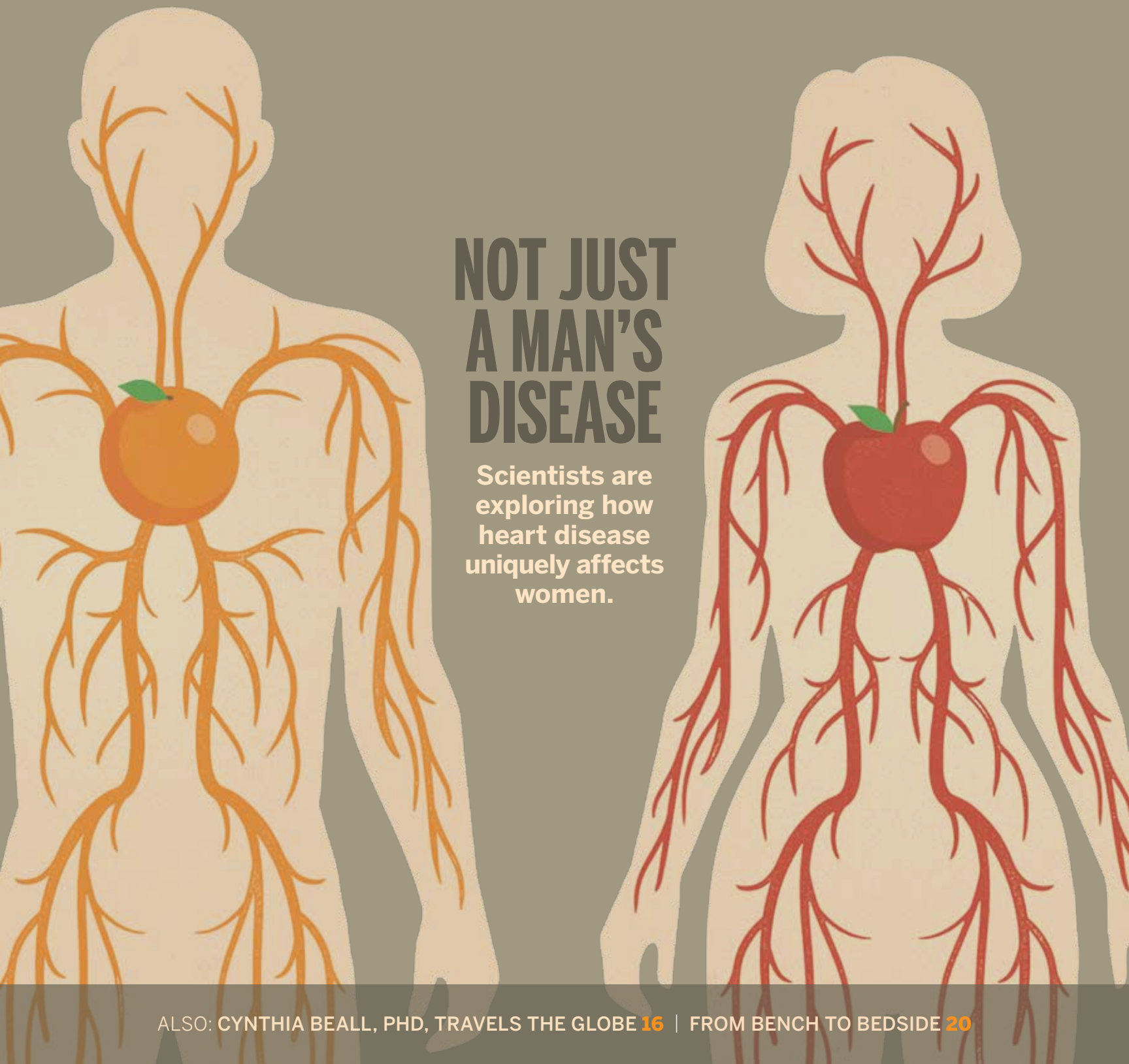
THE Physiologist MAGAZINE

MARCH 2025



NOT JUST A MAN'S DISEASE

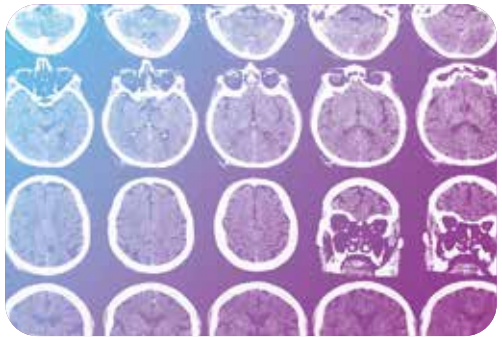
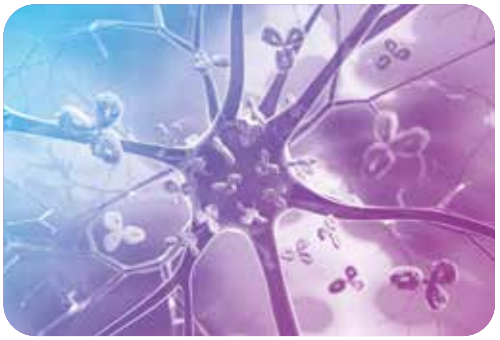
Scientists are exploring how heart disease uniquely affects women.

aps
women's health
research initiative

Raising the Visibility of Women's Health Research

Explore our active cross-journal calls for papers on key women's health research topics.

Alzheimer's Disease • Autoimmune Diseases • Breast Cancer • Cardiovascular Disease
HRT and Menopause • Migraines • Novel Perspectives on Sex as an Investigative Variable
Pregnancy and Postnatal Conditions

