesiologist looked at her as if she were not fully sane. He knew from experience that the postoperative pain was excruciating. When he came by to check on her after surgery, he was astonished to find that she hadn't requested so much as the mild analgesic he'd prescribed. "You haven't even taken paracetamol, have you?" he asked.

"No," Cameron recalls having replied cheerfully. "I told you I wouldn't."

Growing up, Cameron says, she was frequently surprised to discover bruises whose origins were a mystery. When she was nine, she broke her arm in a roller-skating accident, but three days passed before her mother noticed that it was swollen and discolored. Years later, Cameron gave birth to her two children without any pain during delivery.

"I don't really know what pain is," she says. "I see people in pain, and I see the grimace, the strain on their faces, and the stress, and I have none of that."

Cameron's inability to sense physical hurt may be unremarkable to her, but it places her in a rarefied group of individuals who are helping scientists unravel the genetics underlying our ability to feel pain. Her amazed anesthesiologist put her in touch with James Cox, a geneticist at University College London. Cox and his colleagues studied her DNA and found she had two mutations in two neighboring genes, called *FAAH* and *FAAH-OUT*. They determined that the mutations reduce the breakdown of a neurotransmitter called anandamide, which helps provide pain relief. Cameron has an excess of the biochemical, insulating her against pain.

Cox has been studying people like Cameron since he was a postdoc at Cambridge in the mid-2000s, when his supervisor, Geoffrey Woods, learned about a 10-year-old street performer in Pakistan who could walk barefoot over hot coals and stick daggers into his arms without so much as a whimper. The boy would earn money from these stunts and then go to the hospital to be treated for his wounds. He was never the subject of a study—he died from head injuries after falling off a roof while playing with friends—but Cox and his colleagues were able to analyze the DNA of six children from the same clan, who showed similar insensitivity to pain. The children each had a mutation in a gene called *SCN9A*, known to be involved in pain signaling.

The gene makes a protein that is instrumental

in the transmission of pain messages from nociceptive neurons to the spinal cord. The protein, christened Nav1.7, sits on the surface of the neuron and serves as a channel for sodium ions to pass into the cell, which enables electrical impulses constituting the pain signal to propagate along the threadlike axon that connects to another neuron in the spinal cord.

The mutations the researchers discovered in the *SCN9A* gene yield malformed versions of the Nav1.7 protein that don't allow sodium ions to pass into nociceptive neurons. With their nociceptors incapable of conducting pain signals, the children were oblivious when they chewed their tongues or scalded themselves. "The beauty of working with these extremely rare families is that you can identify single genes which have the mutation and essentially are human-validated analgesic drug targets," Cox says.

Mutations in the *SCN9A* gene are also linked to a rare condition called inherited erythromelalgia, or man-on-fire syndrome. Patients who

speaks animatedly and possesses a cheery disposition despite having made pain his life's work. He and his colleagues found, as another group had, that man-on-fire patients had mutations in their *SCN9A* gene. Those mutations have the opposite effect of the one in the pain-free kids from Pakistan, creating Nav1.7 channels that open too easily, allowing sodium ions to flood in even when they shouldn't.

Through lab experiments conducted on neurons in petri dishes, Waxman and his colleagues proved that this was the mechanism by which the *SCN9A* mutations caused the syndrome in patients like Costa. "We were able to put the channel into pain-signaling neurons and cause them to go *BRRRP!* when they should be going *bop-bop*," says Waxman, referring to the hyperactivity that results from the unabated inflow of sodium ions. In patients with the syndrome, this defect causes nociceptors to bombard the brain with pain messages constantly.

The discovery that Nav1.7 can open or close

### **'I see people in pain, and I see the grimace, the strain on their faces, and the stress, and I have none of that.'**

Jo Cameron, a patient with a genetic insensitivity to pain

have it face the extreme opposite of insensitivity to pain: a burning sensation on their hands, feet, and face. In warm surroundings, or with slight exertion, the sensation gets unbearably intense, akin to holding one's hand over a flame.

Pamela Costa, a 53-year-old clinical psychologist from Tacoma, Washington, who suffers from the syndrome, describes the pain as "inescapable." To cope, she has her office temperature set at a chilly 60 degrees. She can sleep only with a complement of four fans around her bed and the air-conditioning on at full blast. In an ironic similarity to individuals with pain insensitivity, the constant burning sometimes makes it hard for Costa to discern hot surfaces, which is how she burned her arm a year ago while ironing.

"I didn't realize until I heard a hissing sound from my skin getting seared," she says. "It was the same sensation as I was already having."

Stephen Waxman, a neurologist at Yale University School of Medicine and one of the world's foremost experts on nerve conduction, has studied Costa and others like her in his lab at the Veterans Affairs Medical Center in New Haven, Connecticut. Gracious and affable, Waxman

the floodgates to nociceptive pain signals has made the channel an attractive target for researchers looking to develop new pain medications that don't pose the risk of addiction that opioids do. Opioids work by binding to a protein on the surface of nerve cells called the mu-opioid receptor, causing the receptor to communicate with proteins inside the cell. While the action of some of these proteins alleviates pain, the receptor's communication with other proteins results in pleasurable feelings. The body develops a tolerance to these drugs, meaning that higher and higher doses are required to trigger the sense of euphoria, which can cause addiction.

Because Nav1.7 is present only in damage-sensing neurons, a drug that selectively turns off the channel promises to be an effective pain reliever. The sole known side effect is the loss of the sense of smell. Likewise, individuals with the mutation also can't smell. Existing local anesthetic drugs such as lidocaine indiscriminately block nine sodium channels in the body, including ones that are key to an array of brain functions, which is why doctors must limit their

use to numbing patients temporarily. Drug companies are searching for compounds that might be able to block Nav1.7 without disabling other sodium channels, but success has been elusive.

Even so, Waxman is optimistic that the research eventually will lead to better drugs. "I'm confident there will be a new and more effective class of medicines for pain that are not addictive," he says, his eyes brightening. Then he pauses for a moment and tempers his enthusiasm. "But I can't begin to attach a time line."

**WHILE THE SEARCH** for new drugs continues, clinicians and researchers are investigating ways to deploy the brain's intrinsic abilities to modulate pain and lessen the suffering associated with it. And those abilities are impressive. After all, our minds and bodies have been coping with pain for a lot longer than we've been studying it.

Take, for example, a recent British study of more than 300 patients with a type of shoulder pain thought to be caused by a bone spur. To relieve the pain, the spur is often removed in surgery. Researchers randomly divided the participants into three groups. One group underwent the surgery. A second group was led to believe it had, but it hadn't. A third group was asked to return in three months to see a shoulder specialist. The group that had the operation and the one that thought it did reported similar relief from their shoulder pain.

"What it showed is that it's just a placebo. The surgery is not mechanistically doing anything for the pain," says Oxford's Irene Tracey, one of the study's authors. "The pain relief the patients are getting is just driven by a placebo effect."

But to Tracey, the outcome isn't any less important because it shows the placebo effect worked. On the contrary, she says, the study reveals the force of a patient's belief in the treatment. "What it's powerfully saying is expectations shape pain," Tracey says.

Other studies have uncovered how a patient's expectation of reduced pain can translate into actual relief. It seems to activate the brain's descending pain pathway, leading to the release of opioids synthesized inside the brain that impede the incoming pain signals from the body.

"This is not just pretend," Tracey says. "The placebo mechanism hijacks this very powerful system in the brain."

Our perception of pain isn't limited to merely sensing it. The feelings of unpleasantness, fear,

Pesach Feldman, 76, takes a break from a swim in Tel Aviv, Israel. Bypass surgery and 15 stents didn't relieve the former paratrooper's chest pain from refractory angina, caused by poor blood circulation in his heart. He underwent a simple procedure perfected by cardiologist Shmuel Banai. A catheter with an inflatable balloon and a stainless steel mesh Reducer (top right) is inserted through a vein in the neck, and the balloon is inflated in the heart's main vein, called the coronary sinus. The Reducer restricts the blood flow leaving the heart, forcing it into areas of the heart muscle that aren't getting enough nourishment. "I got my life back," Feldman said.

FAR RIGHT: DAVID GUTTENFELDER  
NEAR RIGHT TOP: LIOR ZUR, TEL AVIV  
SOURASKY MEDICAL CENTER  
NEAR RIGHT BOTTOM: SHMUEL BANAI,  
TEL AVIV SOURASKY MEDICAL CENTER



and anxiety that accompany the sensation are an integral part of experiencing pain. In a trial at the Cleveland Clinic, researchers led by neurosurgeon Andre Machado used deep brain stimulation (DBS) to target this emotional component of pain in 10 patients who had chronic neuropathic pain after suffering a stroke. The researchers implanted tiny electrodes in a part of the brain involved in processing emotions. Wired to an electronic device inserted in the chest, the electrodes delivered mild shocks to the implantation site at a rate of nearly 200 a second.

"In several patients, we saw an improvement in their quality of life, in their sensation of well-being, in their independence—without improving the amount of pain," Machado says.

Patients who had scored their pain as a nine on a 10-point scale, for example, continued to give it the same score but reported being able to function better. One of the study subjects, Linda Grubb, describes the treatment as



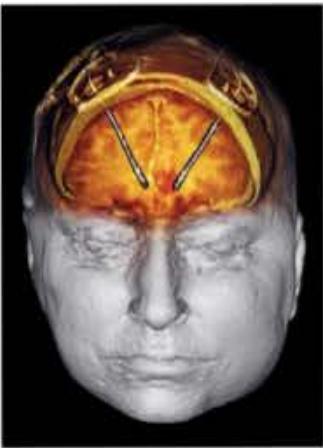
transformative. "It made all the difference in the world as far as being able to go places," she says, adding that her post-stroke pain had compelled her to spend her days on the couch. "I have so much more energy. My husband says I seem so much happier. It really changed my life completely."

A subsequent part of the study involving both healthy subjects and chronic pain patients gave Machado and his colleagues some insight into why deep brain stimulation appeared to have benefited patients like Grubb. The researchers recorded electrical activity from the brains of participants as they watched a screen while they had two devices strapped to their arms. One device delivered a flash of heat to the skin; the other delivered a harmless buzz. From the visual cue that appeared on the screen, the participants could tell which of the two stimuli they were about to get or if they were going to get nothing at all.

The researchers compared the brain activity of participants as they received heat pulses and buzzes or nothing. They found that the brains of chronic pain patients responded similarly when anticipating a painful stimulus and a harmless one, whereas the brains of healthy volunteers showed increased activity in certain regions only when anticipating the heat. When chronic pain patients repeated the experiment while receiving DBS, their brain activity was more similar to that in healthy participants.

To Machado and his colleagues, these findings suggest that the brains of chronic pain patients are conditioned by constant exposure to pain to react as if every stimulus is potentially painful, causing the patients to live in distress. The DBS treatment seems to restore a degree of normalcy, enabling the brain "to again distinguish painful from nonpainful, which is what you need in order to be able to function," Machado says.

Virtual reality may prove to be another way



Linda Grubb, who has suffered from chronic pain since having a stroke, celebrates finishing a so-called zero K, a race of less than 50 feet, on the patio of Buckeye Lake Brewery near Columbus, Ohio. Grubb was treated at the Cleveland Clinic with deep brain stimulation by neurosurgeon Andre Machado. She said it didn't cure her pain but did help her get off the couch and resume many activities. "It's not like I'm jumping rope now," she said, "but I'm going lots more places." Machado said other patients who were treated reported similar improvement in their sense of well-being. In the procedure, two microelectrodes were implanted in Grubb's brain (above) and electrical pulses sent to areas that process the emotional component of pain.

RIGHT: DAVID GUTTENFELDER; ABOVE: STEPHEN JONES, CLEVELAND CLINIC, COMPOSITE OF CT AND MRI SCANS





of reducing pain. I experienced the power of the technique firsthand at the lab of Luana Colloca, a neuroscientist at the University of Maryland. One of Colloca's assistants strapped a little box onto my left forearm as I sank into a comfortable recliner. The device was similar to the one that Machado's group had used: Connected to a computer by a cable, it was capable of heating up and cooling down rapidly. In my right hand, I held a controller with a button that I could press to stop the heating on my arm. "Don't worry; you won't get burned," the assistant reassured me.

In the first few trials, Colloca asked me to press the button as soon as I felt the device getting warm. In the next few rounds, I had to wait a little longer until the device felt uncomfortably hot; in the final series of trials, I had to switch it off only when it felt too hot to bear.

Colloca then led me through the same sequence while wearing virtual reality goggles, which immersed me in an oceanic environment. Soothing music played in my ears as I watched dazzlingly colored fish flitting through the water, which was lit up by sunlight filtering down from above. Large iridescent jellyfish floated past. Periodically I felt the device heating up the skin on my forearm, reminding me that I hadn't gone scuba diving.

When the experiment ended, Colloca showed me the temperatures I had allowed the device to reach in all the trials. The readings for what I felt to be "warm," "hot," and "unbearably hot" were all higher during the immersive experience. Specifically, the hottest temperature I could handle without flinching had gone up by 2.7 degrees Fahrenheit, to 118 degrees Fahrenheit, which in Colloca's view was "huge."

"That means you were tolerating a much, much higher level of pain when you were immersed in this environment along with calming music," she says.

Scientists don't yet know for sure why virtual reality has this positive effect on pain tolerance. Some hypothesize it works through distraction: by engaging networks that would otherwise be involved in signaling and perceiving pain. Others speculate that it works by regulating emotions and altering mood. Colloca has shown that the key driver of the benefit is the entertainment provided by the experience, which helps relax patients and reduce their anxiety. Whatever the mechanisms underlying its effectiveness, doctors already are using virtual reality to help patients

Daniel Boltz kisses his eight-month-old daughter, Peyton, before giving her a bath. Peyton was born with neonatal abstinence syndrome after her mother used heroin during the pregnancy. Peyton spent two months in the neonatal intensive care unit at Penn State Children's Hospital in Hershey, Pennsylvania, being weaned from opioids. Studies on the long-term effects are limited so far, but researchers have found that babies born with the condition are more sensitive to pain than healthy newborns and also may face cognitive, behavioral, and developmental problems.

DAVID GUTTENFELDER



in acute pain, such as those with severe burns. Colloca believes the strategy also could prove useful in treating chronic pain.

**EVERY MONTH,** Norris leads a meeting of a support group that he helped found a few years ago through the American Chronic Pain Association. The goal is to provide members with informal group therapy, applying the emerging scientific insight that our thoughts and feelings can alter our experience of pain.

I joined Norris at a recent gathering at a Los Angeles church, and he introduced me to the members as they trickled in. (To respect their privacy, I decided not to ask for their last names.) One of them, a slender young man named Brian, shook my hand. When I explained to him, as I did with the others, that I'd come to listen, not to participate, he joked: "Maybe we should punch you in the face so you can relate."

There were 10 of us in all—five men and five



women. We arranged our chairs in a circle and sat down. Resting his cane against a table, Norris settled into his seat and asked the members to share how things had been going for them.

Brian, who suffers from severe abdominal pain that doctors haven't been able to diagnose, was the first to speak. He described going to a jujitsu class, which he said helped him temporarily forget his pain. "It's sad that I have to cause myself other pain to forget this one," he laughed. "I thought of all you guys throughout the week. It made me feel better."

The members are familiar with each other's stories. But they seemed bound by an unspoken contract to listen to everyone with full attention, even if they'd heard the same words before. "I called a suicide hot line today," a woman named Jane said. She suffers from fibromyalgia and complex regional pain syndrome, among other issues. "I've complained to my friends so much that I don't want to call them anymore."

Norris told her and the rest of the group that he's just a phone call away. "Sometimes you just need to scream," he said. Turning to another woman in the group who'd admitted earlier to being reluctant to reach out for support, he said, "So please, yell."

When the meeting was over, Norris waited for everybody to file out of the room before turning out the lights. I asked what inspired him to organize the monthly meeting. "I find that my experiences are often helpful to others," he said. But this was just as much about helping himself, he added. "These meetings help me feel like I am still a contributing member of society, and I am not alone in dealing with chronic pain." □

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**Yudhijit Bhattacharjee** has been a contributing writer since 2017. He is the author of a nonfiction thriller, *The Spy Who Couldn't Spell*. **David Guttenfelder, Robert Clark, Robin Hammond, and Craig Cutler** are frequent contributors. **Mark Thiessen** is a staff photographer.





**LEFT**

Fernando Irizarry's addiction began with pain medications he took after an accident. He invited me to observe his life on Kensington Avenue, and I spent two days with him. Unable to find a usable vein in his arm, bruised from repeated injections, he asked an acquaintance to inject a slurry of discarded drugs into his neck. On the street, addicts often look out for each other, administering narcotics but also saving lives with Narcan, an overdose-reversal nasal spray.

**RIGHT**

Those I met could tell me exactly how many lives they'd saved with Narcan. I would witness an overdose, they said, and I did. I found this woman collapsed, unresponsive, and turning blue. A security guard called 911, and emergency medical personnel revived her.

# O

ne thing you should know," one man advised me. "No one on this street imagined they would end up like this. Every person here thought they had it under control." That street could be anywhere in addicted America. This one is Kensington Avenue, a bleak stretch that runs beneath the elevated tracks in Philadelphia. I went there to witness the opioid crisis, to understand how people seeking relief from pain had ended up on the street.