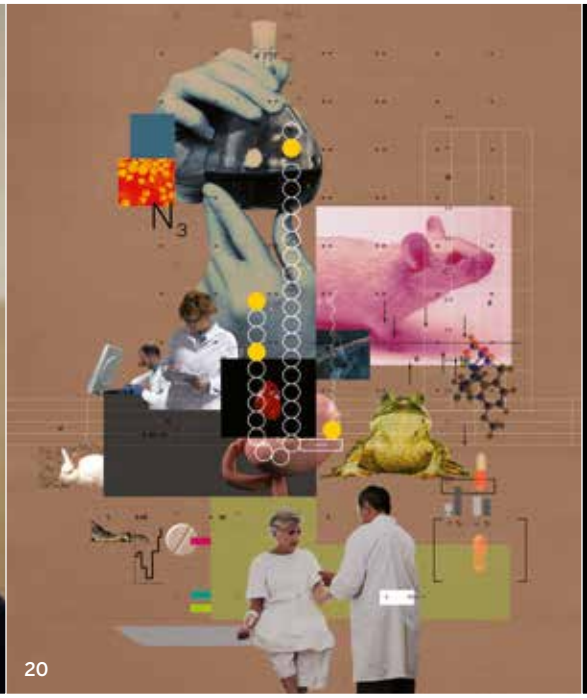


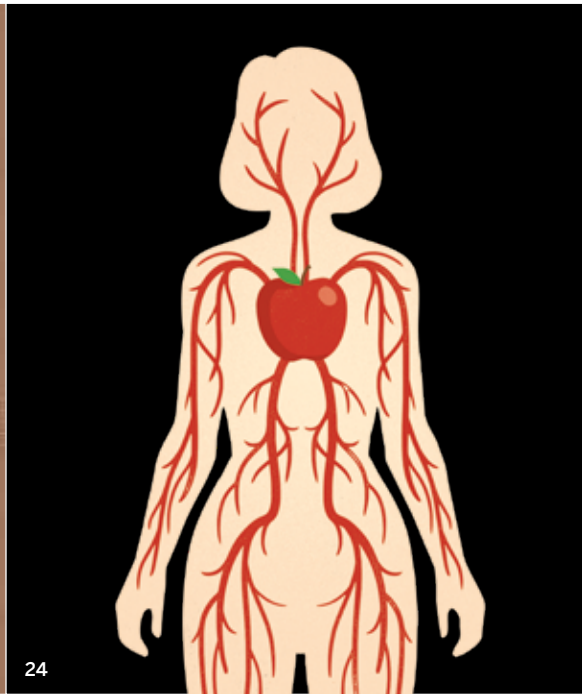


Learn more and submit at journals.physiology.org/womens-health-research-initiative.

CONTENTS

FEATURES



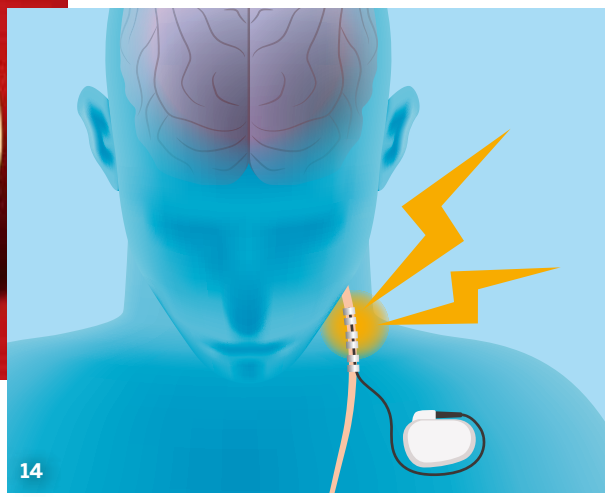


Cover illustration by Chris Gash

CONTENTS

DEPARTMENTS

10



14

8

36

center for physiology education
AN APS INITIATIVE

Elevate the way you teach.

Connect with inspiring education research experts from around the world.

Learn practical tools to incorporate the core concepts of physiology into your curriculum.

Develop a network of life science educators at the undergraduate through medical school levels.

Join us for From Concept to Classroom, April 23–24 in advance of the American Physiology Summit. Register by March 15.

physiology.org/ConceptToClassroom

Keynote Session: "Homeostasis: The Dynamic Balance of Life"

Keynote speaker Mary Pat Wenderoth, PhD, University of Washington, is a physiology education researcher who has published a wealth of articles on student understanding in physiology and how the use of core concepts can enhance their learning.

Rolling Up Our Sleeves for Science

BY AMANDA BERTHOLF, MA

There's something about those first hints of spring—the days start to get longer, the birds are singing, and I am eager to get my hands in the dirt. By now, I'm ready to step into my garden, even if the weather is still roaring like a lion. Rolling up my sleeves, taking in the smell of dirt and flowers, and uncovering earthworms, the garden may be the one place where I can bring order to chaos. But it requires patience and persistence. The summer heat will test me. The rabbits will, too. But with care and effort, life will flourish.

Science is no different. Discovery takes time, and progress isn't always visible at first. But the work you do—planting the seeds of knowledge, nurturing new ideas and refining research—can grow into life-changing breakthroughs. And right now, we all need to roll up our sleeves and dig in—not just in the lab, but as voices for science. More than ever, physiologists and other scientists are stepping forward, sharing their work and advocating for the role of science in improving lives.

"More than ever, physiologists and other scientists are stepping forward, sharing their work and advocating for the role of science in improving lives."

Translational physiology, the focus of one of this month's feature stories, embodies this spirit. In this article, we celebrate physiology's role from bench to bedside—transforming foundational research into real-world medical advancements. Many APS members are conducting critical studies that lead to practical interventions and treatments to improve human health. On page 20, read about their work and what it takes to thrive in this multidisciplinary field.

We also uncover an urgent gap in women's heart research. Many Americans may not realize that women experience worse outcomes from cardiovascular disease than men. Heart disease is the leading cause of death for both women and men, yet much remains unknown about the physiological differences that contribute to these disparities. APS members are working to change that. Learn more in the cover story on page 24.

On page 16, we highlight the remarkable career of biological anthropologist Cynthia Beall, PhD, whose research has taken her to some of the highest-altitude communities in the world. Her research sheds light on how the human body adapts to extreme environments, offering invaluable insights into human physiology.

This issue of *The Physiologist Magazine*, like all those before it, is a celebration of science and the researchers whose passion and perseverance drive real progress. As we step into spring, I take inspiration from you. Just as a gardener nurtures plants, we must nurture science—by conducting rigorous research, sharing knowledge and advocating for its value. It takes persistence, patience and sometimes a willingness to get a little dirt under our nails. But as any gardener, or any scientist, will tell you, the effort is worth it.

Amanda Bertholf, MA, is APS director of communications and the editor-in-chief of *The Physiologist Magazine*. Send questions or comments to the editor at tphysmag@physiology.org.

THE Physiologist MAGAZINE

VOL. 68 | MARCH 2025

CONTACT US
The Physiologist Magazine is distributed to members as part of their membership. For non-member subscription information or to update your contact information, email **subscriptions@physiology.org**.

tphysmag@physiology.org | 301.634.7118 | **physiology.org/magazine**

The Physiologist Magazine (ISSN 0031-9376) is published six times a year by the American Physiological Society (APS), 6120 Executive Blvd., Suite 575, Rockville, MD, 20852-4911.

APSselect

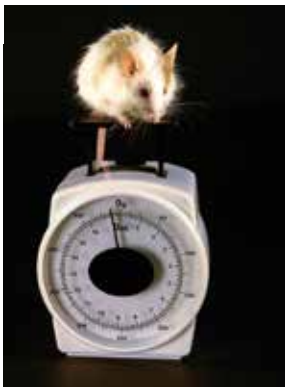
Rethinking Menopause and Heart Health

Cardiovascular disease is the leading cause of death in women, and new research shows it's not just a postmenopause concern. A recent review reveals troubling trends among women ages 25 to 54, with signs of heart disease appearing earlier than expected. Researchers analyzed vascular and hormonal changes in 140 women ages 18 to 70. They found that changes in blood pressure, weight gain and higher cholesterol and blood sugar levels started to appear in women in their 40s. In addition, endothelial function begins to decline, and aortic stiffness increases around ages 47 to 48—several years younger than previous studies have indicated (age 53). The findings suggest that blood vessel dysfunction in women begins before the average age of menopause (51) and may not be solely influenced by sex hormones. While factors like diet, exercise, sleep and mental health weren't addressed, this research highlights the need for earlier interventions to protect women's heart health.

Source: doi.org/10.1152/ajpheart.00373.2024

APSselect

What Genes in Fat Tissue Tell Us about Obesity



Researchers have found that hundreds of genes in mice are expressed differently in different types of fat tissue found in the body. Most of the genes are involved in processes relating to inflammation, metabolism and heart health. The changes in genetic expression also varied depending on whether the mice were lean or obese. Visceral adipose tissue—the fat that surrounds the internal organs—is already associated with chronic inflammation. Multiple genes involved in inflammatory signaling pathways were upregulated in the visceral adipose tissue of obese mice. Cardioprotective genes, on the other hand, were expressed more abundantly in the subcutaneous adipose tissue—the fat that sits under the skin—of the leaner mice. This study may improve our understanding of factors that contribute to obesity and how genes respond to obesity.

Source: doi.org/10.1152/physiolgenomics.00080.2024

Unless otherwise noted, all images: iStockphoto

IN BRIEF

The Latest Research from APS Journals

Highlights from research articles recently published in one of the Society's 10 journals.

Artificial intelligence plays a role in the classification, prediction and research advancement for glioblastoma multiforme, one of the most aggressive forms of brain cancer.

doi.org/10.1152/physiolgenomics.00011.2024

A guinea pig model of placental insufficiency helps researchers understand how therapies designed to improve fetal growth may affect the placenta.

doi.org/10.1152/physiolgenomics.00131.2024

Researchers explore using arginine vasopressin as a promising treatment for neuropathic pain.

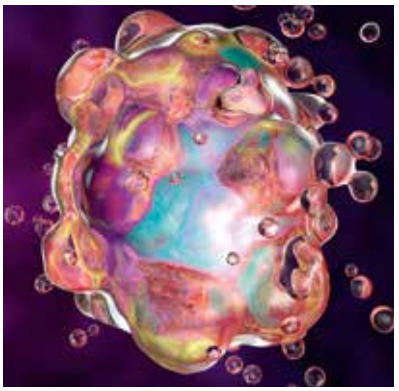
doi.org/10.1152/ajpendo.00361.2024

A study of vascular and hormonal changes throughout women's lives finds endothelial function declines and aortic stiffness increases in their late 40s.

doi.org/10.1152/ajpheart.00731.2024

AGING

How Cellular Cleanup Slows over Time



Autophagy—the body's process for breaking down old and damaged cell parts—is essential for handling the stresses our bodies experience, especially during exercise and heat exposure. However, age may weaken this critical function, according to a recent study on women's cellular response to exercise. Researchers examined blood cells of pre- and postmenopausal women who completed 30-minute high-intensity cycling sessions. They found the older women (average age of 69) had a weakened autophagy response compared to the younger women (average age of 23). This could put older women at a higher risk for heat-related cellular damage.

Source: **doi.org/10.1152/ajpregu.00178.2024**

NEUROPHYSIOLOGY

Sleep's Role in Neurodegenerative Disease Risk

Sleep not only provides the body and brain with needed rest, but it also removes neurotoxic molecules, such as amyloid beta, which is found in the brains of people with Alzheimer's disease. Disturbed or interrupted sleep can lead to a buildup of neurotoxins in the brain and nerve cell death. Impaired sleep has been found to be a precursor to neurodegenerative conditions such as Alzheimer's and Parkinson's diseases. Improving sleep physiology through several means may help the brain clear these toxins. Sensory (e.g., auditory, vestibular) or transcranial (e.g., magnetic, ultrasound, infrared light) stimulation, antiepileptic or antidepressant medications, exercise and changes in sleep position are explored in a recent review.

Source: **doi.org/10.1152/physiol.00019.2024**

Top right: Shutterstock; bottom left: iStockphoto

Changes in fat fraction in lumbopelvic muscles occurring in low gravity highlight the importance of targeting this area to protect astronauts' spine health.

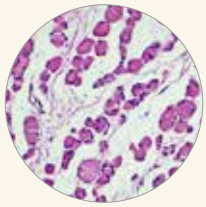
doi.org/10.1152/japplphysiol.00502.2024

Researchers find exposure to air pollution particles leads to liver inflammation, fibrosis and fat accumulation.

doi.org/10.1152/ajpcell.00385.2024

Blood flow restriction as a potential preventive tool for inactivity-induced muscle atrophy does not appear to affect muscle size or satellite cell concentration in men.