I've seen extreme misery in wars and natural disasters, but I was stunned by what I found in my own country. The rules of society seemed to have vanished. What remained was a raw struggle for one thing: the rush of relief from pain.

In Philadelphia 1,116 people died from a drug overdose in 2018, more than twice the number five years earlier, and eight out of 10 of those deaths involved opioids.

Hundreds of people live on the street. High, or searching for a high, they slump against storefronts, they drift through parking lots. Many are emaciated, weak, scarred from shooting up. Desperate, they pierce their arms, ankles, necks with needles.

Fernando Irizarry (far left) lives on this street. He is 33, small and thin, with a dark beard. He walks with difficulty, shuffling on atrophied legs. He is funny, thoughtful, and kind, but distracted, searching constantly for discarded bottle caps used to mix drugs. When he collects enough of them, he scrapes together the dregs for his next shot.

On September 11, 2005, he hit the back of a car on his motorbike. As a kid, he'd loved school. The strongest substance he'd tried was chewing tobacco. After months in rehab, he was discharged on Percocet. When his family physician passed away, his new doctor refused to renew his prescription. He found the pills on the street. But there, he could pay \$10 for two or \$5 for a shot of stronger heroin. "That was the choice I made."

At first I was intimidated, unsure how to approach people. When I did, though, their stories were familiar. Stories about their pain, but also about college days, fulfilling jobs, loving families, plans for the future. On cracked screens of mobile phones, I saw evidence of their former lives. And I saw them cling to the vestiges. Recalling her days as a dancer, a young woman, bone thin, took off a boot and performed an *en demi-pointe* pirouette.

The opioid addicts I met are our children. They are our mothers and fathers. They are college students and professionals. Enduring a chronic illness or striving to recover from an accident, they could be any one of us.



**The rules of society seemed to have vanished.  
What remained was a raw struggle for survival.  
One thing: the rush of relief from pain.**

**Seeking relief from pain, many Americans get addicted to prescribed opioids and then turn to heroin, fentanyl, or other drugs. It's a crisis that touches every part of the country. On Philadelphia's Kensington Avenue, the misery of lives**

**derailed by drugs**

**is in plain sight.**



STORY AND PHOTOGRAPHS BY DAVID GUTTENFELDER

nished.



**CLOCKWISE  
FROM TOP LEFT**

I talked with this woman about her life on the streets and looked at photos of her from an earlier time. After she woke up against a wall where she'd been dozing, I watched her peer into a mirror shard to apply mascara. I caught a glimpse of the woman in those old photos.

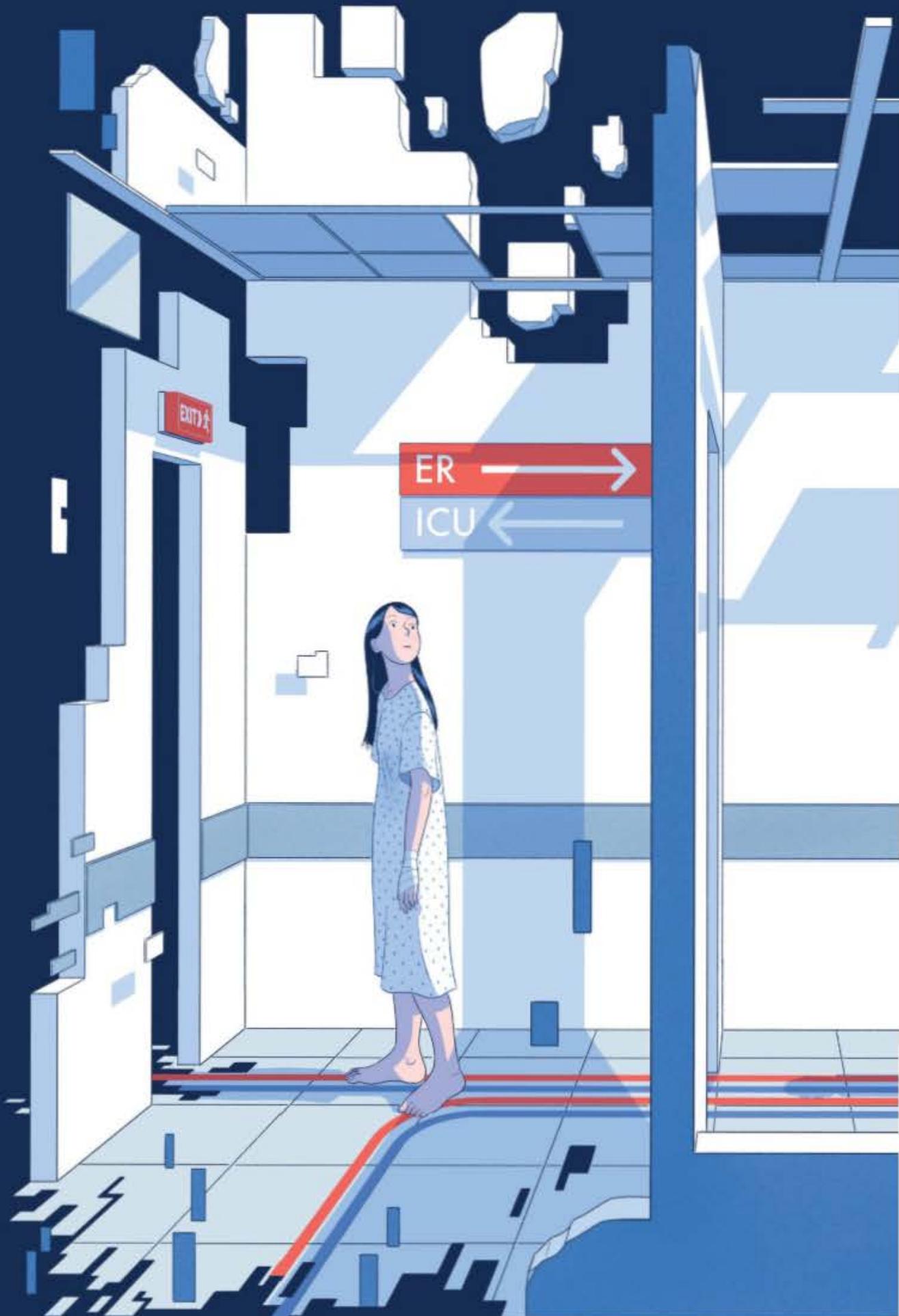
This young man told me he started using Percocet when he was about 18 and then switched to heroin. He was jailed for stealing to pay for his habit. His mother lives nearby, but, starting to cry, he told me he couldn't go home while he was still using. "I don't want her to see me like this."

Kensington Avenue runs for many shadowy blocks under the elevated tracks of the rapid transit system. The cross streets, like this one, thread through one of the city's poorest neighborhoods.

Volunteers from many organizations seek to help those who are addicted. On this day, members of The Table Philadelphia, a Christian community, pray after distributing food and drinks to the homeless.

**Women's health and wellness concerns are dismissed and politicized more than men's and researched and prioritized less, says this female physician. Her Rx for changing that: Women must speak up.**

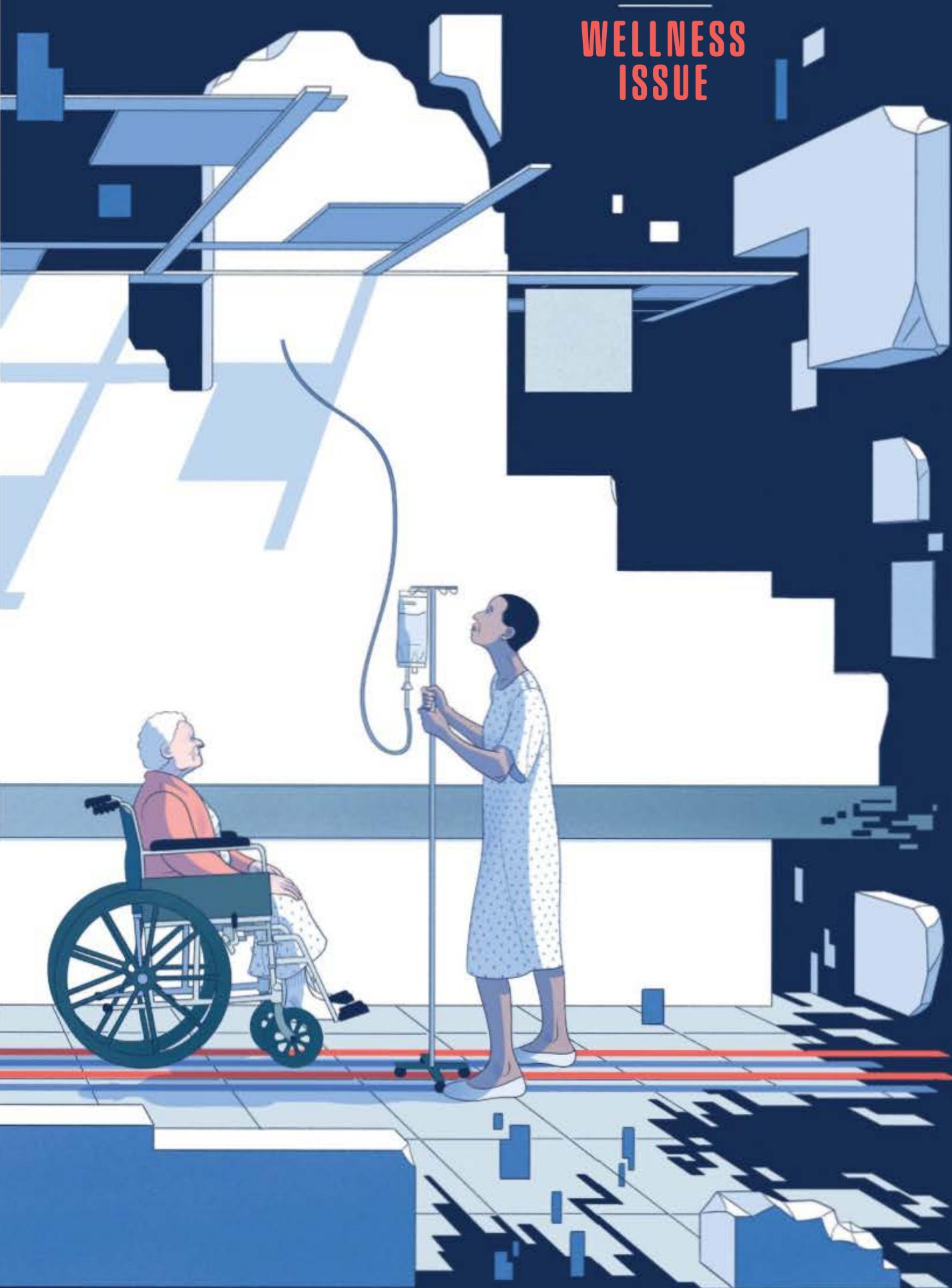
BY  
**ZOANNE CLACK**  
ILLUSTRATIONS  
BY BIANCA  
BAGNARELLI



# HOW WOMEN'S HEALTH

JANUARY 2020

WELLNESS  
ISSUE



GETS SHORTCHANGED



## S AN EMERGENCY MEDICINE PHYSICIAN

since the mid-1990s, I've cared for all sorts of patients: old and young, rich and poor, male and female. I've also observed the companions who arrive with the patients, as they scramble to handle this health crisis amid work, family, and financial obligations. Often that burden lands chiefly on women, doing double, triple, quadruple duty to care for children, partners, parents, and other loved ones. It's a global phenomenon: The Organization for Economic Cooperation and Development

says the world's women spend more than 1.1 trillion hours a year on unpaid care of children and the elderly. Men spend about a third as much.

As an executive producer on the television drama *Grey's Anatomy*, I write these women into scripts. They are mothers, partners, wives, sisters, daughters, CEOs, and secretaries. The woman who just had a baby, thinks she has a blocked milk duct, and finds out too late that it's breast cancer.<sup>1</sup> The woman who doesn't want to admit to being raped because she thinks she'll be blamed for being where she was or wearing what she wore.

They're women who have a terminal illness, or need an organ transplant—and have to break it to their daughters. Women confronting their sexuality head-on; getting pregnant at older ages and choosing alternate paths to motherhood, or being childless by choice. Women with brain tumors, mental illness, and depression; women with no insurance, and women who could buy the world.

I write these women because I see these women. Because I am these women. I am firmly stuck in the "sandwich generation," taking care of an aging mother and three young children. Working full-time. Juggling schools, schedules, extracurricular activities, babysitters, deadlines, caregivers, and professional goals, all while trying to have a semblance of a social life. I am a physician, I am a writer, I am a mother, I am a single woman. I am everywoman, we are multitudes—and we are frequently, quietly, overwhelmed.

If this is the script of so many women's lives, how do we find the means to nurture health and wellness?

There's plenty to fault in the medical care, treatment, research, and support that are available to the female half of humanity. But there also are reasons for optimism, in discoveries and advances that show real promise for girls and women. I'm especially hopeful when I see us do the single best thing we can do to promote well-being: Speak up!

More women need to open their mouths and talk. About their miscarriages or their infertility or their contraception scares. About their cancer or their heart disease. About depression. Anxiety. Weight. Eating disorders. Alcohol abuse. Prescription drug abuse. Domestic violence. The stigma attached to such conditions keeps many of us silent.

### 1. BREAST CANCER

#### Cancer cell conversion

Sometimes breast cancer cells avoid medical treatments by drifting away from tightly packed tumors and changing their internal machinery. They then resemble adult stem cells and can travel in the body and start new tumors elsewhere. By using existing drugs that target these tumor turned stem cells in mice, a team of biomedical researchers redirected their development so they became harmless fat cells. The treatment has shown the potential "to repress tumor invasion and malignant progression," as scientists from the University of Basel, Switzerland, reported in the journal *Cancer Cell*. —THERESA MACHEMER

But without loud-and-clear advocacy, the research will not get funded and the policies will not get overhauled. It's only by finding our voices that we can strengthen each other and grow together into a force for healthy change.

**IN MY ROLE AS A WRITER**, obviously I'm a storyteller. I adapt real women's stories to fashion characters' stories; they're the everywomen who appear in my TV show's plots and in this essay. It's my belief that good physicians also must be good storytellers. I practice what's known as narrative medicine, which means essentially this: intently listening to a patient's story, reading the story the patient's body tells, and using both to craft a narrative for diagnosis and treatment.

Take the story of Meredith, for example. She's a surgeon, a widow with three young children, and manages to not only win accolades professionally but also spend time with her children and have a social life. She went to medical school in the early 2000s, when not even half the entering students were women. By 2018, 52 percent of those enrolling were women—progress! More broadly, by 2017, women earned 57 percent of bachelor's degrees, 59 percent of master's degrees, and 53 percent of doctorates in the United States, the National Center for Education Statistics reports. That's truly progress, because the number one element of improving health care is educating women.

Even with Meredith's advanced degree—and though she introduces herself with the title doctor, wears the white coat, and sports a visible stethoscope—she's regularly referred to as nurse while going about her hospital business. And if there's a male medical student in the room when she makes rounds, patients will often tell their story to him instead of her. Stereotypes and bias are a real part of women's lives, and gender bias is a real problem in medicine.

Another example of that is Miranda—a successful surgeon, having made it through the glass ceiling to become chief of surgery at her hospital. She's on her second marriage because her first husband couldn't understand the demands of her job (a common refrain for professional women). She goes into a hospital complaining of the nonspecific symptoms that often signal a heart attack in women<sup>2</sup>—more subtle symptoms than men's, such as upper abdominal pain, light-headedness, or unusual fatigue. Miranda is sure she is having a heart attack. (Spoiler alert: She is.) But when women—and especially women of color—raise concerns about their health and demand they be investigated, they are much likelier than men to be brushed aside, not believed, even mocked into silence by health-care professionals. According to author Leslie Jamison, whose writings include the essay "Grand Unified Theory of Female Pain," women's pain<sup>3</sup> often is "perceived as constructed or exaggerated," and women's symptoms may be ignored or treated less aggressively than male patients' would be.

This dismissive attitude has consequences not only for women's treatment now but also for the medical research that will produce the cures of the future. Historically in the

## 2. HEART ATTACK

### Gender and resuscitation

When women suffer cardiac arrest in public settings, they're less likely than men to have bystanders attempt resuscitation—and more likely to die, according to a study conducted in the Netherlands and published in the *European Heart Journal*. One probable reason: Bystanders who see a woman collapse don't realize she's having a cardiac arrest (heartbeat that gets fast and irregular, then stops) and so don't call for help or try a defibrillator to restore normal rhythm. As a result, men have about twice the chance that women have of living long enough to get out of the hospital.

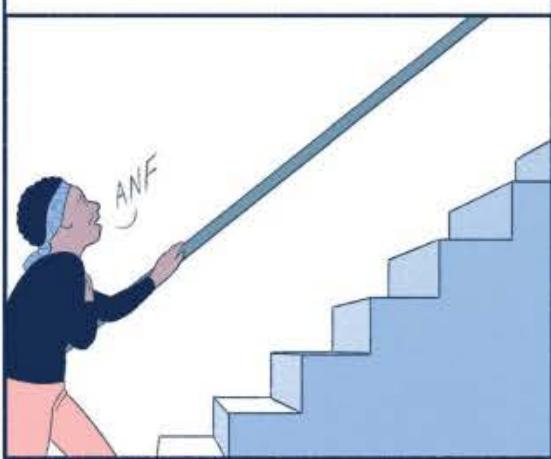
—PATRICIA EDMONDS

## 3. PAIN MEDICATION

### Women's pain undertreated

For decades, studies have found that women are significantly more likely than men to be undertreated for pain. **1989:** Research on a group divided evenly between men and women found that in the three days after they had coronary bypass surgery, the men were twice as likely as the women to be given narcotics for pain. **1996:** A 20-month study at a hospital emergency department found that among people who reported acute chest pain, women were less likely than men to be admitted, and also less likely to be given an exercise stress test at a follow-up visit. **2008:** Research by a female emergency room doctor found that when patients came to the ER complaining of acute abdominal pain, men waited an average of 49 minutes before being given a painkiller, while women waited an average of 65 minutes. —PE

I WAS AT WORK, GOING BACK TO MY OFFICE AFTER LUNCH.



AND I SUDDENLY FELT SO TIRED.



FOR NO REASON.



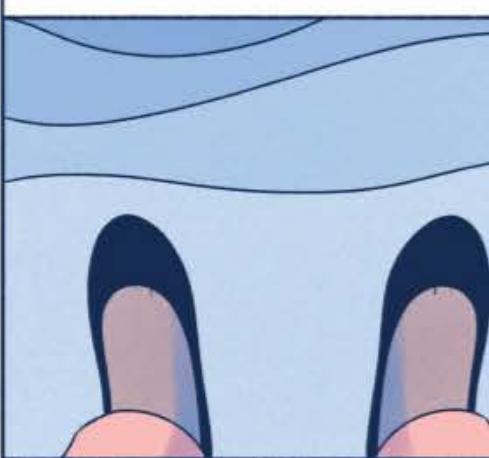
I WAS SITTING ON THE STAIRS TRYING TO CATCH MY BREATH.



BUT I COULDN'T. IT WAS LIKE THERE WAS NO AIR.



I FELT LIGHT-HEADED

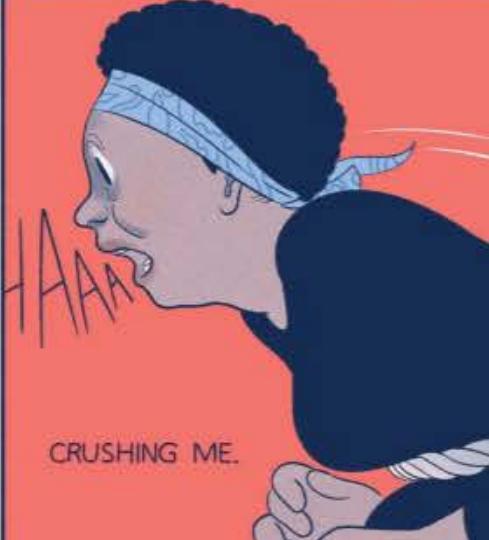


AND A TERRIBLE PRESSURE.



LIKE A ROPE...

BEING TIED AROUND ME



CRUSHING ME.

SO I CALLED 911 AND HERE I AM.

M-HM...



YEAH, I WOULDN'T WORRY ABOUT IT.



YOU PROBABLY JUST NEED TO RELAX.



(male-dominated) medical profession, clinical trials were conducted with male subjects; they were considered the “norm,” and their reactions to a new drug were assumed to be representative of how both sexes would react. Women of reproductive age were excluded “for safety reasons”; so were women in general, to eliminate hormonal differences as a factor in the research. In 1993 the U.S. National Institutes of Health called for women to be included in more trials. In 2016 a medical journal analysis found that clinical trials were including more women, but not always in numbers representative of the female population. It also found that the research didn’t always involve “sex-specific analysis of the safety and efficacy” of a product.

We need women-specific research to help address differences in biology, and discrepancies<sup>4</sup> in health outcomes, between women and men. Women are more likely to be diagnosed or living with chronic diseases and/or immune diseases; in the United States, 38 percent of women have one or more chronic diseases compared with 30 percent of men. Coronary artery disease causes more severe impairment and more deaths in women than in men (but greater research funding is devoted to studying it in men). New drugs and products come on the market ostensibly for women’s benefit, but some actually harm women.<sup>5</sup> This suggests a need for more research and testing, with women playing a role as subjects and as decision-makers.

**IN CERTAIN GIRLS AND WOMEN** who turn up at hospital emergency departments, physicians see health problems that probably are treatable. But the social and cultural crises that complicate these patients’ lives often seem to defy resolution.

Jo is so frightened of her past that she has run away from it, changed her name, and disguised her identity. She was a victim of intimate partner violence so severe that she was hospitalized multiple times and feared for her life. Emergency physicians see plenty of domestic violence victims, some with bruises and broken bones, others with unseen scars. But Jo’s not a patient; she’s a physician on the hospital staff. She belies the common misconception that domestic violence occurs mostly in poor, uneducated households. The reality is that on average in the United States, about 20 persons every minute are abused by an intimate partner. And worldwide, domestic violence is the leading cause of injury to women—more than accidents, muggings, or assaults by strangers.

Nadia is a 10-year-old girl who is outside an emergency department, alone and apparently in pain, when a stranger alerts the doctors. An exam shows the girl has a large abdominal tumor and needs emergency surgery. Hospital staff is about to summon child protective services when the “stranger” confesses: She is Nadia’s mother, afraid to show herself because of her undocumented status. This fear of deportation is also why she waited so long to get Nadia examined. Because of the delay, the procedure is much more costly (both physically and financially) than open and preventive medical care would be.

#### 4. HEALTH AND SAFETY

##### Drug effects differ

Some of today’s most commonly used drugs produce different effects, and side effects, in women than in men—a variability not always considered by prescribers or communicated to patients. For example, Americans had been using the popular prescription sleep drug zolpidem (sold under names including Ambien) for more than 20 years when the Food and Drug Administration announced in 2013 that what had been the recommended dose for both sexes was actually twice as much as women should take. Similarly, research has shown that women have a 1.5 to 1.7 times higher risk of adverse drug reactions than men do. For instance, women experience liver failure caused by acetaminophen (the active ingredient in the over-the-counter analgesic Tylenol) more often and more severely than men, because men’s livers have a greater capacity to metabolize acetaminophen safely. —PE, TM

#### 5. HEALTH AND SAFETY

##### Banned birth control

Nearly 47 million women in the United States ages 15 to 49 use contraception, but not every method available to them has been reliable or safe. In 2002, the FDA approved a permanent birth control product called Essure, a metal device that is inserted into the fallopian tubes, where the body covers it with scar tissue. After about three months, this creates a permanent blockage so an egg cannot pass from the ovary to the uterus. The FDA has received more than 26,000 reports of side effects attributed to Essure, including pelvic pain, allergic reactions to nickel, device breakage, and pregnancy. By the end of 2018, Essure use was considered a possible factor in 15 women’s deaths. Sales of the product ended in the United States in December 2018; a study of its long-term effects is ongoing. —TM

Today's immigration crises have no simple remedies. But when undocumented U.S. residents lack access to preventive medicine and care, they bring all their care needs to emergency departments—where use by the uninsured costs about \$38 billion a year more than non-emergency care would.

Uninsured patients suffer from lack of health-care access, and a woman's risk of being uninsured increases if she has a low income or is Hispanic/Latina. Women living in rural communities are more likely than women in other areas to struggle with poor health; they have limited access to mammograms and other screenings, and maternity care, because only 6 percent of the nation's ob-gyns work in rural settings.

Other factors discourage women from accessing the system. Although the Affordable Care Act attempted to lower financial barriers, seeking care still takes money—for child-care, transportation, and out-of-pocket costs. That can be prohibitive for women because they often earn lower wages, have fewer financial assets, and have higher rates of poverty than men. In the United States, a woman also is statistically likelier than a man to be covered by health insurance as a dependent and is thus at greater risk of losing coverage if she then is widowed or divorced or if her policy-holding spouse or partner becomes unemployed. For these reasons and more, about one in four U.S. women has had to delay or forgo health care in the past year because of costs, a Kaiser Women's Health Survey found.

**IN THE QUEST FOR WELLNESS, WOMEN CONTEND** with one variable that men do not: a reproductive system designed to bear offspring. Whether or not they ever give birth, most women are equipped to do so for some portion of their lives. Depending upon circumstances, that can become a blessing, a burden, a political football, a societal issue. Ultimately, it's the most personal health issue of all.

Arizona is a pediatric surgeon who loves kids and wants to have her own with her same-sex spouse. Fortunately for them, and for singles and couples who need help to conceive, there are options, including surrogacy, embryo donation, egg donation—and sperm donation, a global industry valued at about four billion dollars. Arizona and her partner decide on sperm donation. She has an IUI (intrauterine insemination) and is elated when her pregnancy test is positive. Unfortunately, on her first ultrasound, there is no heartbeat.

Infertility<sup>6</sup>—not being able to get pregnant or to sustain a pregnancy—affects about 10 percent of U.S. women ages 15 to 44 (some 6.1 million women), according to the Centers for Disease Control and Prevention. But the good news about infertility is that the majority of cases can be treated by conventional therapies such as surgery or medication (and only 3 percent require the use of in vitro fertilization, or IVF). Compared with decades ago, there's much more hope.

What of the women who don't want children yet? Or ever? Roughly 60 percent of U.S. women ages 15 to 44 years use

## 6. INFERTILITY

### Factors affecting male fertility

If a woman is unable to get pregnant after one year of trying, she and her partner may be facing infertility. In the United States, about 8 percent of infertility cases are caused by a male factor alone. Risk factors for male infertility include obesity and substance use, but some risks are beyond an individual's control. A study conducted in Sweden found that men with fathers who smoked had a 50 percent lower sperm count than those with nonsmoking fathers. And while men can avoid the high temperatures of hot tubs, climate change may also pose a risk. A 2018 study in beetles found that one heat wave reduced sperm production by about 75 percent, but females were not affected. —TM

a contraceptive method, the Guttmacher Institute reports. And of women in that age range, the abortion rate in 2017 was 13.5 abortions per thousand—the country's lowest rate ever.

Cristina is a take-no-prisoners kind of person who proclaims herself “childless by choice.” Even when she was married to a man she deeply loved, and he wanted a child, she stayed true to herself (at the price of the marriage). She aligns with the growing wave of women who, for a variety of reasons, are voluntarily child free—a decision as valid as the opposite choice.

Then there are the postponers, those who want to wait to bear children after a career or for other reasons. My advice to them: Look at what the current generation of older, professional women has gone through. Women who wait too long have a much harder time getting pregnant (and it gets very expensive—the average cost of a single IVF treatment is around \$12,000). Even with my medical training, I looked at the age-at-conception statistics and somehow thought they didn’t apply to me. Certainly I’d be like the people in the media, or the television characters I write for, who get pregnant at the drop of a hat no matter their age. Guess what? Wrong!

Here’s the truth: A woman’s best reproductive years are in her 20s. Fertility gradually declines in the 30s, as both the quality and quantity of her eggs decrease. Each month that she tries to get pregnant, a healthy, fertile 30-year-old woman has a 20 percent chance of doing so. By age 40, a woman’s chance is less than 5 percent a cycle.

This is why I’m a strong advocate of fertility preservation<sup>7</sup> via egg or embryo freezing, to avoid “panic parenting” moves such as entering into unwise relationships just to have a child. Izzy, a surgical resident struggling to beat stage 4 melanoma, has her eggs removed to preserve future fertility if she survives her treatments. Others use the technology in less dire circumstances. Yes, egg and embryo freezing are expensive processes, and not a guarantee, but they do offer a choice. Think of them as investments in your future life!

For those who have the desire and have timed everything right, there’s the joy of pregnancy and birth. But even these happy times can be scary. Karen is a quirky woman married to the love of her life, a paramedic who rushes to her bedside when she is in labor. He gets there in time to witness the birth of their baby girl, and it’s a happy day for all until Karen starts feeling some pain that doesn’t seem right. She begins bleeding profusely so is taken to the operating room, where doctors perform a hysterectomy. After the operation, she suffers multiple-organ failure and has a cardiac arrest from which she does not recover. Karen dies of pre-eclampsia, a high blood pressure disorder that can be treated if caught soon enough.

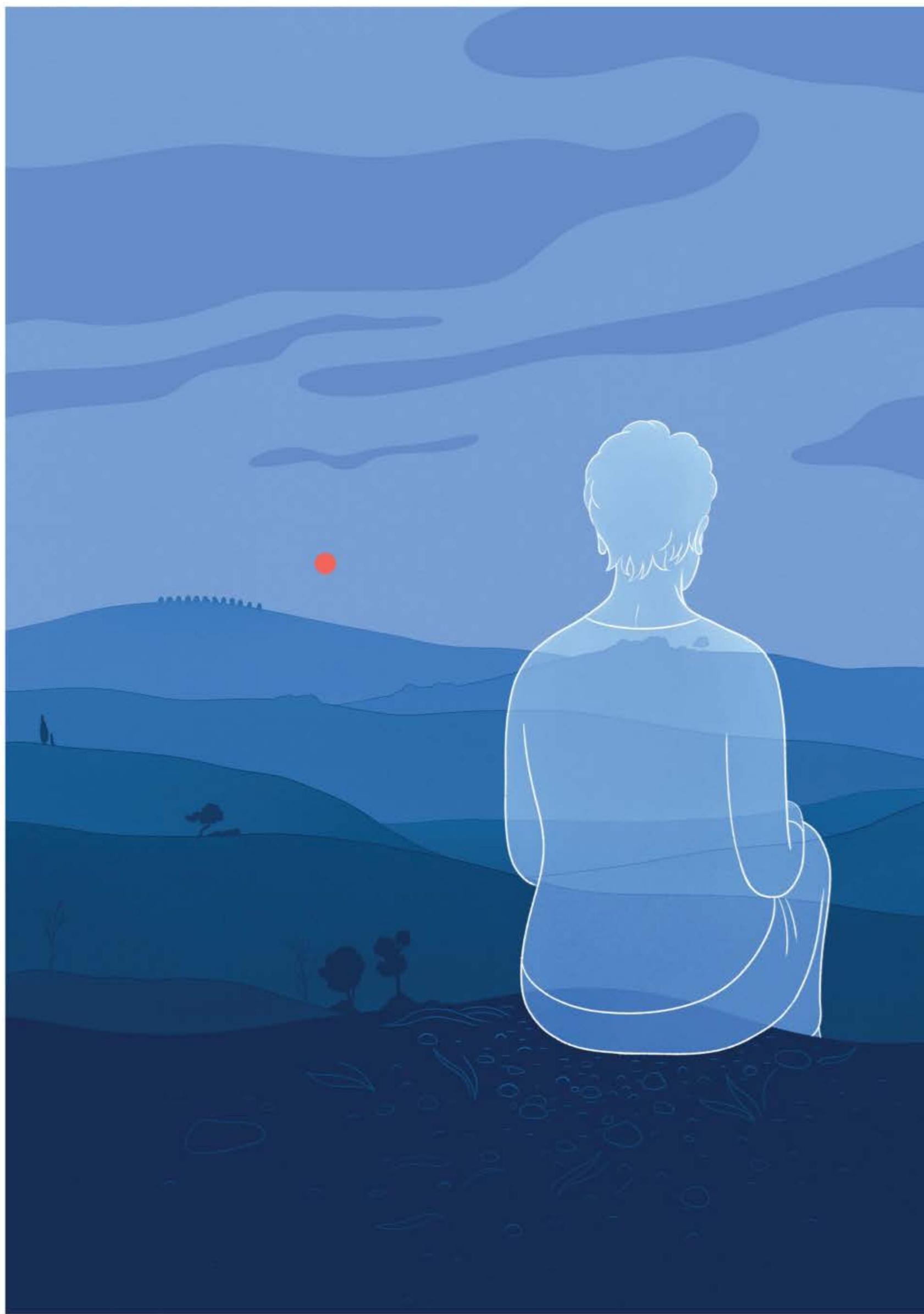
Maternal mortality statistics track what fraction of deaths of women ages 15 to 49 are maternity related. From 2000 to 2017, maternal mortality decreased significantly in the world overall—but increased in the United States. Many elements contribute to such increases; among them are obesity, chronic conditions, socioeconomic factors, access to care, and having

## 7. TECHNOLOGY

### ‘Femtech’ tools and childbearing choices

For women struggling with infertility or maternity issues, a fledgling “femtech” industry is developing new devices and services. Computer apps and wearable monitors track a woman’s fertile periods—or, once she’s pregnant, her unborn baby’s development. A cloud-based company offers all-in-one clinical and financial plans for patients having IVF or egg freezing.