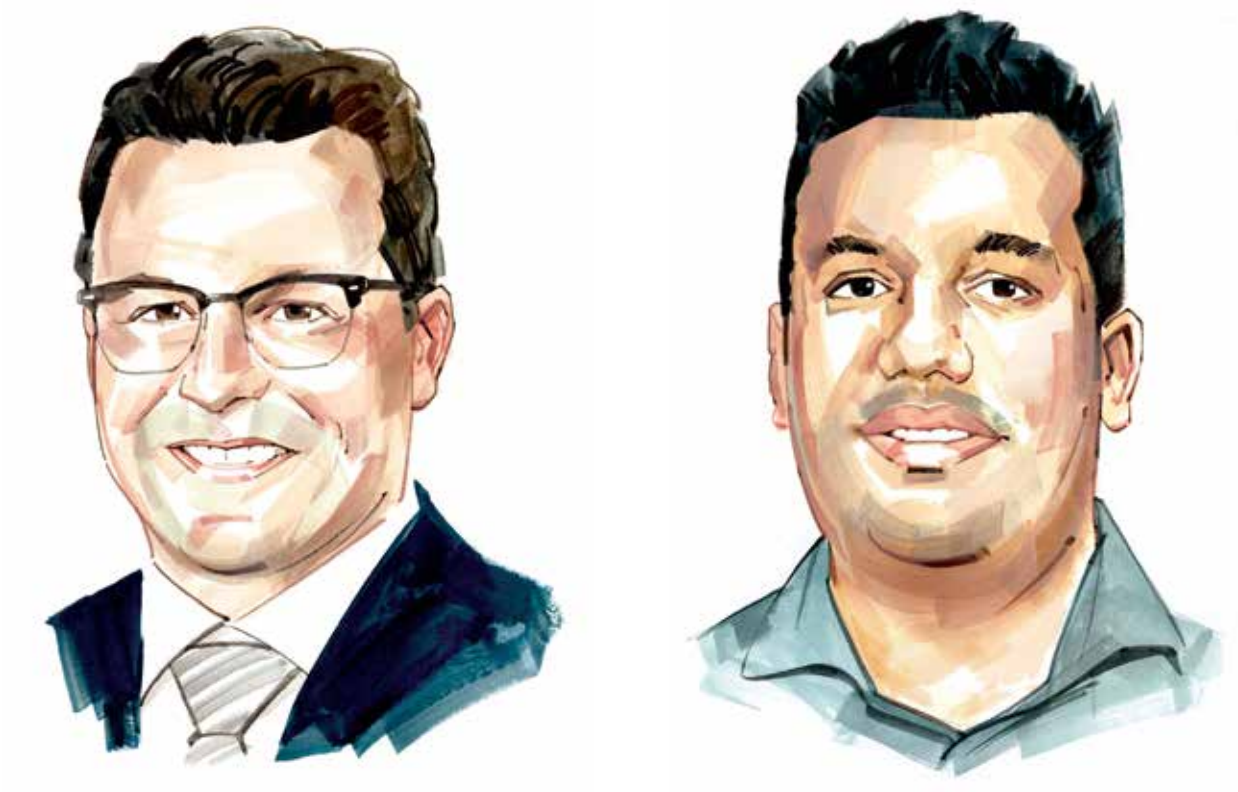
doi.org/10.1152/japplphysiol.00461.2024



A recent review explores differences in chemotherapy-related muscle wasting by age, sex, cancer type and drugs used.

doi.org/10.1152/ajpcell.00773.2024

LAB NOTES



Ian M. Greenlund

Naveen Sharma

MENTORING Q&A | EARLY CAREER

Progress in Motion

How to chart your course for success as new faculty.

Each issue, we ask a student or early-career member to pose their career questions to an established investigator and mentor. Here, **Ian M. Greenlund, PhD**, assistant professor of medicine and a senior research fellow at Mayo Clinic, asks **Naveen Sharma, PhD**, professor in the School of Health Sciences at Central Michigan University, for successful strategies to move from postdoc life to faculty.

Illustrations by Kagan McLeod

Q: What traits or strategies do you employ that you attribute to your personal and professional success?
A: Self-awareness has been a key trait for my professional success. The ability to better understand my strengths and limitations has been important in my interactions with everyone ranging from supervisors to colleagues to trainees. By being more self-aware I can be a better collaborator and teacher, which ultimately makes my work environment really enjoyable.

Q: What was one of your largest challenges in your academic career path and how did you overcome it?
A: Unlike all my previous training, my current faculty position requires a considerable amount of classroom teaching, which initially led to feelings of self-doubt and anxiety. Fortunately, on campus I have excellent resources for improving teaching and classroom instruction. Seeking out those resources and using them has allowed me to become a more effective instructor in the classroom and the lab.

Q: Research is filled with trials and tribulations, especially as a postdoctoral fellow or as early-career faculty. How do you keep your line of academic inquiry stimulating and exciting?
A: It was a whole new ball game transitioning from a postdoc to an early-career faculty member. The safety net is gone, and it is truly up to you to run the team that, until this point, you've only been a player on. Even if your line of research was similar to what you were working on as a trainee, the independent start-up is going to be very exhilarating and sometimes overwhelming. While you are still trying to get your feet under you, don't be afraid to reach out to those who helped you get there. They are willing to provide encouragement and answer questions that you didn't know to ask when you were still a trainee. Once you get settled in, one of the greatest perks of being an independent researcher is that you get to answer questions in whatever way you want. That itself is very stimulating and exciting.

Q: What is the most rewarding part of your current position?
A: I often tell my friends that I have the best job. I have flexible hours, I am compensated well, I have fantastic colleagues, and by working at a university I literally never left school. But truly, the most rewarding part of this job is seeing a student from my class or lab get accepted into grad school since I know the best is yet to come for them in their academic journey.

Q: What's one thing you wish someone had told you when you were a senior postdoc fellow?
A: I feel extremely fortunate to have received great advice from my postdoc supervisor and other mentors. But that was then, and it was a much different time in terms of technology and communication. The use of social media is more second nature to trainees now, more so than those who graduated 15–20 years ago. I see how so many of my earlier-career colleagues are great at information delivery and self-promotion via social media. This is the current norm, so excel at using these tools to stand out from the crowd and attract people to your research as it may open up boundless opportunities.

"Once you get settled in, one of the greatest perks of being an independent researcher is that you get to answer questions in whatever way you want."

Got a career question you'd like to submit? Email it to tphysmag@physiology.org. We may use it in an upcoming Mentoring Q&A.

STATS & FACTS

No. 1

Heart disease is the leading killer of women, causing 1 in 3 deaths a year, killing more women than all forms of cancer combined.

Go Red for Women

Women can have different heart attack symptoms than men, including shortness of breath, nausea, severe fatigue and back or jaw pain.

New York-Presbyterian

33%

of maternal deaths are caused by cardiovascular disease.

Go Red for Women

Women are more likely than men to have microvascular dysfunction and spontaneous coronary artery dissection.

New York-Presbyterian

A CLOSER LOOK | THE NOBEL PRIZE

Celebrating Science

Since 1901, the Nobel Prize has honored groundbreaking discoveries that deepen our understanding of life and health. Alfred Nobel—a chemist, engineer and inventor who built a vast fortune—stipulated in his will that his wealth be used to establish prizes honoring those who provide the "greatest benefit to mankind" in physics, chemistry, physiology or medicine, peace, and literature. Past laureates have uncovered DNA's structure, insulin's role and immune system mechanisms. Today, it remains one of the most prestigious honors in science. On page 32, learn how APS member Joseph Erlanger, MD, received the Nobel Prize in Physiology or Medicine (alongside Herbert Gasser, MD) in 1944 for Erlanger's work on the properties of nerve fibers. This year, more than 80 years later, Erlanger's family has generously donated his Nobel medal to APS, where it will be displayed in honor at Society headquarters.

Up until 1980, the medals were made of 23 karat gold and weighed 200 grams. Since then, they have been made of 18 karat recycled gold plated with 24 karat gold.

Swedish sculptor and engraver Erik Lindberg designed the medals in 1901.

Alfred Nobel's year of birth (1833) and death (1896).

The medals for chemistry, literature, physics, and physiology or medicine have an identical portrait of Alfred Nobel in left profile.

The reverse is inscribed "Inventas vitam iuvat excoluisse per artes." It means "it is beneficial to have improved human life through discovered arts," from "Aeneid" by the Roman poet Virgil.

Shutterstock

POLICY IQ | ADVOCACY

New Congress, New Opportunities

With dozens of new members of Congress, it's time to highlight the importance of federal research support.

The November election returning President Trump to the White House brought significant political change to Washington, D.C. Along with a Republican president, the Senate and the House of Representatives will be controlled by Republicans, with narrow majorities in both chambers.

While federal research agencies have long enjoyed strong bipartisan support in Congress, disagreements over the handling of the COVID-19 pandemic by federal officials have eroded trust in science. A recent poll by the Pew Research Center shows that the percentage of Americans who trust scientists to act in the best interest of the public remains high at 76%, but still well below the pre-pandemic peak of 87% in early 2020.