Increasingly, would-be parents get embryos or gametes tested for chromosomal abnormalities before deciding whether to use them. In a U.K. study reported last year in *Human Reproduction*, about a third of patients who chose to test expressed some regret that they’d done so—especially if abnormalities were revealed, but even if they weren’t. As a result, study authors suggested that “additional counselling and support” be offered in concert with testing. —PE



children at older ages. Even so, the CDC estimates that about 60 percent of maternal deaths are preventable. And between white women and women of color, the discrepancy is staggering, with black women three to four times as likely to die from pregnancy or childbirth complications.

Our health-care system has done a wonderful job of protecting and improving the outcomes for newborns and preterm babies, but at the expense of ignoring the mothers. In 2018 Congress took a step in the right direction, passing legislation to fund and support states' efforts to reduce maternal deaths.

**JUST AS THEY'RE INTEGRAL** when new lives enter the world, women are guardians and anchors when long lives reach the end. Women tend to live longer than men (those 85 and older outnumber their male counterparts two to one). Many are doubly exposed to health-care problems because they're caring for the young and the old in addition to themselves. Ellis is an award-winning, intelligent, driven surgeon in the prime of her career when she is diagnosed with early onset Alzheimer's dementia.<sup>8</sup> It ruins her career and eventually leads to the end of her life. Alzheimer's disease disproportionately affects women, on two levels. Almost two-thirds of adults 65 or older with the disease are women. And of the more than 16 million Americans who provide unpaid care to a person with Alzheimer's or other dementias, 66 percent are women.

As Americans over 65 become a larger share of the population, that almost certainly will mean more women with Alzheimer's and fewer younger women to be caregivers. It's one more reason to take a hard look now at our approaches to health and wellness needs, and make improvements.

In 2015, United Nations member states agreed to try to provide basic health care for every child, man, and woman by 2030. Today, when hundreds of millions of people can't find or afford health care, we're a long way from that. But it's a goal worth fighting for. Each of us can start by advocating for what she personally needs, and what her family and community and country will need, to live lives of health and well-being.

On *Grey's Anatomy* a few seasons ago, Meredith Grey—the Meredith I mentioned earlier—barely survives a brutal assault. When she recovers, she offers some powerful advice about the importance of speaking up. I'll give her the last word here:

"Don't let fear keep you quiet. You have a voice, so use it. Speak up. Raise your hands. Shout your answers. Make yourself heard." □

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Physician **Zoanne Clack** is an executive producer on the ABC series *Grey's Anatomy* and has been one of the writers since the show began in 2005. She's also an adviser for all medical aspects of the show. Clack completed a residency in emergency medicine, has a master's degree in public health, and spent a year at the Centers for Disease Control and Prevention working in international emergency medicine. She has one son and twin daughters.

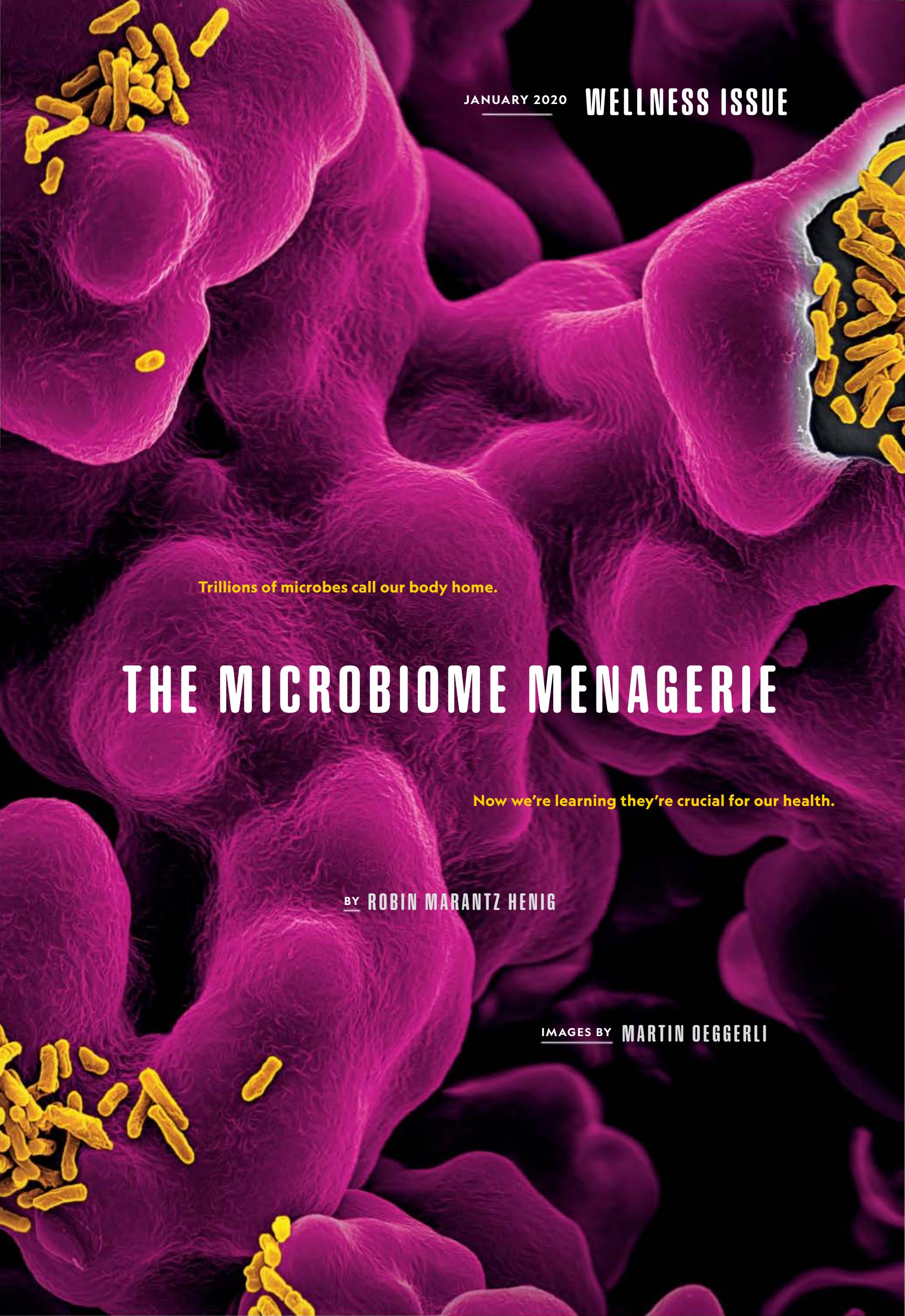
*National Geographic Partners and the ABC Television Network are owned by The Walt Disney Company.*

## 8. ALZHEIMER'S DISEASE

### Dementia differences

Women outnumber men roughly two to one among Americans with Alzheimer's disease, and scientists are unraveling the factors behind this disparity.

Lifestyle may play a role: Women who spent time in the paid workforce show less memory decline than those who didn't. But physiological factors also differ. The cognitive tests used to catch the disease early are less effective for women because they tend to have better verbal memory than men, and catching the disease later may lead to faster cognitive decline. There are also different genetic risk factors for men and women. And compared with men's brains, the connections in women's brains might provide paths for greater spread of protein plaques. —TM



JANUARY 2020

WELLNESS ISSUE

Trillions of microbes call our body home.

# THE MICROBIOME MENAGERIE

Now we're learning they're crucial for our health.

BY ROBIN MARANTZ HENIG

IMAGES BY MARTIN OEGGERLI



*Escherichia coli*, the yellow rods clustered on a purple substrate, can cause food poisoning, but most strains are not only harmless, they're beneficial. *E. coli* inhabit the human gut and perform essential functions, such as making vitamins K and B<sub>12</sub> and repelling disease-causing bacteria.

## FECES

The gut microbiome flaunts its diversity in this sample of human feces, which includes an enormous bacterium that's about 50 times longer than *E. coli*. Everyone's mix of microbes is unique. Scientists are learning the many ways these microbes affect our health, weight, mood, and even personalities.





# T

HE MORE SCIENTISTS investigate the microbes living inside us, the more they learn about the surprising impact of these tiny organisms on how we look, act, think, and feel. Are our health and well-being really driven by the bacteria, viruses, fungi, and protozoa that live in our intestines, in our lungs, on our skin, on our eyeballs? What a weird concept—that the bugs we lug around appear to be essential to establishing the basic nature of who we are.

The effects of the microbiome, this menagerie of microorganisms, can be profound—and can start incredibly early. In a study published last year, scientists showed that something supposedly as innate as a child's temperament might be related to whether the bacteria in an infant's gut are predominantly from one genus: the more *Bifidobacterium* bugs, the sunnier the baby.

This observation, from Anna-Katariina Aatsinki and her colleagues at the University of Turku in Finland, is based on an analysis of stool samples from 301 babies. Those with the highest proportion of *Bifidobacterium* organisms at two months were more likely at six months to exhibit a trait the researchers called "positive emotionality."

Microbiome science is still relatively young. It's been just 15 years since the research took off in earnest, which means most studies to date have been preliminary and small, involving only a dozen or so mice or humans. Scientists have found associations between the microbiome and disease, but can't yet draw clear cause-and-effect conclusions about our vast critter inventory and what it all means for us as hosts. Still, the inventory itself is mind-boggling—it's now thought to be around 38 trillion microbes for a typical young adult male, slightly more than the number of actual human cells. And the prospects for putting that inventory to use are tantalizing.

In the not-too-distant future, according to the most enthusiastic researchers, it might be routine to deliver a dose of healthy microbes in the form of prebiotics (compounds that act as a substrate on which beneficial microbes can grow), probiotics (the beneficial microbes themselves), or fecal transplants (microbe-rich feces from healthy donors)—helping us realize the promise of operating at top form, from the inside out.

When we talk about the microbiome, we're talking primarily about the digestive tract, home to more than 90 percent of a

## STREP

*Streptococcus pneumoniae*, shown dividing into daughter cells, can cause serious illnesses, such as meningitis and pneumonia, but like *E. coli*, some *Streptococcus* species are harmless. The bacteria are found on the skin and in the mouth, respiratory tract, and gut.

### Behind the Images

Martin Oeggerli made these images with a scanning electron microscope. The samples were dried, coated with gold, and placed in a vacuum chamber. The microscope's electron beam has a shorter wavelength than visible light and can capture smaller objects, but without color. When the color of a microbe is known, Oeggerli uses it. If not, he chooses colors to discriminate between types of microbes and their features.





## LIPS

Moist lips are rich in microbes. A woman pressed her mouth on a petri dish to let her microbiome grow, and grow it did. Days later a colony bloomed.

People who often kiss each other will develop similarities in their oral microbiomes.



body's microorganisms. But other regions are also crawling with life. Microbes colonize wherever the inside of the body meets the outside: eyes, ears, nose, mouth, vagina, anus, urinary tract. There are also microbes on every inch of skin, with high concentrations in the armpits, the groin, between the toes, and in the belly button.

And here's the really amazing thing: Every one of us has a particular mix of microbes that's different from everyone else's. Based on current observations, it's possible for two individuals to have zero overlap in the microbial species of their microbiomes, says Rob Knight of the Center for Microbiome Innovation at the University of California, San Diego. The unique nature of microbiomes might even have forensic applications, he says. "We can track objects or surfaces people touch back to that person by matching the skin microbiome traces." Maybe someday police investigators will go through crime scenes taking samples of skin microbes, much the way they now dust for fingerprints.

Here are some highlights of what scientists are learning about how the microbiome affects us across our life span, from infancy to old age.

## INFANCY

**THE FETUS IN UTERO** lives essentially microbe free. Then it squeezes down the birth canal, where it confronts a riot of bacteria. During a vaginal delivery, the baby is awash in microbes that live in the vagina; it's also exposed to the mother's gut bacteria as its face passes by her perineum and anus. These maternal gut microbes immediately start to colonize the newborn's own gut, engaging in a kind of conversation with developing immune cells. In this way, the very early microbiome prepares the immune system for healthy functioning later in life.

When a baby is born by cesarean section, though, it misses out on this exposure. Its gut is seeded with different microbes—not those from the mother's gut and vagina, but from her skin and breast milk, the nurse's hands, even the hospital bedding. These early differences might have implications that last a lifetime.

In 2018 Paul Wilmes of the Luxembourg Centre for Systems Biomedicine at the University

of Luxembourg published a study of 13 babies born vaginally and 18 by C-section. He and his colleagues analyzed the microbes in the stool of the newborns and their mothers, as well as vaginal swabs from the mothers. C-section babies had significantly lower levels of bacteria that make lipopolysaccharides, which are a primary stimulus of the developing immune system. The reduction lasted for at least five days after birth—enough, Wilmes believes, to have long-term consequences for immunity.

Eventually, usually by the first birthday, the microbiomes of C-section babies and vaginally born babies are pretty much the same. But Wilmes thinks the differences he observed in the first few days of life mean C-section babies might be missing a period of "priming," when immune cells are set up to respond appropriately to foreign agents. The scantier microbial populations of C-section babies during these initial days could explain why they are more prone to a host of immune system problems later on, including allergies, inflammatory diseases, and obesity.

Wilmes says one day it might be possible for babies born by C-section to be given probiotics derived from specific strains of bacteria found in their mothers, which would, in theory, seed their intestines with helpful microbes. Such probiotic therapy is still far in the future, though.

## CHILDHOOD

**FOOD ALLERGIES HAVE BECOME** so widespread that many schools restrict what lunches kids can bring from home, like peanut butter and jelly sandwiches, for fear of setting off a classmate's allergic reaction. In the United States, 5.6 million children suffer from food allergies—which translates to two or three in every classroom.

Many factors are thought to account for this rise, including an increase in C-section births and an overuse of antibiotics, which can wipe out protective bacteria. Cathryn Nagler and her colleagues at the University of Chicago wondered whether the rise in childhood food allergies might be linked to the microbial mix in children's guts. Last year they published a study of eight six-month-old babies, half of whom were allergic to cow's milk, half of whom

were not. The microbiomes of the groups were quite different, they discovered: The healthy babies had the bacteria expected in typically developing babies their age, while the babies with a cow's milk allergy had bacteria more characteristic of adults.

In the allergic babies, the normally slow progression from an infant microbiome to an adult one took place "at warp speed," Nagler says.

Using fecal samples, Nagler and her colleagues transplanted gut bacteria from the babies in her study into germ-free mice—mice born by C-section and raised in sterile conditions so they had no microbes at all. When the mice received transplants from healthy babies, they received protective bacteria that prevented an allergic response to cow's milk. But when the transplants were from allergic babies, the mice didn't get the protective bacteria and had an allergic response.

Further analysis showed that one species of bacteria in particular that's unique to human infants—*Anaerostipes caccae*, from the Clostridia class—seems to have been most relevant in protecting the first group of mice. This species was from the same family within Clostridia that Nagler's team had identified in an earlier study as protective against peanut allergy.

Nagler, who is president and co-founder of the Chicago-based drug start-up ClostraBio, hopes to test the therapeutic potential of these bacteria in lab mice—and eventually in allergic patients. The first challenge has been finding somewhere in the gut for the beneficial bacteria to land. Even in an unhealthy microbiome, Nagler says, all the niches are already filled; for Clostridia to go in, something else has to come out. So ClostraBio developed a drug that clears out a niche in the microbiome.

Nagler and her colleagues have been giving the drug to mice and then infusing them with a variety of Clostridia bugs, along with dietary fiber that encourages their growth. She hopes to begin clinical testing on a Clostridia treatment in humans within the next two years, with the eventual goal of giving it to children with food allergies.

Gut microbes also might be related to other childhood diseases, such as type 1 diabetes. In Australia scientists collected stool samples from 93 children with a family history of type 1 diabetes and found that those who went on to develop the disease had higher levels of enterovirus A in their

stool than those who didn't develop diabetes.

One of the scientists involved in the study, W. Ian Lipkin of the Columbia University Mailman School of Public Health, cautions researchers against rushing to explain diseases—whether diabetes or any other—by differences in the microbiome alone. "This is still largely a descriptive science," he says; all that's known for sure is that certain microbes are associated with certain conditions.

Even with this caveat, Lipkin is excited about where microbiome science might lead. He expects that in five or 10 years, scientists will understand the mechanisms of how the microbiome affects the body and will have begun clinical trials on human subjects to demonstrate the health impact of altering it. Once microbiome science "becomes mechanistic and testable," he says, "then it will become real."

## ADOLESCENCE

**THE VAST MAJORITY OF TEENAGERS** in developed countries are pimple-prone—and for them, there does seem to be such a thing as an "acne microbiome." Many kids have skin that's especially hospitable to two strains of *Cutibacterium acnes* (until recently called *Propionibacterium acnes*) that have been closely linked to acne. Most strains of this bacterium, despite the *acnes* in its name, are either harmless or helpful, keeping pathogenic microbes at bay; in fact, *C. acnes* is the predominant component of the normal microbiome of the face and neck.

But having a bad-guy strain of *C. acnes* can be a problem. It's one of the elements needed for acne to arise, says Amanda Nelson, a dermatologic researcher at Penn State University College of Medicine. The others are sebum (the oil produced by sebaceous glands to keep the skin moist), which *C. acnes* uses as a food source; plugged-up hair follicles; and an inflammatory response. These four factors work in concert, Nelson says, adding, "We actually don't know what happens first."