In the last Congress, budgets for both the National Institutes of Health (NIH) and the National Science Foundation (NSF) were held flat—or cut—as lawmakers sought to rein in spending. Members of the House and Senate launched efforts to reauthorize and reform NIH, with some proposals including a consolidation of institutes and centers. These efforts faltered at the end of 2024 but are expected to be revived, particularly with an increased focus on government efficiency.

SENATE OUTLOOK

With a 53–47 seat majority in the Senate, Republicans will need to work with Democrats and Independents to reach the 60 votes needed to pass most legislation. At least 12 new senators have joined the 119th Congress, with additional vacancies possible as Cabinet officials are selected and confirmed.

HOUSE OUTLOOK

House Speaker Mike Johnson (R-Louisiana) returns to an even slimmer majority, with Republicans expecting to hold 220 seats to the Democrats' 215. With three representatives likely joining Trump's Cabinet, the Republican majority will shrink even further until special elections are held. At least 62 newly elected representatives will hold office for the first time.

NEW OPPORTUNITIES

With at least 74 new members of Congress, now is the time to share why federal support for research is important. Members of Congress may be unaware that the budgets for NIH and NSF flow to institutions in their states or districts and that those funds are used to support cutting-edge research and train the next generation of scientists.

Sharing information about how federal funding supports physiology research on the local level is crucial to building strong support in Congress.

Learn more at **physiology.org/career/advocacy**.

Sharpen Your Advocacy Skills

Learn how to effectively advocate for science funding and policy with APS online advocacy course, "How to Advocate for Science." Discover strategies to engage lawmakers, craft meaningful messages and drive support. Equip yourself with tools to champion science. Start today at **physiology.org/career/advocacy/how-to-advocate-for-science**.

STATS & FACTS

Nearly 50%

of women ages 20 or older are living with some form of cardiovascular disease.

Go Red for Women

Women are more likely than men to have microvascular dysfunction and spontaneous coronary artery dissection.

New York-Presbyterian

About 57.5%

of total stroke deaths are in women.

Go Red for Women

An analysis of data from ClinicalTrials.gov, one of the largest trial registries in the world, found that women represented less than 40% of the people enrolled in heart disease and stroke clinical research.

Circulation

UNDER THE MICROSCOPE | PHYSICIAN-SCIENTIST

Bridging Science and Care

This researcher cherishes the privilege of being a physician-scientist.

Jeanie Park, MD, is an associate professor of medicine and interim associate director of renal medicine at Emory University. She is a staff nephrologist and deputy associate chief of staff for research at the Atlanta VA Healthcare System. Her research interests are in autonomic regulation and neural control of blood pressure in patient populations at increased cardiovascular risk, such as those with chronic kidney disease and hypertension. Here's what she shared with us:

BUILDING RELATIONSHIPS. As a nephrologist, I really enjoy building relationships with my patients and helping them improve their health. I was also drawn to science because of the opportunity to improve health at a community level. As a physician-scientist, I am privileged to care for people living with kidney diseases, as well as developing and testing new solutions to improve their health and quality of life.

DRIVING CHANGE. My favorite parts of my job are related to making a positive impact on my patients, students and mentees, while contributing to scientific knowledge. I enjoy the scientific process of identifying gaps in knowledge and testing hypotheses that could have a real clinical impact and improve outcomes. I also find it very rewarding to mentor and help early-career investigators develop their academic careers.

TAKING IT OUTSIDE. When I first started the human integrative physiology laboratory at Emory and the Atlanta VA, the only manufacturer of the nerve traffic analyzer that was used for microneurography stopped making the device. I partnered with another company to build the device from scratch. During one of our troubleshooting sessions, I wasn't sure if we weren't getting the nerve recording because of an issue with the device itself or because of interference inside the building. So, I took the nerve traffic analyzer, along with a stretcher, outdoors to test the device. I did microneurography on the lawn in front of the VA hospital!

> "I am privileged to care for people living with kidney diseases, as well as developing and testing new solutions."

OLD SCHOOL? Not true. Some may say that physiology is "old school" and no longer relevant. This is a major misconception! Physiology is all about how the body works and is central to developing new therapies.

Do you know someone we should meet? Email us at tphysmag@physiology.org and tell us more.

Courtesy of Jeanie Park, MD

PUBLISH WITH POLISH | OPEN ACCESS

Creative Commons License Options

APS' Subscribe to Open expands authors' licensing choices.

The landscape of open access has evolved significantly over the years. APS has been there every step of the way, creating initiatives that prioritize author needs and funder requirements. From hybrid open access in the early 2000s to Read-Publish-Join agreements in 2021, APS has continually adapted to support its communities.

Now, with the launch of Subscribe to Open (S2O) in 2025, APS is expanding its licensing options for authors, offering greater flexibility and control. Through S2O, APS authors can now select from three Creative Commons (CC) licenses: CC BY, CC BY-NC and CC BY-NC-ND. This marks an important step in empowering researchers to share their work while aligning with funder mandates.

What Are Creative Commons Licenses?

CC is an international nonprofit that facilitates the sharing and reuse of creative works. The licenses are designed to promote the dissemination of knowledge while allowing authors to retain copyright. Choosing the right license boils down to your goals and funder requirements.

CC BY. The most permissive license, CC BY allows others to distribute, remix, adapt and build upon the work, even for commercial purposes, as long as the original author is credited. Many funders designate CC-BY as the only license allowed for compliance with their open access mandates. This license even allows for commercial reuse.

CC BY-NC. The reuse terms are nearly identical to CC BY, but there is an added restriction: Only noncommercial uses of the work are permitted. Under APS open access publishing terms, authors retain the copyright of their work, so the CC BY-NC terms protect authors' commercial interests in their published text and images. For example, when APS transitioned *Advances in Physiology Education* to a no-cost open access model, it adopted CC BY-NC to safeguard physiology educators' instructional materials while enabling open sharing for educational purposes.

CC BY-NC-ND. This license restricts commercial reuse and also prohibits sharing of derivatives. ND, or "no derivatives," means that if you "remix, transform or build upon the material you may not distribute the modified material." As limiting as this license sounds, it allows for the redistribution of the original material, ideal for authors who want to ensure their work is shared but not altered.

Supporting Author and Funder Needs

APS' expanded licensing options reflect a shift in open access publishing—acknowledging that one size does not fit all. While CC BY remains the most popular and widely required license, many authors and funders recognize the importance of protecting commercial rights or maintaining the integrity of original works. For authors navigating these choices, it's crucial to consider the requirements of their funding bodies. Most funders outline specific licensing mandates, which can often be found on their websites.

Why Subscribe to Open Matters

By adopting S2O, APS gives authors eligible for open access the opportunity to publish their work without additional fees while selecting the licensing option that best fits their needs. This combination of flexibility and accessibility ensures that APS continues to champion innovation and inclusivity in publishing.

Send questions or comments to tphysmag@physiology.org.

iStockphoto

STATS & FACTS

4

Nobel prizes (at least) have been awarded resulting from research about C. elegans, a one-millimeter nematode.