The acne microbiome was the focus of a study at Washington University School of Medicine in St. Louis, where researchers found that the only acne treatment leading to long-term remission—isotretinoin, sold as Accutane and other

## SMELLY FEET

Cultured from damp feet, these bacteria, attached here to a fiber, thrive in sweat, which is odorless. But when sweat collects, it creates a breeding ground for odoriferous microbes. More sweat glands are concentrated on our palms and on the soles of our feet than anywhere else.

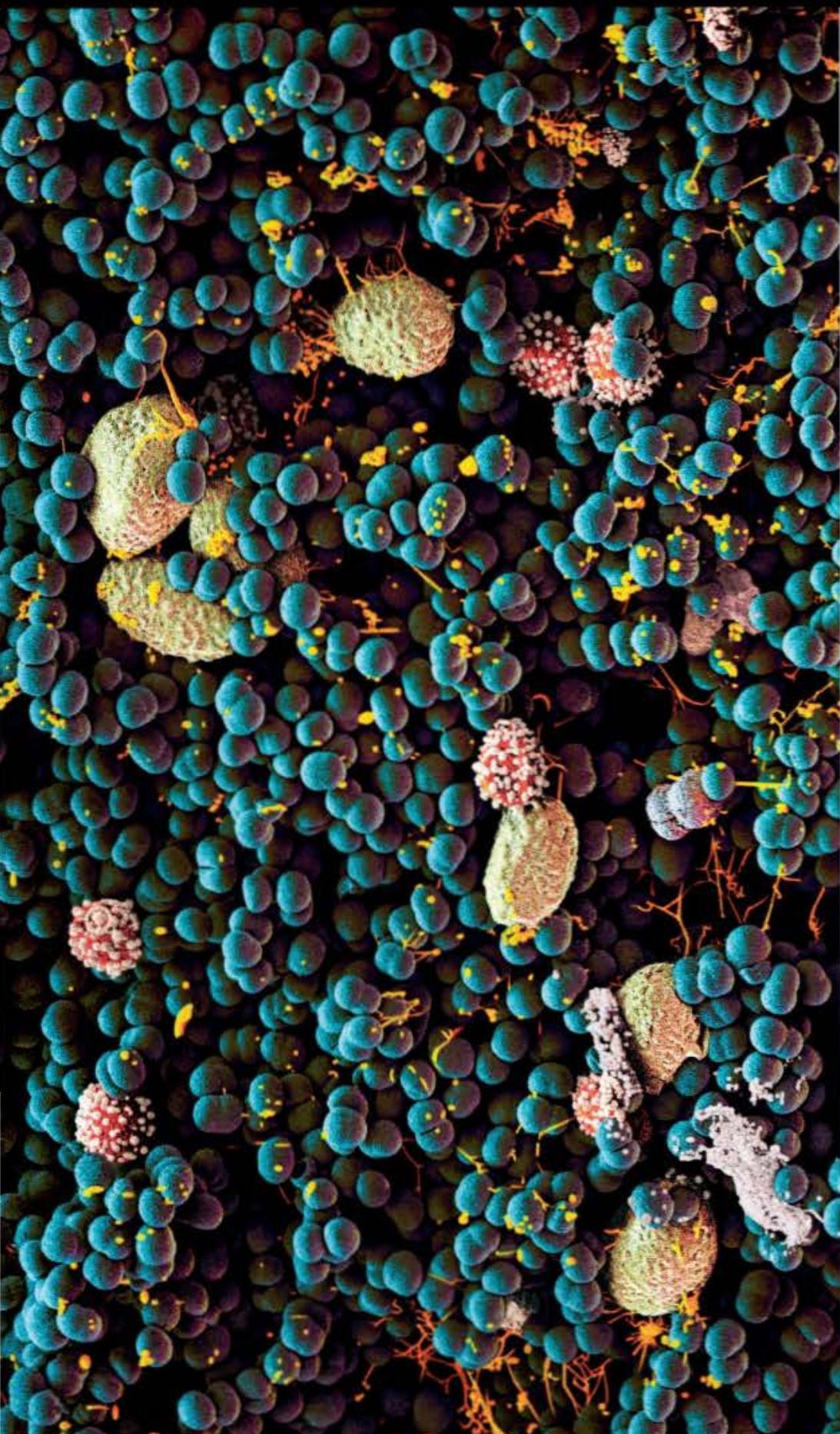
[NEXT IMAGE](#)

## BELLY BUTTON

A half dozen types of microbes predominate in the navel. But many other species of bacteria and fungi are also found there. Like the microbiome inside, the microbes outside vary from person to person.







## THE MICROBES WITHIN

Approximate number\*

38 trillion

LARGE  
INTESTINE

# GUT INSTINCTS

Our bodies host trillions of microbes, a collection of bacteria, fungi, and protozoa that starts developing at birth and is unique to each of us. These microorganisms can communicate with our brains to regulate bodily functions and even influence our mood, as well as chronic conditions such as anxiety, through chemical communication pathways known as the gut-brain axis.

## HOW THEY COMMUNICATE

### VIA BLOODSTREAM AND NERVES

Chemicals released by microbes into nerves or the bloodstream influence brain areas that deal with memory. Chemicals in the bloodstream can also signal the limbic system—a brain area that processes emotion and stress—to change our moods.

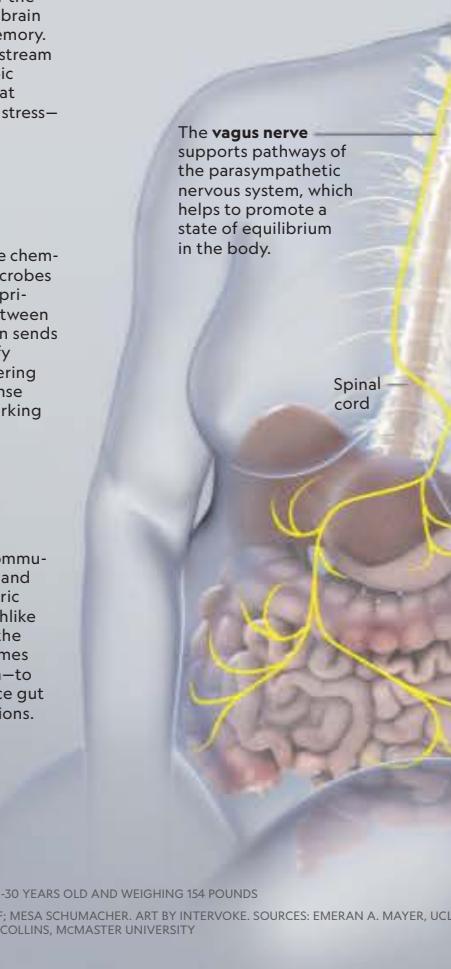
### THROUGH THE VAGUS NERVE

Sensory neurons receive chemical signals from gut microbes and relay them up this primary signaling path between gut and brain. The brain sends back signals that modify function, such as tempering an inflammatory response so the gut will keep working even if a person is sick.

### USING THE 'SECOND BRAIN'

Microbes can bypass communicating with the brain and directly signal the enteric nervous system—a meshlike network of neurons in the digestive tract, sometimes called the second brain—to independently influence gut movements and secretions.

The vagus nerve—  
supports pathways of  
the parasympathetic  
nervous system, which  
helps to promote a  
state of equilibrium  
in the body.

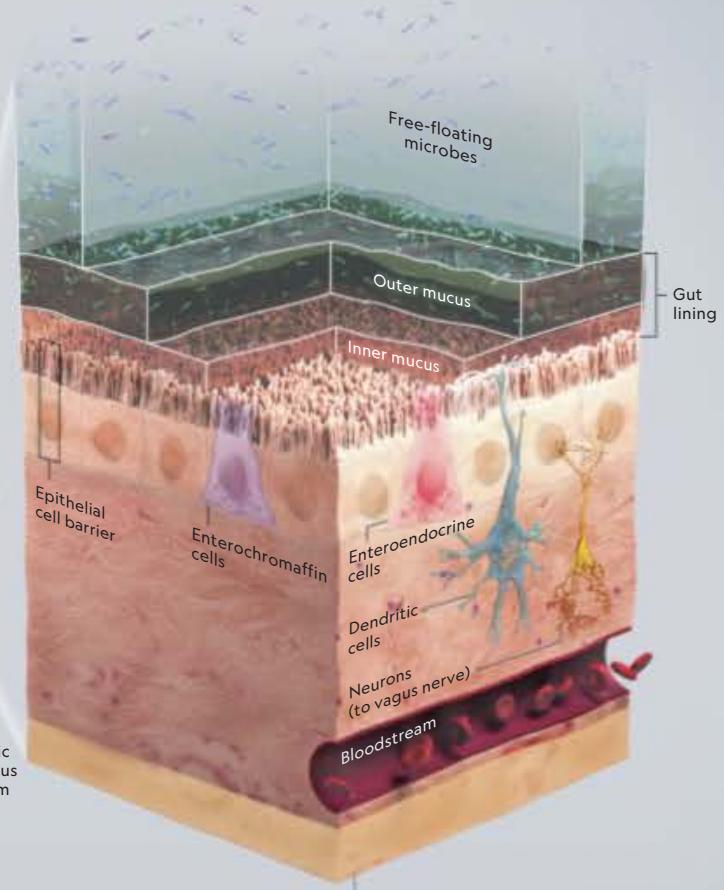
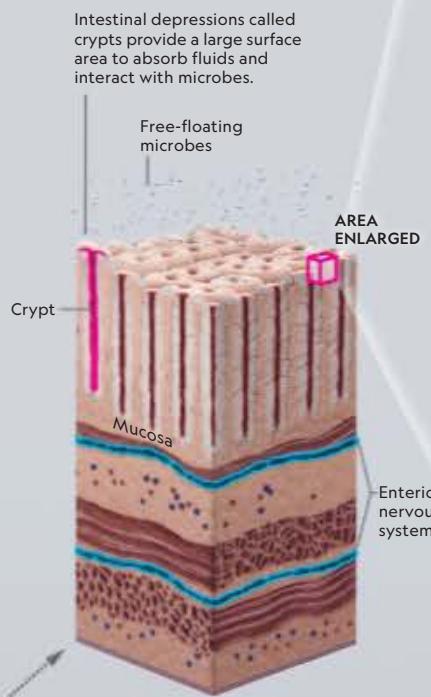


\*BASED ON A TYPICAL MALE, 20-30 YEARS OLD AND WEIGHING 154 POUNDS  
MONICA SERRANO, NGM STAFF; MESA SCHUMACHER. ART BY INTERVOKE. SOURCES: EMERAN A. MAYER, UCL DIGESTIVE DISEASES; STEPHEN COLLINS, MCMASTER UNIVERSITY

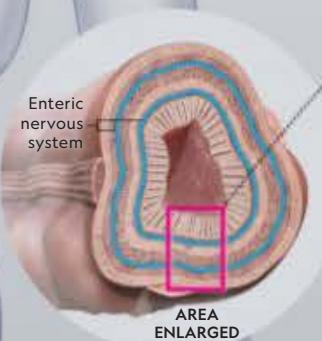


### FRIENDS AND FOES

Microbes in mucosa can work with us. But those floating free inside the intestine tend to focus more on their own survival, sometimes to our detriment, especially if they're harmful parasites.



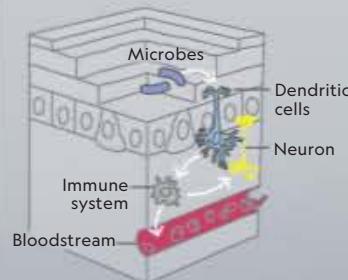
The biggest community of microbes, more than 90 percent of the body's total, thrives in our **large intestine**.



## WHAT MICROBES CAN TELL US

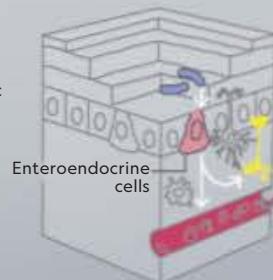
### WE NEED AN IMMUNE BOOST

Microbial disturbance in the gut lining can be sensed by immune messaging (aka dendritic cells). They can then activate other immune cells or signal distress to the brain.



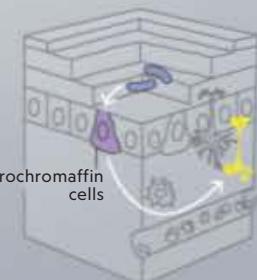
### PUT DOWN THE FORK

Scientists suspect that microbes get enteroendocrine cells to release chemicals signaling the hypothalamus—the brain area that keeps our body in balance—to tell us we're full.



### WE'RE HURT, OR HAPPY

Microbes can trigger enterochromaffin cells, which hold most of the body's "happy chemical," serotonin, to signal the brain, influencing perceptions of pain and well-being.



brand names—works in part by altering the skin microbiome, reducing the number of *C. acnes* bacteria while increasing the diversity of the skin microbiome overall. In this healthier, more diverse environment, they found, it's harder for the bad strains of *C. acnes* to take hold.

Now that scientists have learned that isotretinoin works by changing the acne microbiome, they might try to develop microbial treatments that have the same effect—treatments, they hope, that are safer than isotretinoin, which can cause birth defects if taken during pregnancy.

These alternatives can include what the Washington University researchers call “prebiotic fertilizers”—microbes that provide conditions for a healthy skin microbiome to flourish—and “strain-selective ‘weed killers’”—agents that wipe out the deleterious strains of *C. acnes* while allowing the beneficial ones to remain. Also in the mix, they say, might be probiotics, oral or topical supplements that contain direct doses of beneficial *Cutibacterium* strains.

## ADULTHOOD

**WHAT IF YOU COULD GET MORE** out of your workout just by transferring microbes from an athlete's gut into yours? That's the question scientists at Harvard University wanted to explore. They collected daily stool samples over the course of two weeks from 15 runners in the 2015 Boston Marathon—starting one week before the race, ending one week after—and compared them with daily stool samples taken for two weeks from a control group of 10 non-runners. A few days after the marathon, the scientists found, the runners had significantly more *Veillonella atypica* bacteria in their stool than did the non-runners.

“It set up a bit of a light bulb because of the unique metabolism of *Veillonella*, which uses lactate as its preferred source of energy,” says Aleksandar Kostic, of the Joslin Diabetes Center and Harvard Medical School. Lactate is generated by muscles during intense exercise. “That got us thinking: Is it possible that the *Veillonella* is metabolizing muscle-derived lactate in the athletes?” And if it was, could infusions of *Veillonella* help nonathletes perform better?

Next they turned to lab mice. They extracted

*Veillonella* from one runner's stool and infused the bacterium into 16 mice with normal microbiomes that had been screened for pathogens. Then they put the mice on tiny treadmills and had them run to exhaustion. They did the same with 16 control mice, using a different bacterium that isn't involved in lactate metabolism. The *Veillonella* mice could run for 13 percent longer than the control mice, leading the investigators to conclude that the microbiome might play a critical role in physical performance.

Kostic says the experiment offers “a really elegant example of how symbiosis comes to happen.” The *Veillonella* benefits when the muscles of the host, through exercise, generate the lactate it lives on. The host, in turn, benefits because *Veillonella* turns lactate into propionate, which enhances the capacity for exercise by, among other things, increasing heart rate and oxygen metabolism, and possibly by reducing muscle inflammation.

“This kind of relationship, I think, underlies most human-microbiome relationships,” Kostic says. “Ultimately, there's this kind of mutualistic relationship happening.”

The microbiome might account for some less advantageous traits too, including mental states such as anxiety and depression. In 2016 scientists at University College Cork in Ireland published a demonstration of the microbiome-depression link when they transplanted stool from depressed humans into rats. Would the rats become depressed too?

The scientists divided 28 lab rats into two groups. The experimental rats received fecal transplants from a pooled preparation from three severely depressed male patients; the control rats got transplants of pooled feces from three healthy males.

It turned out that getting fecal transplants from the depressed men made the rats depressed. Compared with the controls, they exhibited a loss of interest in pleasurable activities (as measured in rats by how often they chose to drink sugar water), and increased anxiety (which in rats means avoiding open or unfamiliar sections of a laboratory maze).

While acknowledging it's a leap from rats to humans, the scientists say their work adds to the evidence that the microbiome of the gut could play a role in how depression develops. Targeting these microorganisms, they say, might one day help treat depression and other mood disorders.

# OLD AGE

THE MICROBIOME IS AT ONCE PERSISTENT and ever changing. Your unique microbiome profile is pretty much set by age four, and only significant changes—altering diet or exercise routines, moving to a different place, changing the time spent outdoors, taking antibiotics or certain other drugs—can really change it. But in one sense, the microbiome is constantly in flux, varying in tiny ways with every meal. And throughout adulthood it changes along a predictable course—so predictable, in fact, that it's possible to estimate your age just by looking at your gut microbes.

This handy trick, known as a “microbiome aging clock,” involves artificial intelligence, as demonstrated recently at the Hong Kong-based start-up Insilico Medicine. The scientists gathered information on the microbiomes of 1,165 people in Europe, Asia, and North America from publicly available data sets. Roughly one-third of the samples were from people in their 20s and 30s, one-third from people in their 40s and 50s, and one-third from people ages 60 to 90. The scientists put the age-tagged microbiomes of 90 percent of the subjects through a round of machine learning; then they applied the patterns found by AI to the other 10 percent of the microbiomes, untagged, to see if they could determine the ages. The microbiome aging clock came up with a suggestion that was accurate to within four years of the actual age.

What does this say about the physical changes that occur with age, in particular weakened immunity, systemic inflammation, and frailty? Researchers at Babraham Institute in Cambridge, England, tried to find out using fecal transplants. They knew the immune system functions more poorly with age, and they wondered whether transplanting feces from young mice into old mice would have a restorative effect.

Before the transplant, the old mice showed a significant decline in the immune reaction of cell masses lining the small intestine known as Peyer's patches. When the old mice were given fecal transplants from young mice, the immune response of their Peyer's patch cells reverted to a more youthful state. Apparently, the scientists concluded, the sluggish immune reaction in old mice is reversible; it can be “rescued”

by an infusion of gut microbes from young mice. It's enough to make you wonder whether a dose of youthful poop could be the secret to a healthier old age.

**FECAL TRANSPLANTATION** is a hallmark of microbiome research in animals. It's also one of the main clinical interventions being studied for people as a way to introduce microbes that could fight a wide range of diseases.

This is not mere speculation; fecal transplantation has been used for the past decade or so to treat recurrent infections of drug-resistant *Clostridium difficile*, a severe, potentially fatal intestinal infection. About 12,000 to 15,000 medically supervised fecal transplants are done each year in the U.S. alone, according to Colleen Kelly of Brown University, co-chair of the Fecal Microbiota Transplantation National Registry. Generally the results are good, but last June the FDA reported the death of one patient from an infection after a transplant performed with feces that had not been adequately screened for drug-resistant bacteria.

Besides fecal transplants, scientists are studying other methods of manipulating our microbiome, including prebiotics, probiotics, and changes in diet or exercise that might alter the mix of microbes in the gut. But even the biggest boosters of microbiomics say it's hard to draw conclusions yet about the connection between the microbiome and human health, and they urge caution about rushing into therapies.

“There's a lot of excitement around fecal transplantation and the development of the microbiota as drugs,” says the University of Luxembourg's Wilmes, noting that companies are working on new probiotics to “restore an imbalanced microbiome to one that would be in equilibrium to the host.” Which is all very well—as an ecologist himself, Wilmes knows the value of “restoration ecology” in the environment—but it's a bit premature.

“Before we are able to really properly and rationally do this,” he says, “we need to understand what really constitutes a healthy microbiome and what are the functions that the microbiota confer to the human host. I don't think we're there yet.” □

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**Robin Marantz Henig** is a journalist based in New York City and the author of nine books. **Martin Oeggerli**, a Swiss molecular biologist, specializes in capturing the beauty of the microscopic world.

# FOODS

## OKINAWA

Yoshiko Shimabukuro, the 91-year-old founder of the Daiichi Hotel, drinks miso soup for breakfast. She and her daughter Katsue Watanabe specialize in creating elaborate plant-based meals that feature some 50 local ingredients.

DAVID MCLAIN

# TO



JANUARY 2020

WELLNESS ISSUE



**Traditional diets  
with whole grains,  
greens, nuts,  
and beans offer  
the promise of  
eluding disease and  
staying healthy.**

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BY

**DAN BUETTNER**

# LIVE BY

# M

**MORE THAN 14 YEARS** have passed since Dan Buettner first wrote about the world's longest-lived people for the magazine. Today he's still uncovering the secrets of centenarians in regions he calls the blue zones. He recently returned to four of them to learn more about the foods that contribute to this remarkable longevity, collecting time-tested recipes and investigating why certain foods seem to promote long lives.

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HOME TO THE WORLD'S  
HIGHEST CONCENTRATION OF  
MALE CENTENARIANS

## SARDINIA, ITALY



Carbohydrates from Sardinian sourdough bread enter the bloodstream at a slower rate than those from plain white bread.



**NINETY-NINE-YEAR-OLD ASSUNTA PODDA** vigorously stirs an earthen pot and flashes a toothy smile. "Minestrone," she explains with a swooping hand gesture.

I peer into the mélange of beans, carrots, onions, garlic, tomatoes, fennel, kohlrabi, herbs—all under a golden veneer of olive oil. Behind her, a shaft of evening light angles through a window and illuminates a table with a medieval spread: sourdough loaves, foraged greens, a carafe of garnet red wine.

"Sit," she insists, deploying the region's generous albeit predatory hospitality. I join her family and Gianni Pes, an epidemiologist who studies the region.

Podda's traditional embroidered blouse, filigreed necklace, and black sweater contrast sharply with her nimble movements: With the steady hand of a younger woman, she pours wine into stout glasses and ladles steaming soup into dishes.

"Now eat."

We're on the eastern slopes of Sardinia's Gennargentu mountains in Arzana, a village in a region with the world's highest concentration of male centenarians. In the years after

World War II, 38 people in this village—one out of every 100 of their peers—have reached a century.

Pes discovered this phenomenon in the late 1990s. Since then, he's meticulously interviewed more than 300 centenarians, using extensive questionnaires. He believes that steep streets, zeal for family, reverence for elders, a matriarchal culture in which women bear most of the family stress, and a simple traditional diet explain much of this longevity. Pes says he's found that the spouses of centenarians live longer than the siblings of centenarians, suggesting to him that diet and lifestyle may make a bigger difference than genes.

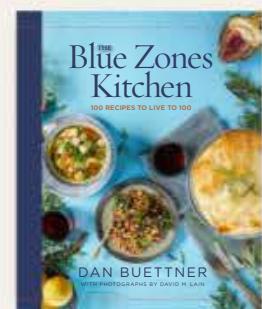
Pes, who favors blue-framed glasses and a silver goatee, slurps a spoonful of soup. "*Delizioso!*" he proclaims, glancing admiringly at Podda, who closes her eyes and shrugs.

Minestrone serves up essential amino acids, a potpourri of vitamins, and a range of fibers. Pes has found that centenarians have specific strains of bacteria in their digestive systems that convert fiber into unusually high levels of odd-chain fatty acids. These saturated fats are associated with a lower risk of heart disease and may prevent cancer.

Cruciferous vegetables, like the cabbage and especially kohlrabi that find their way into almost every bowl of Sardinian minestrone, also may play a role. After observing the high percentage of centenarians with goiters—a condition that accompanies a low-functioning thyroid—Pes speculates that thiocyanate from a steady diet of kohlrabi may blunt thyroid function. That may help Sardinians live longer by reducing their rate of metabolism, Pes says, just as a lighter with a low flame lasts longer.

In Seùlo, another centenarian-blessed village, Pes and I visited a century-old community bakery. A dozen women were making the distinctive bread eaten with most meals. We watched them build a blazing fire in a brick bread oven and knead dough with strong arms, their faces flushed. The senior baker, a short, vigorous octogenarian named Regina Boi, hovered over the process in her black dress and head scarf, dispensing advice and signaling when the dough was ready and the oven hot enough.

Boi had provided the starter dough, a gooey froth resembling curdled milk that her family has cultivated for generations. The starter contains yeast and native *Lactobacillus* bacteria. The



Best-selling author Dan Buettner reveals recipes to promote longevity in his debut cookbook, *The Blue Zones Kitchen*, available wherever books are sold.



SARDINIA, ITALY



Franca Piras (at right), with help from neighbors Angela Loi and Marisa Stochino, and Piras's daughter, Michela Demuro, and granddaughter Nina, prepares *culurgiones*, a traditional dish of the Ogliastra area. The pasta dough is shaped into pockets and stuffed with potato, pecorino cheese, and mint.

ANDREA FRAZZETTA

yeast and lactobacilli produce carbon dioxide that leavens the bread, and the lactobacilli also break down the carbohydrates to produce lactic acid. The acid imparts a sour taste, but more important, Pes tells me, the bread's carbohydrates enter the bloodstream 25 percent slower than those of plain white bread.

As dinner with Podda's family winds down with a spirited exchange of village gossip, Pes, in a flush of revelry, raises his glass and belts out the signature toast of the island, delivered in the local dialect: "A kent' annos!" "May you live to 100!"

"And may you be here to count the years!" the family bellows. A beat later, Podda softly repeats it. Indeed, since our dinner together, she's celebrated her 100th birthday.

ADULTS HERE HAVE  
THE LONGEST LIFE EXPECTANCY  
IN THE AMERICAS.

## NICOYA, COSTA RICA



Easy access to fruits such as pineapples and papayas from home gardens extends the plant-based diet year-round.



**WHEN PES BEGAN HIS STUDY** of centenarians, he denoted areas with long-lived residents with blue marks on a map. He noticed such a profusion in Sardinia's Nuoro Province that he began to refer to the area as the "blue zone." I met Pes while canvassing the world in search of longevity hot spots, and I adopted his term for similar areas I uncovered: Nicoya, Costa Rica; the Greek island of Ikaria; Japan's Okinawa island; and a community of Seventh-day Adventists in Southern California.

I've examined dietary surveys of each region and inventoried their foods of the past century. Until the late 20th century, these diets consisted almost entirely of minimally processed plant-based foods—mostly whole grains, greens, nuts, tubers, and beans. People ate meat on average only five times a month. They drank mostly water, herbal teas, coffee, and some wine. Notably, they drank little or no cow's milk; soda pop was largely unknown to them. As globalization spreads, processed foods, animal products, and fast foods are supplanting the traditional diets. Not surprisingly, chronic diseases are on the rise in the blue zones.

A healthy diet is just one part of a web of longevity-promoting factors that also include having a circle of lifelong friends, a sense of purpose, an environment that nudges one into constant movement, and daily rituals that mitigate stress.

I found all of those factors in Costa Rica's Nicoya region, as well as what might be the world's healthiest breakfast, in

an open-air building with a vaulted red-tiled roof blackened with smoke.

Every morning at daybreak in the city of Santa Cruz, María Elena Jiménez Rojas and a dozen or so other women at Coopetortilla stoke wood fires in long, clay ovens and stir cauldrons of spicy beans. Rojas, wearing a smudged apron over an immaculate white T-shirt, pinches off a golf ball-size piece of corn dough, plops it down on waxed paper, and rotates it with mechanical precision into a round patty. She slaps it onto a hot clay plate called a *comal*, where it roasts briefly before expanding into a puffy pancake and collapsing into a perfect tortilla.

Three women mix black beans with onions, red peppers, and herbs. The beans will cook to tender perfection and then be mixed with rice and sautéed bell peppers, onions, and garlic to produce a uniquely Costa Rican version of *gallo pinto*.

Nearly 30 years ago, Rojas tells me, the cooperative was just a tortilla shop. But young single mothers came to her for work, and she's helped dozens lift themselves out of poverty.

A few minutes before 6 a.m., the first customers file in. They sit on benches at long, green tables, where waitresses, wearing simple dresses and flip-flops, serve giant cups of weak coffee, plates of gallo pinto, and baskets of warm tortillas. As lilting ranchera music drifts in from a distant radio, customers fill their tortillas with beans, top them with hot sauce called *chilero*, and wash them down with black coffee, savoring a recipe for longevity reflecting thousands of years of culinary genius.

Costa Rica's blue zone is a roughly 30-mile-long strip that runs along the spine of the Nicoya Peninsula; it doesn't include the tourist resorts on the coast. The region consists mostly of dry pastureland and forests. Until about 50 years ago, people here were mostly subsistence farmers or ranch hands, supplementing a corn-and-bean diet with tropical fruits, garden vegetables, and, occasionally, wild game and fish.

The region's Chorotega people, who most influenced the diet, have been eating essentially the same food for millennia. That may help explain why adults here have the longest life expectancy in the Americas and men older than 60 have the lowest reliably measured rate of mortality for their age group in the world.

Corn tortillas might contribute to that longevity. They are an excellent source of grain, with complex carbohydrates rich in vitamins, minerals, and fiber. The wood ash the women add when they soak the corn breaks down the cell walls of the kernels and releases niacin—which helps control cholesterol.

Black beans contain the same pigment-based antioxidants found in blueberries. They're also rich in colon-cleansing fiber.

The magic comes in pairing corn with beans. Our bodies need nine amino acids—the building blocks of protein—to make muscle. Animal products such as meat, fish, and eggs provide all nine, but they also contain cholesterol and saturated fat. Together beans and corn provide all of these amino acids—with none of those unhealthy elements.

Researchers are looking into whether the combination

**Costa Rica's blue zone is a roughly 30-mile-long strip that runs along the spine of the Nicoya Peninsula; it doesn't include the tourist resorts on the coast.**



NICOYA, COSTA RICA

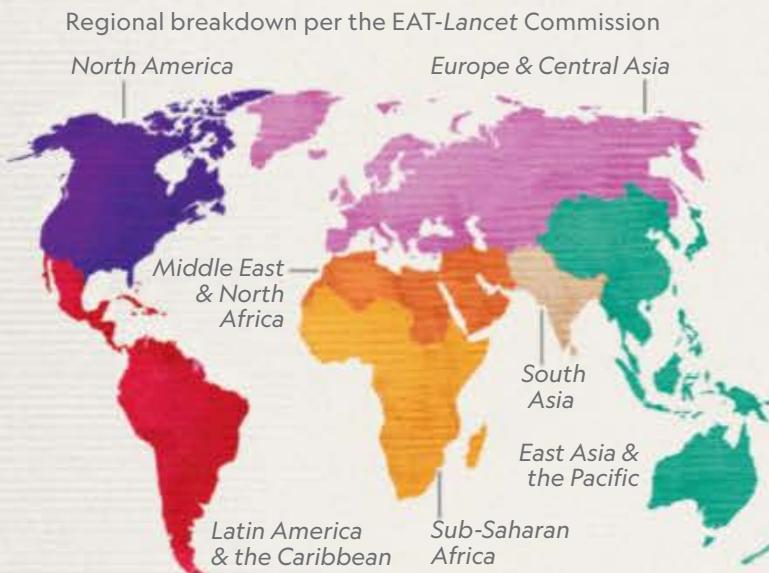


Paulina Villegas serves a hearty breakfast that's typical in the Nicoya region to her 102-year-old father, Pachito, and her nephew Sixto. The meal includes coffee, eggs, rice and beans, and tortillas cooked on a traditional wood-fired stove known as a *fogón*.

NICOLE FRANCO

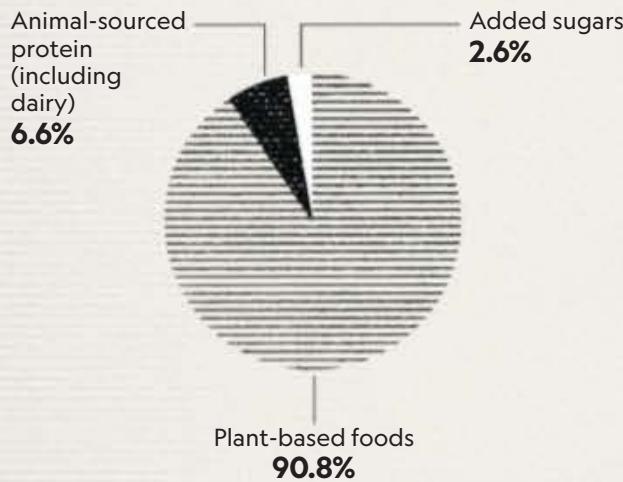
# PUTTING THE PLANET ON A DIET

Can we feed 10 billion people by 2050 and also protect the environment? A group of scientists from 16 countries say the answer is yes. They've devised targets for a nutritionally sound and sustainably produced planetwide diet; global consumption of foods such as fruits and nuts would double, while that of red meat and sugar would be cut in half.



## PLANT VS. ANIMAL

Not all foods are created equal. The global diet emphasizes plant-based foods and limits animal products, which are linked to chronic disease and often involve environmentally harmful production practices.



\*RECOMMENDED GLOBAL DIET IS BASED ON CONSUMPTION OF 2,500 CALORIES A DAY.

SUSTAINABILITY FACTORS INCLUDE GREENHOUSE GAS EMISSIONS, AND LAND AND ENERGY USE.

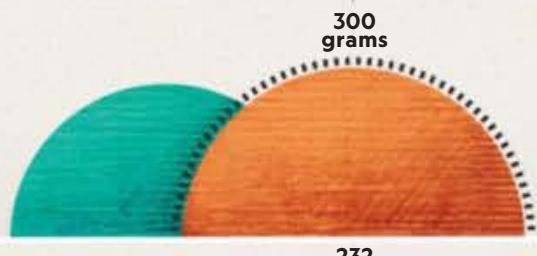
MANUEL CANALES, NGM STAFF; ALEXANDER STEGMAIER  
SOURCES: BRENT LOKEN, EAT; THE EAT-LANCET COMMISSION ON FOOD, PLANET, HEALTH

## THE WORLD ON A PLATE

Scientists devised the diet by first analyzing a food's nutritional data and then its environmental impact. Here that diet is broken down by food type and compared with consumption in world regions.



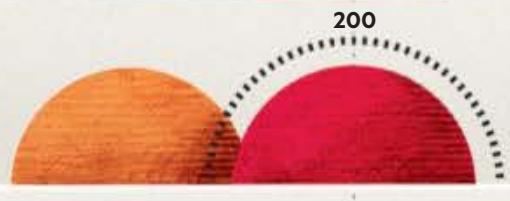
Regions closest to the targets, shown by dotted semicircles, are most aligned with the diet's recommended daily consumption\* for that food type.