The New York Times

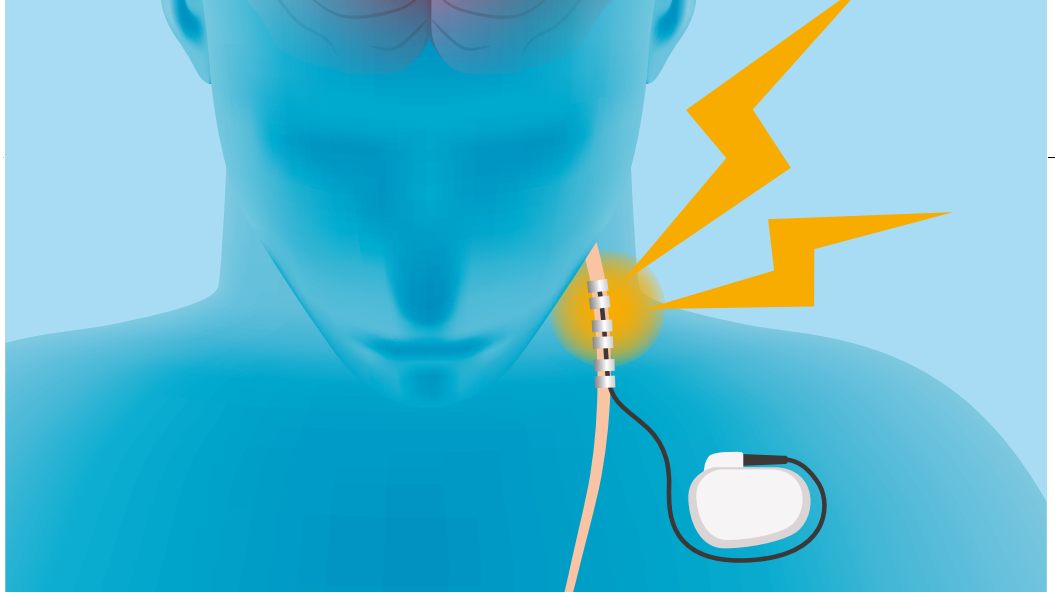
"The Nobel Prize disciplines "remind us that it is not blind destiny that decides on our future as humanity. This also offers hope. It lies in our hands to change the world."

Astrid Söderbergh Widding, board chair of the Nobel Foundation, Nobel Prize Award ceremony, Dec. 10, 2024

627

Nobel prizes have been awarded in physics, chemistry, medicine or physiology, literature, peace and economics.

Nobelprize.org



Reshaping Recovery

Vagus nerve stimulation rewires neural circuits to promote healing for conditions such as stroke, depression and PTSD.

Michael Kilgard, PhD, is the Margaret Fonde Jonsson Professor of Neuroscience in the School of Behavioral and Brain Sciences at the University of Texas at Dallas, where he also serves as executive director and chief science officer of the Texas Biomedical Device Center. His groundbreaking research focuses on using vagus nerve stimulation to rewire neural circuits to improve recovery from serious psychiatric or neurological conditions. This empowers patients to actively participate in their recovery rather than relying on lifelong medications or managing symptoms passively.

How did you become interested in developing new tools for treating people with neurological and psychiatric disorders?
This is very personal for me. I've known people with nearly every neurological and psychiatric disorder—psychosis, addiction, depression, Alzheimer's, spinal cord injuries, strokes—either as family, friends or colleagues. Although these disorders were once thought to stem from specific genes or brain regions, this turned out to be wrong. These conditions aren't about chemistry; they're about wiring problems, which are potentially changeable.

If we can develop tools to rewire the brain, we can push it away from pathological states and toward healthy states. That's true for recovery from stroke or spinal cord injuries and also for mental health conditions like depression and post-traumatic stress disorder (PTSD).

How is your work game-changing?
The key innovation is shifting the focus from brain areas—of which there are only a few hundred—to individual synapses, of which there are trillions. It's a big change in perspective. Our goal is to enable targeted rewiring of the specific parts of the brain that are malfunctioning, without affecting the healthy parts. This is an incredibly challenging task that took us 30 years to figure out. Now that we have the technology platform, we can explore how to use it to change the nervous system in a variety of conditions.

Our personalized approach fosters collaboration between patients and clinicians, making therapy more effective. By focusing on changing neural connections rather than unchangeable factors like genes or past injuries, our work aims to revolutionize how therapists help patients achieve meaningful and lasting improvements.

Tell us more about the technology and devices you developed.
The vagus nerve connects to all the body's organs and plays a key role in the "rest and digest" parasympathetic system, promoting relaxation. When you stimulate the part of the vagus nerve that connects to the brain, it briefly activates the brain. The brain momentarily perceives a disconnect, triggering a powerful but brief release of acetylcholine and norepinephrine—lasting only half a second.

Unlike prolonged effects from substances like amphetamines, this short burst signals to the brain that something significant has occurred. It doesn't feel rewarding or aversive but does prompt the brain to adjust and pay attention. These chemicals are crucial for forming new memories, learning skills and creating new neural connections.

Our team has developed implantable vagus nerve stimulators that reward the brain when someone

iStockphoto

does the right thing, such as staying calm, moving their hand or holding a memory longer.

What is the current status of this technology, and how is it applied in real-life applications?
The first generation of our vagus nerve stimulation system, called Vivistim, is being used in an FDA-approved treatment to help stroke patients. This involves patients getting the implant and then working with a physical therapist who evaluates what they can do, focusing on small movements they can manage such as partially turning their hands. The therapist stimulates the nerve when they exceed their personal baseline, with the goal of eventually turning their hand fully, for example.

We have also developed a device that measures movement—like how hard someone squeezes or turns their hand—and provides feedback directly to specific neurons. This allows at-home therapy that can target and strengthen the neurons active during correct movements, much like perfecting a tennis serve or violin note, to drive better performance and recovery.

In the lab, we created a vagus nerve stimulator that is 50 times smaller than the Vivistim, making it cheaper, easier to implant and more comfortable. These improvements are key to scaling this technology to tens or hundreds of thousands of people with serious conditions.

What's unique about your approach to this research and technology development?
We challenge traditional clinical methods by prioritizing personalization and collaboration with participants. Unlike the straightforward "fix a broken process with a pill" model of biochemistry, our research acknowledges that brain function is deeply individual. Each person has unique goals, challenges and needs, so the focus shifts to identifying and rewiring circuits that help participants achieve their aspirations.

The interdisciplinary nature of this work is key. At the Texas Biomedical Device Center, engineers, clinicians, biochemists and students collaborate closely, often within 50 feet of each other, to design devices, study animal models and engage with patients. This tight integration fosters innovation and ensures that ideas flow freely across disciplines.

For me, it's all about caring for people with real needs. When you focus on treating actual conditions, it forces you to do very practical, useful things. This has exposed new biology and opened our minds regarding the mechanisms at work. My focus on translation has deepened my understanding of the basic science, making it even more meaningful.