Low in calories and providing essential macronutrients, vegetables are also an inexpensive food source.



Enough grain to feed the 2050 population is grown today, but much of it is fed to livestock.



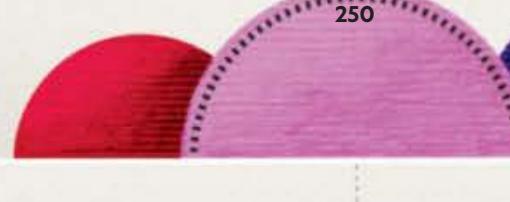
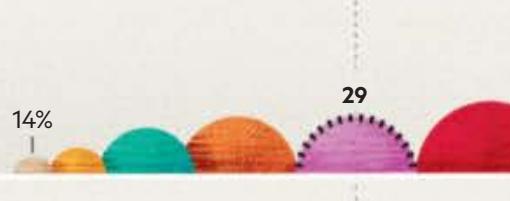
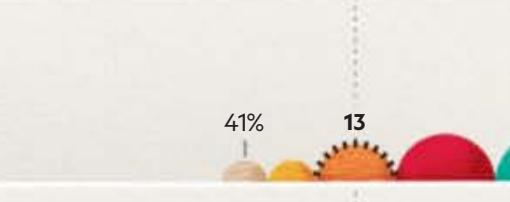
People worldwide are not eating enough fruit. Fruits and vegetables should make up half our daily diet.



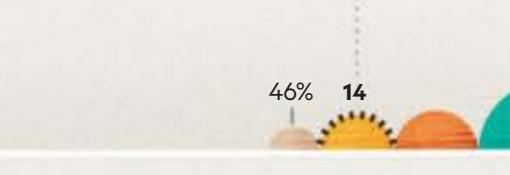
Beans and peanuts provide protein; soy is already heavily consumed in East Asia.



729%  
above  
target



Dairy is a renewable source of protein, calcium, and other nutrients.



CLOSE TO TARGET

OVERCONSUMED

may preserve cellular health too. Stanford social epidemiologist David Rehkopf and Costa Rican demographer Luis Rosero-Bixby have found that Nicoyans have longer telomeres on average than Costa Ricans overall. Telomeres are protective “caps” on the ends of DNA strands, which wear down over time, a rough marker of biological age. Rehkopf, who joined me in Costa Rica, told me that Nicoyans seem to be up to a decade younger biologically than their chronological age. Another group with longer than average telomeres? The poor—who may be more likely to subsist largely on beans, tortillas, chilero, and black coffee.

At Coopetortilla, I dig into my breakfast, chasing chilero-topped beans wrapped in fresh tortillas with gulps of coffee. Sweat beads on my forehead, and tears roll down my face. “Are you okay?” Rojas asks, flashing me a look of sincere concern. “Don’t worry,” I say. “These are tears of joy.”

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RESIDENTS ARE THREE TIMES  
AS LIKELY TO REACH 100  
AS AMERICANS.



## OKINAWA, JAPAN

Goya, or bitter melon, is a vitamin-packed local favorite that can protect cells and lower blood sugar.



**HALF A WORLD AWAY ON OKINAWA,** I prepare to sample yet another contender for the world’s healthiest breakfast at the Daiichi Hotel in Naha with Craig Willcox, another researcher seeking dietary clues to longevity.

On Okinawa, as compared with the United States, residents are three times as likely to reach 100, women suffer about half the rate of breast cancer, both sexes are afflicted by a third to a quarter the rate of heart disease, and elderly people die from Alzheimer’s dementia at a tenth to a twelfth the rate.

Each morning the hotel founder, Yoshiko Shimabukuro, 91, a short energetic woman, and her daughter Katsue Watanabe, a certified vegetable sommelier, prepare plant-based dishes from some 50 ingredients, about half of which are unique to Okinawa. Before us, in appetizer-size plates and bowls, lies a starburst of colorful foods, many of which helped create what remains, by several measures, the world’s longest-lived population despite a decline in the health of younger generations.

Willcox, an anthropologist and gerontologist, points out that everything in this 20-course meal—including tofu soup, carrot salad, a boiled fern called otani-watari, and papaya stir-fry—is light on calories. Okinawan food, he tells me, is nutritionally dense and calorically poor, while in the U.S. it’s the reverse.

With his twin, Bradley, and their mentor, Makoto Suzuki, Willcox has written books that lay out most of what we know about the island's traditional diet. The brothers showed up in Okinawa in 1994 interested in studying centenarians and hooked up with Suzuki. For a quarter century the trio has chronicled what people here eat and investigated why it helps them elude disease. Now I'm getting a hands-on lesson.

Willcox points a chopstick at a tofu stir-fry with sea green crescents of goya, or bitter melon, a key ingredient in goya champuru, a classic Okinawan dish. Goya is high in vitamins A and C, folate, and powerful antioxidant compounds that can help protect your cells against damage, he says. It's anti-cancer, protective of liver and cell membranes, a free radical scavenger, inhibiting of bacteria such as *E. coli*, and capable of lowering blood sugar. I bite down on a piece, unleashing a flavor explosion redolent of chewing a mouthful of aspirin—only more piquant. As with beer, which people often don't like at first, the bitter taste grows on you.

With a tuft of sandy brown hair and round spectacles that make him look like a middle-aged Harry Potter, Willcox moves on to the tofu, which is denser and more cheeselike than other Japanese tofu. As the protein centerpiece of the daily Okinawan diet, it often replaces less healthy proteins, such as meat or eggs. Traditionally made with seawater, Okinawan tofu is rich in calcium, magnesium, zinc, and other minerals that most Americans lack in their diet. It's also high in genistein and in daidzein, which metabolizes into equol. Genistein and equol are isoflavonoids that Willcox notes are associated with reducing the risk for cancer and cardiovascular disease.

Willcox hoists a porcelain cup containing a bright yellow brew. "Turmeric tea," he says. He takes a sputtering sip and explains that dozens of studies have shown the active ingredient in turmeric can help our bodies protect against diseases, including cancer, heart disease, and dementia. Islanders have co-opted the Japanese trick of using pungent flavors, such as turmeric, to enhance the taste of healthy vegetables. Most recipes rely on dashi, a rich broth commonly made from bonito flakes or sea kelp. Dashi can convert a pile of vegetables into an explosion of deliciousness, resulting in a dish with fewer calories than a hamburger but with five times the nutrients—and it tastes good enough to eat every day.

As I fill up my plate with more delicacies, Willcox fixes on a glutinous mass of seaweed resembling green spaghetti. Islanders consume more than a dozen varieties of seaweed, which he calls "sea vegetables." This particular one, mozuku, boasts an abundance of fucoidan, an anticancer, antiviral compound that Willcox says may help reverse inflammation, manage blood sugar, and also grow blood vessels.

Even more intriguing, another compound in seaweeds, called astaxanthin, has been linked to a gene that, when activated, seems to tell cells to clean up waste and reduce inflammation, which are at the root of the majority of age-related diseases.

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**LOMA LINDA, CALIFORNIA**



Krystal Gheen and her three-year-old son, Austin, pick beets in their garden for dinner, a meal she designs around what's ripe. The Gheens, like many residents of the inland Southern California city, are Seventh-day Adventists and follow a vegetarian diet inspired by the Bible.

NICOLE FRANCO

After two hours of learning and eating, I regard the sea of empty dishes. “I feel like a total glutton,” I say. “Don’t feel guilty,” Willcox replies. Our whole meal, he explains, contained fewer than 600 calories—about the same as eating a big cookie.

**ADVENTISTS WHO FOLLOW A  
VEGETARIAN DIET TEND TO LIVE LONGER  
THAN THOSE WHO EAT MEAT.**

## LOMA LINDA, CALIFORNIA



The vegetable-based Adventist diet is based on passages in the Bible and mirrors modern dietary recommendations.



**THE FINAL STOP** on my journey is Loma Linda, California, where a community of Seventh-day Adventists has long followed a diet inspired by the Bible. Their guidelines originate from passages such as Genesis 1:29: “And God said, Behold, I have given you every herb bearing seed, which is upon the face of all the earth, and every tree, in the which is the fruit of a tree yielding seed; to you it shall be for meat.”

Adventists who follow the diet tend to live longer. One study showed that life expectancy for Adventists in California was 7.3 years greater for men and 4.4 years greater for women than for similar Californians. Being both vegetarian and Adventist boosted life expectancy by an additional two years.

When I asked researchers studying the diet to find someone who follows it, they sent me to 90-year-old Dorothy Nelson, who answers her door wearing a bright red T-shirt and running shoes, with schoolgirl bangs cut just above her hazel eyes. She welcomes me and leads me to her well-lit kitchen.

Moving with the energy of a Chihuahua, Nelson begins cooking a savory lunch. When I compliment her cooking, she reveals her secret: “This kitchen is seasoned with love.”

Over lunch she tells me about her life. When she was younger, she’d had an adventurous career as a pilot-nurse for church missions. Once, while she and her copilot were hopscotching across the Arctic, the plane’s engine sputtered, and they plummeted toward the earth, spotting a flat area on an ice floe between Canada and Greenland at the last minute. She figured they’d be all right, “as long as the good Lord wants me around,” she recalls. When the plane touched down, it skidded but stayed upright. “I got out and knelt down and thanked the Lord.”

The half-frozen pair were picked up five days later. The rescuers gave them hot coffee. “I’d never tasted coffee,” she says. Caffeine and alcohol are discouraged for Adventists. Today Nelson limits her adventures to tending her vegetable garden.

As a proponent of vegetarian ways, Nelson is a direct culinary

descendant of Ellen G. White, who helped found what became the Seventh-day Adventist Church, a Protestant denomination. In the late 1800s and early 1900s, White first articulated the dietary prescriptions that have since guided this subculture of long-lived Americans.

White praised the consumption of whole grains, fruits, nuts, and vegetables, which “impart a strength, a power of endurance, and a vigor of intellect, that are not afforded by a more complex and stimulating diet.” She warned against cooking with grease, spices, and salt, among other things, and discouraged the use of sugar, which “causes fermentation and this clouds the brain and brings peevishness into the disposition.” Her recommendations seem remarkably prescient, mirroring today’s dietary guidelines from the American Cancer Society and the American Heart Association.

Most of the newest insights on the Adventist diet come from Gary Fraser, an Adventist and researcher at Loma Linda University, and a vegetarian who sometimes eats fish. With his combed-over sandy brown hair, Fraser looks a bit like a scoutmaster. Trained as a doctor, he noticed that Adventists had healthier hearts than non-Adventists, and he began to wonder whether science could validate his diet’s health claims. He now leads the Adventist Health Studies, which have monitored the health of tens of thousands of American Adventists.

Their research indicates that, at a given age, vegetarian Adventists are about 12 percent less likely to die than non-vegetarian ones who eat only a small amount of meat. By contrast, among younger Adventists, those who eat the most meat suffer a 46 percent higher rate of premature death than those who get their protein from nuts, seeds, and legumes. “It’s clear that a plant-based diet is the way to go,” Fraser says.

When I smell Nelson’s cooking, I’m inclined to agree. The aromas wafting from her stove make me hungry. After combining black beans with steamed cabbage and cauliflower, she adds slices of browned tofu, sesame seeds, and a dash of soy sauce. It’s a satisfying mix of complex carbs, protein, vitamins, minerals, and antioxidants, with fewer calories than a bag of french fries. “I’ve never tasted meat,” Nelson brags.

She tells me she has perfect blood pressure and a resting heart rate of 60. She walks three miles a day.

And there you have it: The vast majority of the calories eaten in the traditional diets in the blue zones come from plant-based whole foods. Grains, greens, nuts, and beans are the four pillars of every longevity diet on Earth.

Nearly half the people who die this year in the U.S. will likely do so from cardiovascular disease, cancer, or diabetes. In blue zones, far fewer suffer from these diseases. Why? For most of their lives, they’ve simply eaten what was readily available and, luckily for them, it was a whole food, plant-based diet. Trial and error yielded recipes that make these foods taste delicious enough to eat day after day. Therein, perhaps, lies the secret to a healthier you. If you want a good starter recipe, I know a feisty centenarian who makes a mean minestrone. □

**‘I’ve never tasted meat.’ Ninety-year-old Dorothy Nelson has perfect blood pressure and a resting heart rate of 60. She walks three miles a day.**

JANUARY 2020

WELLNESS  
ISSUE

BY FRAN SMITH

PHOTOGRAPHS BY ANDY RICHTER

# FINDING CALM

The ancient practice of yoga offers  
an antidote to modern stress.









**PREVIOUS PHOTO**

**Yoga on the Rocks**  
draws sellout crowds of  
2,100 practitioners to  
Red Rocks Amphitheatre  
outside Denver, Colorado.  
In the United States, yoga is an  
increasingly popular  
way to reduce stress  
and enhance health.

**LEFT**

In the West, yoga often focuses on the asanas, or postures, of hatha yoga, one of its many branches. In India, where the discipline began more than 4,000 years ago, followers of Krishna perform bhakti, or devotional, yoga, by moving 108 stones the length of their body during repeated prostrations on a 13-mile circuit of Govardhan Hill.

Followers of the late Yogi Bhajan, a spiritual leader who brought kundalini yoga to the West from India, chant and walk with their eyes closed at an annual summer solstice celebration in the Jemez Mountains near Española, New Mexico.





# J

**JUDGE ELENI DERKE** cuts an imposing figure, shrouded in her black robe and seated behind the elevated wood-paneled bench in the county courthouse in Jacksonville, Florida. From the jury box and lawyers' tables, you can't see what else she's wearing: wildly patterned yoga pants.

More than 25 years ago, Derke discovered yoga. She was suffering from the searing abdominal pain of Crohn's disease. Her doctor recommended surgery. Hoping to avoid it, she went to see a cousin who was a yoga master. He taught her the upside-down poses known as inversions. They are said to clear the body of toxins, though there's no scientific evidence to support the claim. Derke's symptoms quickly subsided. "Yoga saved my life."

She trained as a yoga instructor, and if it's not too hot, she holds free monthly classes on the courthouse lawn. When lawyers drone on at trial, she will order a break and lead jurors in standing stretches and breathing exercises. But she's best known in legal circles as the judge who sentences offenders to take yoga behind bars.

Derke handles misdemeanors, such as shoplifting, minor drug possession, and driving under the influence, punishable by up to a year in jail. Offenders can cut their time by 40 percent or more if they take a weekly program called Yoga 4 Change. She sees yoga as a way to quiet self-defeating chatter in the mind and quell rage, fear, anguish, and compulsions that drive bad behavior.

"Once you let go," she said, "you make room for the positive things." Her colleagues, though, didn't buy it at first. "Come on, *yoga?*"

Many offenders had a similar reaction. "I thought it was really weird," said Cecil Reddick, an inmate at Jacksonville's Montgomery Correctional Center.

An evaluation of the program in three Jacksonville facilities found that after six weeks, participants reported significant improvements in sleep, overall health, and the ability to manage anger and anxiety. At least two more county judges now offer the yoga option.

Some offenders choose to do their full sentence rather than try yoga, but Reddick grabbed the get-out-of-jail-quick offer from one of Derke's colleagues. He was surprised by how much the classes relaxed him, soothed his sore back, and stirred a sensation he'd never felt: "Serenity."



In a state prison near San Diego, California, Patrick Acuña rests in Savasana, a deep relaxation position, with Zeus, a service dog he's training, during a class sponsored by the nonprofit Prison Yoga Project. Acuña has practiced yoga behind bars for more than 20 years.



**YOGA, A SPIRITUAL PRACTICE** that began in India, has extended its limbs widely. In the United States, it's held up as a fitness regimen, a path to transformation or enlightenment, and a treatment for so much that ails us—from addiction, headaches, and hearing loss to post-traumatic stress disorder, heart disease, and yes, Crohn's.

More than 14 percent of U.S. adults used yoga for health reasons in 2017, up from 9.5 percent five years earlier, a government survey found. Since 2018, Harvard Medical School students have studied it as part of a required course on building resilience. Parents tote infants to Itsy Bitsy Yoga, which purports to improve a baby's sleep, digestion, and brain development.

Validating health claims for yoga is difficult.

Most studies involve too few participants to be conclusive, in large part because yoga does not generally attract big government grants or have an industry like drugmakers to finance research.

Sat Bir Singh Khalsa, a yoga instructor, Harvard neuroscientist, and expert on the science of yoga, acknowledges the research has a long way to go. "But I would say we have demonstrated our credibility." Khalsa has investigated yoga for insomnia, PTSD, anxiety, and chronic stress, where he's seen the most compelling evidence of yoga's benefits.

Stress plays a major role in many illnesses that kill us. It also drives unhealthy eating, poor sleep, alcohol and drug misuse, and other bad habits. "Modern medicine really sucks at preventing chronic disease," he said.





Sri Dharma Mittra practices asanas with aspiring teachers at his studio in New York City. Born in Brazil, he served in the country's air force and ran a bodybuilding gym before leaving to study yoga in the U.S. more than 50 years ago. He's devised his own approach to yoga.