What are some of the next steps for this research?
Our brains are complicated, and it's going to take us time to figure out how to prevent someone from being psychotic or depressed or unable to move their hand. We're currently carrying out a randomized controlled trial examining vagus nerve stimulation for post-traumatic stress disorder where both groups receive psychotherapy but only half get vagus nerve stimulation. We're also testing the technology's use in spinal cord injuries and exploring its potential for other conditions, such as multiple sclerosis and treatment-resistant depression, while continuing to advance the basic science.

Interview conducted by science writer Nancy D. Lamontagne. Send questions or comments to tphysmag@physiology.org.

Meet the Game Changers

Michael Kilgard, PhD, will speak in a Game Changer session at the American Physiology Summit titled "Bioelectric Medicine and the Power of Vagal Nerve Stimulation." Learn more at **physiology.org/gamechangers**.

STATS & FACTS

25

Lawrence Bragg was the youngest scientist to win a Nobel in 1915 at the age of 25 "for his services in the analysis of crystal structure by means of X-rays."

Nobelprize.org

In May 1968, the editor of the *New England Journal of Medicine* used the term "bench-bedside interface" to describe two papers published in the issue that demonstrated for the first time that chronic granulomatous disease of childhood could occur in females.

New England Journal of Medicine

97

John B. Goodenough was the oldest scientist to win a Nobel in 2019 at the age of 97 "for the development of lithium-ion batteries."

Nobelprize.org

Her Research Is a TRIP

Biological anthropologist Cynthia Beall, PhD, wrangles multiple disciplines in her research on biological variation.

BY JENNA SCHNUER

While growing up on what used to be farmland in upstate New York, Cynthia Beall, PhD, never dreamed of trekking the Andes or the Himalayas. She wasn't one of those kids who disappeared into their minds, imagining far-off adventures while their parents stood five feet away asking them to finish their chores.

Beall's route into the mountains was both more direct and completely by chance. It was the fall semester of her senior year at the University of Pennsylvania, and she needed to fulfill a general education requirement for her diploma. Beall's course of choice for that requirement? A class called physiological anthropology. "And wow, I loved it," she says. "I thought, 'Well, this brings everything together. It's people, it's the environment, it's biology.'"

The love stuck. Beall became a biological anthropologist. She has been a professor at Case Western Reserve University in Cleveland since 1976. She is also co-director of the university's Center for Research on Tibet.

"My field, biological anthropology, is focused on understanding why there's so much human biological variation. And not only why, but how. The 'why' is the big question—are they adapted to the environment—the evolutionary questions. The 'how' is the genetics, the physiology, the anatomy, the biochemistry."

THE IMPORTANCE OF ALTITUDE

After earning her undergraduate degree in 1970, Beall went on to get her master's and PhD at The Pennsylvania State University. The focus of her research came into view during her PhD program. Her adviser was researching how people adapt to high altitude in the Andes. He was studying the Quechua people, who lived in a remote high-altitude village.

Beall joined a team of other PhD students helping him with his research. "It was fascinating because of what we could see about how

Photos courtesy of Cynthia Beall, PhD

Beall spent years trekking into the field, including in the Tibet Autonomous Region, to study human adaptation to high-altitude hypoxia.

their biology in many cases mirrored, or was qualitatively similar, to the biological response you and I would make," Beall says. "Not in everything, but in a number of traits."

When, say, lowlanders from the U.S. or Europe go to high altitude, their hemoglobin concentrations will increase and stay high. Oxygen saturation goes down. It's the same for Andean highlanders.

But things are different when it comes to breathing. When somebody who lives at low altitude decides to trek up a mountain, their breathing increases. But over time, that ventilatory response becomes blunted. Andean highlanders also have a blunted response. "With the hemoglobin, it does not seem to be a function of how long you've been in altitude, but with the breathing it does," Beall says.

Beall's early work with her adviser also helped her understand why working at altitude was essential for the kind of research she wanted to do. Altitude remains the same. "At high altitude it's easy to measure the environmental stress by measuring barometric pressure. Everyone at a given altitude has the same stress," she says.

That's unlike, for example, looking at the environmental stress of temperature. "If you and I went to the Sahara, you might have different gear than I do, so we might be exposed to temperature slightly differently. Or maybe I went one year, and you went a different year, and it was hotter one year than another," she says. "So, for some environmental stresses, it's harder to measure the stress."

One of the other elements that Beall considered when she began her work was evolution, but she says it alone could not explain the variation among people, partly because evolutionary changes occur over long timeframes. Instead, the Andean highlanders displayed signs of developmental adaptation, having grown up in an environment with constant exposure to high-altitude stress. This adaptation led to the development of barrel chests, which accommodate larger lungs.

HEADING TO THE MOUNTAINS

Beall's first visit to the field didn't quite make it to the heights she would eventually work up to. Instead, she and several other graduate students were on the coast of Peru studying Quechua highlanders who had migrated down to lower elevation.

She started to learn just enough Spanish to hold rudimentary chats. Beall enjoyed talking to the research participants, collecting biological measurements and household data. She continued her work in the Andes throughout graduate school. After completing the program, one of her colleagues at Case Western Reserve University asked, "Have you ever thought about working in the Himalayas?" Her response? "Only in my dreams."

At the time, most of the Himalayas were not open to foreigners. But a new colleague had worked in Nepal at high altitude. He wasn't interested in researching biology, but he had some experience, and he knew how to organize a high-altitude trek. Even more importantly, he had contacts in the area who could help make essential introductions to locals Beall could work with along the way.

In less than a year after defending her dissertation, Beall began organizing her first trip to the Himalayas. It would kick off years of research centering on human adaptations to high-altitude hypoxia, mostly focused on Andean, Tibetan and East African highlanders.

Beall outlined the criteria her research required, and her colleague set off to figure out the perfect location. Before long, he came back with good news: "I found the perfect place. It's only an eight-day walk." Beall thought she misheard. "You mean eight hours?" No, eight days.

Beall had no experience with camping or hiking on the flat farmland where she grew up. While her graduate work in the Andes exposed her to high-altitude research, it didn't involve trekking or camping. "I was used to being outside," she says, "but we didn't do anything like that. It was all new to me."

Her mom helped outfit her for the trip by buying her a tent. "She bought a really brightly colored one so if anything happened, it would be easy to spot me," Beall says. "And I headed out." With her for the trek were an interpreter, a cook and a guide. She had one very simple question: Did Tibetans adapt to high altitude the same way that Andean highlanders did?

She says that first trek into the Himalayas was a very basic pilot study using minimal equipment. It was monsoon season "so it was dark and kind of crappy weather." She and the interpreter spent time explaining to locals what they were doing and why. The first publication from that study—which she says is the first observation that has carried through to this day—came out in 1981.

"One nice thing about people who live at high altitudes is they know they're special," Beall says. That literal pride of place made it easy for Beall to be honest and tell potential research subjects that she wanted to understand what made them so different from her.