**CLOCKWISE  
FROM TOP LEFT**

A woman lies in Savasana at a Beijing studio belonging to Yogi Yoga, one of the country's largest chains. Yoga was slow to take off in China, with some wary of its spiritual aspects, but it's now spreading quickly.

Ashley Craven (front) and Carla Torres attend a class at Naval Medical Center San Diego for pre- and postnatal mothers who are active-duty personnel or spouses and have a doctor's recommendation.

Ashtanga yoga emphasizes a vigorous sequence of postures. This class in India was taught by Saraswathi Jois, who trained with her father. She was the first woman in Mysore to teach men and women together.

Bob Gregory, who has cerebral palsy, does an upward salute pose with an assist from Paris Kaye as part of an adaptive yoga class for adults living with disabilities at a rehabilitation center in Minnesota.



Khalsa, who took up kundalini yoga in 1971, told me with excitement that epigenetics and neuroimaging are revealing how the body and brain interact—and unraveling the mysteries of yoga's power. In other words, the benefits aren't just in a devotee's mind.

Researchers in Norway analyzed blood from 10 volunteers before and after two-hour sessions of a yoga practice with rhythmic breathing and saw significantly increased gene activity in circulating immune cells. Scientists at UCLA studying breast cancer survivors discovered yoga decreased the expression of genes involved in inflammation, believed to be a root of many complex diseases.

Scientists at the National Institutes of Health found that longtime yoga practitioners don't

display the usual age-related declines in the brain's gray matter. Yogis also had larger volume in several brain regions, including the hippocampus, critical to memory and emotional regulation, and the precuneus and posterior cingulate cortex, involved in attention and self-awareness.

Studies like these bring scientific legitimacy, but they're not why the ancient discipline has caught on in a frazzled, fast-paced society. "Yoga is a strategy for making people basically happy and able to cope with modern life," Khalsa said.

**THIS MAY BE THE MOMENT** to admit that yoga stressed me out. I went on the recommendation of a physical therapist who had healed my injured shoulder after others had failed. When



On a tower over the sacred Yamuna River in Vrindavan, a man meditates at Keshi Ghat, a Hindu holy site. In India yoga retains more of its origins as a harmony between body and mind. The spiritual and physical practice is believed to help yogis overcome worldly suffering and attain a state of liberation.

he spoke, I dutifully listened. In the 2.4-square-mile New York City suburb where I live, yoga is abundantly available in storefront studios, community recreation rooms, the continuing education program, and the chain health club. I started there, accompanied by my husband. Classes were packed. People jostled for space like subway commuters. Supple spandex-clad bodies bent, curled, and twisted in ways that defied me. It felt like one more competitive arena where I didn't measure up. I took refuge in restorative yoga, where I seemed as adept as anyone at splaying across comfortable bolsters and trying not to snore. Meanwhile, my husband learned to stand on his head.

I'm not the only one to have a hard time

reconciling the yoga scene with the potential of a serious practice. "I would get feedback that my playlist wasn't cool enough," said teacher Olivia Mead. "I thought, I cannot handle this anymore. I didn't become a yoga instructor to wear cute shorts. I actually wanted to make a difference."

Mead founded Yoga for First Responders. The nonprofit has brought yoga to police departments, fire stations, and training academies from Los Angeles to Thunder Bay, Ontario. Classes tailor the traditional yoga elements—physical postures, breath regulation, deep relaxation, and meditation—to help people endure the challenges of putting their lives on the line.

"The whole goal is to harness the mind," she said, "not to touch your toes."

**NINETEEN WOMEN WEARING** identical inmate T-shirts and pants took their spots on mismatched yoga mats arranged in a U-shape in a cramped room at Jacksonville's Montgomery Correctional Center. Two uniformed officers stood watch over me; one of them, Sgt. Rhonda Warren, held an iPad and videoed my interviews.

It seemed an unlikely setting to release stress, not to mention harness the mind. Kathryn Thomas, a former Navy aviator who founded the nonprofit Yoga 4 Change, led the women through deep inhales and exhales, and then the fluid series of poses known as the sun salutation. Gradually, a sense of calm became palpable.

Most inmates weren't required to come. Some signed up, as Melissa Bruce told me, "basically to have something to do." Many wanted a break from the tension and clamor of living among inmates, an hour to sink into oneself. If they hadn't all achieved enlightenment or transformation, at least a dozen told me they'd learned skills to help them survive another day. Philieza Lopano said she used the breathing exercises and gentle stretches during lockdowns to relieve anxiety.

Watching each woman stretch and fold and blow out her breath in loud, unembarrassed whooshes, it occurred to me that I might have fared better in yoga if I'd focused less on other people and more on myself, without judgment. After the women filed out of the room, I mentioned to Warren that I would try yoga again.

"I know," she said, nodding slowly. "Me too." □

**Fran Smith** has written about precision medicine and the science of addiction for the magazine.

**Andy Richter**, a yoga devotee, photographed the discipline for his book, *Serpent in the Wilderness*.

As part of the photographer's project, elderly people were asked to imagine how they would interact with a robot. A resident at Maison Ferrari, a retirement home in Clamart, France, volunteered to act as the robot's godmother. She pictured herself celebrating its birthday and decorated her chair with balloons.



JANUARY 2020

WELLNESS  
ISSUE

TAKE ME TO

**In the future,  
robots could be  
used to assist  
and comfort  
the elderly—and  
help meet the  
escalating demand  
for caregivers.**



BY CLAUDIA KALB

PHOTOGRAPHS BY YVES GELLIE

# YOUR SENIORS



Loneliness is common among seniors. This woman at a long-term care facility in Montgeron, France, treated the robot as a confidant. They were indoors, but she imagined relaxing with it under the sun.



ISSUE DE SECOURS  
WE PAS DÉCONSEILLE



# IN

**HEN GOLDIE NEJAT BEGAN** developing robots in 2005, she spent much of her time knocking on doors in hopes of demonstrating her high-tech prototypes. Back then, the health-care world was hesitant. “Now, it’s the opposite,” says Nejat, a professor of mechanical engineering at the University of Toronto. “I have people calling from around the world saying, When’s your robot going to be ready?”

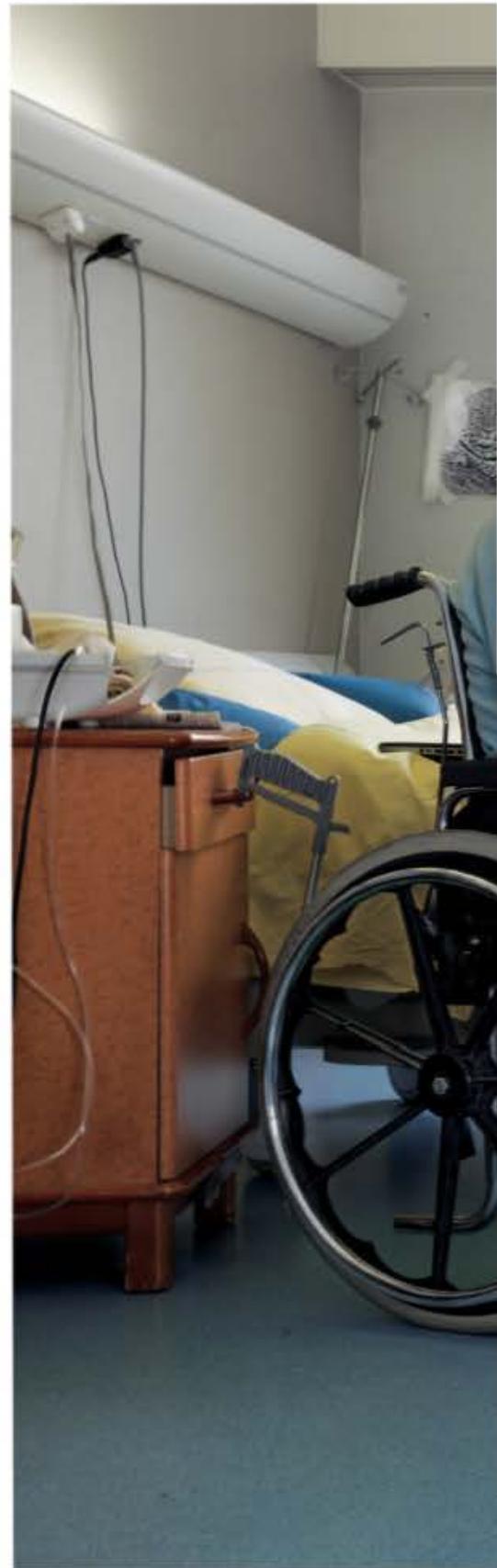
Nejat’s machines, a special type known as socially assistive robots, are designed to engage with humans and could help fill an urgent need: caregiving for the elderly. The population of people over age 80 is projected to almost triple worldwide, from 143 million in 2019 to 426 million in 2050.

Such robots could be especially useful for patients with Alzheimer’s disease or dementia because the robots can be programmed to assist with everything from providing medication reminders to leading exercises. Nejat’s robots also can help run bingo and memory games to keep patients cognitively active.

Inspired by robots’ potential to help the elderly, French photographer Yves Gellie spent two years creating the award-winning 2019 film, *Year of the Robot*, which documents interactions between elderly people and social robots in long-term care facilities in France and Belgium. In the film Gellie and his assistant, Maxime Jacobs, humanize robots by allowing active engagement between person and machine. In scenes that appear futuristic, people play piano, dance, and even tearfully divulge secrets with their robotic companions.

After completing his film, Gellie embarked on a related photography project in which he asked some of the same subjects to imagine their dream scenario with a robot. What would they most like to do? In the images shown here, Gellie documented people’s interactions with robots after months of observation. The project was not intended to be therapeutic or to show the robots’ actual capabilities. Instead, it explored humans’ capacity to form relationships with machines.

Critics have worried that caregiving robots might eliminate human interaction and jobs. But the goal is to support human care, not replace it, says Brian Scassellati, head of Yale University’s Social Robotics Lab. He’s tested robots with a range of patients, and has found that daily interaction with robots can help children with autism spectrum disorder improve



Photographer Yves Gellie introduced the robot to elderly people over several months. He didn’t expect everyone to warm to it. Some weren’t interested, but others were eager to engage. This woman, at the Broca Hospital in Paris, said the robot helped her forget her surroundings. She loves books and said she’d read to the robot.



eye contact and social skills.

Cognitive psychologist Maribel Pino, executive director of the Broca Living Lab at the Broca Hospital (Greater Paris University Hospitals), one of the locations where pictures were taken, describes the engagement of the people photographed with the robots as authentic. After people spent time with a robot, many became attached to it.

As the field grows, scientists aim to better understand human-robot dynamics. Do robots

offer an advantage because they aren't judgmental? Is a lack of emotion helpful? Will patients lose interest?

One benefit is clear, Scassellati says: Robots can provide personalized, on-demand care—and the need for that will only increase in the future. □

**Claudia Kalb** has covered the science of genius, Pablo Picasso, and Leonardo da Vinci for *National Geographic*. **Yves Gellie** photographed Pitcairn Island for the French edition of the magazine.

TARMAK



TARMAK



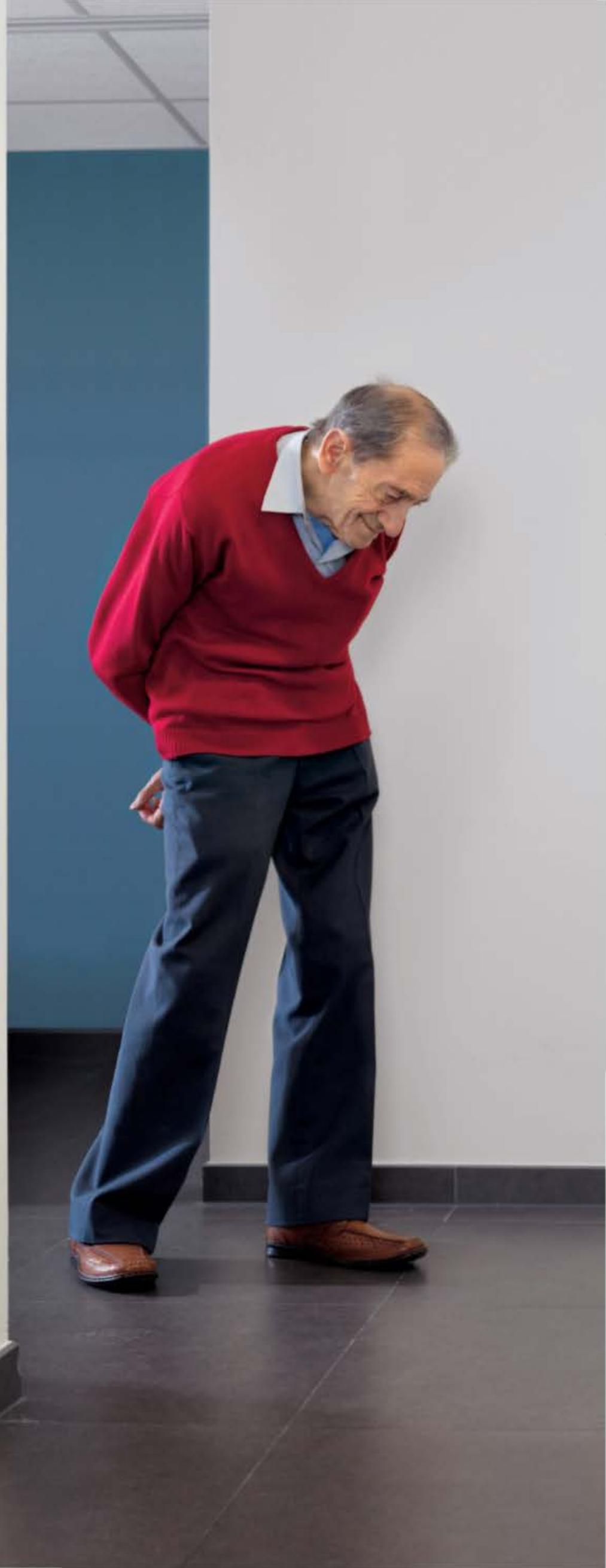
This resident of Maison Ferrari said she would like a robot to teach her basketball. Manufactured by Tokyo-based SoftBank Robotics, this robot is not programmed for that. However, its software, designed by ZoraBots in Belgium, can help people complete a range of tasks, including exercise.



At Weverbos Long Term Residential Facility in Ghent, Belgium, this 94-year-old resident wanted a robot that would dance while she played the piano. Fabrice Goffin, co-CEO of ZoraBots, believes the robot's diminutive size makes it appear child-like, appealing to the elderly. "The honesty of a child also has no judgment," he says.



The robot, known as NAO, has another advantage, says Gellie: It never gets angry or changes its mood. This 78-year-old man at Weverbos Long Term Residential Facility is an arts lover and admired the robot as if it were a sculpture. "If I had this robot with me in a museum," he told Gellie, "he would teach me everything."







INSTAGRAM

## JASPER DOEST

FROM OUR PHOTOGRAPHERS

**WHO**

Doest, a photographer in the Netherlands, captures interactions between humans and the natural world.

**WHERE**

A veterinary practice run by his cousin, Odette Doest, on the Caribbean island of Curaçao.

**WHAT**

Doest took photos of this bird, Thomas, with everything from his smartphone to his DSLR camera. For this shot he used a 100mm lens.

On Curaçao to photograph animals in rehabilitation at his cousin Odette's veterinary practice, Doest met two flamingos: Bob, who became an internet sensation after recovering from a concussion, and Thomas (above), impaired by a serious foot infection. Odette is often faced with euthanizing injured animals if she can't find creative treatments—such as the makeshift socks she fashioned to bandage Thomas's wounds. In time, Doest says, Thomas was walking normally and was returned to the wild. Because Bob has arthritis that would make him vulnerable in the wild, he remains with Odette, who takes him to visit Curaçao schools to teach children about conservation.

This page showcases images from National Geographic's Instagram accounts. We're the most popular brand on Instagram, with more than 120 million followers; join them at [instagram.com/natgeo](https://instagram.com/natgeo).



### Snowy Owl (*Bubo scandiacus*)

**Size:** Body length, males 53 - 64 cm (20.9 - 25.2 inches); females 59 - 66 cm (23.2 - 26 inches)

**Weight:** Males 710 - 2,500 g (1.6 - 5.5 lbs); females 780 - 2,950 g (1.7 - 6.5 lbs) **Habitat:** Predominantly Arctic

**Surviving number:** Estimated at 28,000 mature individuals



Photographed by Markus Varesvuo

## WILDLIFE AS CANON SEES IT

Safe zone. The snowy owl allows no predators near its nest, and other birds take advantage of this safety by moving in nearby. Unlike most owls, the snowy owl hunts during the daytime, with lemmings and other voles being favored prey. Nesting success is tied to lemming numbers; in times of plenty the owl lays more eggs and practices bigamy. But this canny hunter has

no strategy to escape the effects of climate change on prey availability or the danger of collisions with man-made objects. Nowhere is truly safe.

As Canon sees it, images have the power to raise awareness of the threats facing endangered species and the natural environment, helping us make the world a better place.



EOS System

Canon



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