FINDING HER PLACE

That monsoon season trip made Beall question her enthusiasm for trekking through rainstorms, but it didn't stop her. She returned again and again. Once, while working with a group of Tibetan nomads, she camped midwinter at 17,000 feet on the Tibetan plateau. "I can tell you it's cold," she says. "The lowest it got was 29 below—without factoring in the windchill."

Those trips led to several comparative studies where she looked at Tibetans in the Himalayas and Quechua in the Andes who lived at the same altitude. Her most recent research started in 2012 and continued through last fall "in various forms."

One project involved five months of trekking to 48 villages. Along the way, Beall learned the importance of involving villagers in the research process and ensuring clear communication to build trust. To address concerns and encourage participation, she and her team held public demonstrations to explain their work and answer questions. "Otherwise, rumors start to fly: 'Oh, she's collecting blood and she's going to sell it,'" Beall says. And when people told her they weren't comfortable with some form of collection or another, then the researchers just had to make do or find another way. "Any field worker will tell you [that] you have to be flexible," she says.

She has also learned that it helps to team up with cultural anthropologists who know local dialects and have built up trust from village to village. Then it's a matter of respectfully asking about collaborating, without jeopardizing what the anthropologist has worked so hard to build.

Beall's research has gone far beyond lung function into rates of birth and many other areas. She continues to build on the layers she's learned over 40 years of trekking. And, over time, she has also helped bring people from the Tibet Autonomous Region to the U.S. to learn English or get degrees so they could return home and do their own research.

As for the future, Beall says her trekking days might be over. Though she retired from teaching a year ago, she has plenty of in-office work organizing data and writing up years of research. Overall, she says organizing the 48-village trek sounds easier. "The trek was very goal oriented," she says. "This cataloging past work is organizing on a different scale."

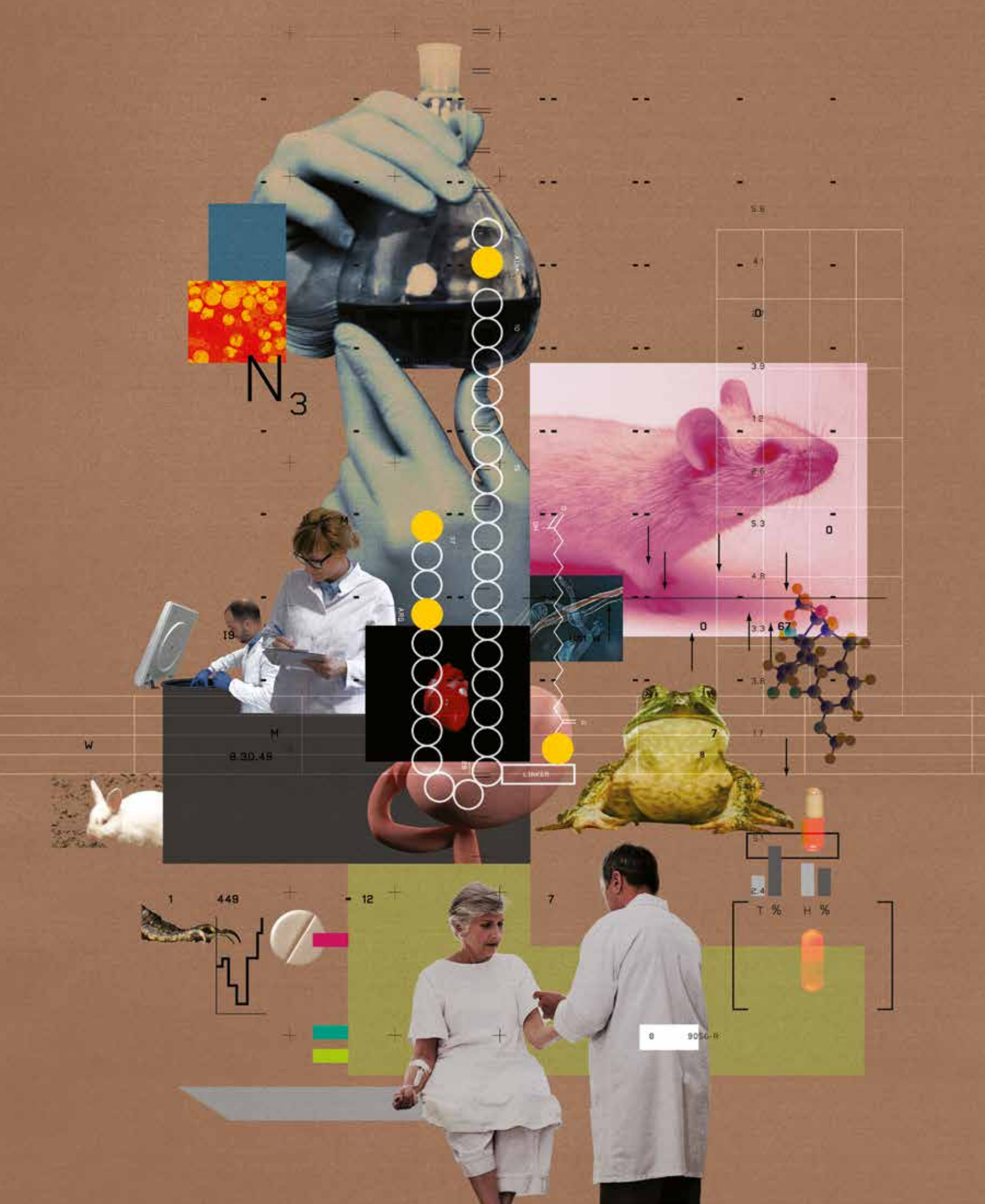
INSIDE THE STORY

Trust and Boundaries

Like all fieldworkers, Cynthia Beall, PhD, knew from the get-go that she would need to build rapport with the people she hoped to recruit. Strangers can't just walk up to someone and ask for a blood pressure or a blood sample. What's helpful? Introductions to influential local people. Research assistants speaking the local dialect. Learning to speak the local language—or at least a few important phrases. Living in the community and participating in everyday life. Collaborating with researchers with experience in the community is also possible and carries the extra responsibility of preserving what they have already built.

No two villages responded the same way to Beall's requests. She learned the importance of clear explanations and public demonstrations of research activities. "Otherwise, rumors start to fly," she says. "We always spend time keeping our ear to the ground to hear what is it that people are saying that we are doing. How are they interpreting what we are doing? Do we need to clear up misunderstandings?"

Communities vary in their willingness to provide information. At times that means settling for less-than-ideal samples. For example, collecting pedigree data for genetic studies can be challenging in cultures that don't say the names of dead people. In one set of villages in Nepal, people said no to blood but offered to provide urine samples. "You have to be flexible," Beall says.


N3
T %
H %

From Bench *to* Bedside

How physiologists move from foundational findings to patient care.

BY JENNIFER L.W. FINK

From the clinic to the lab, Mark Donowitz, MD, has built his career around one goal: unraveling the mysteries of human physiology to improve health. Donowitz's journey began on the front lines of patient care, but it was in the laboratory during his medical fellowship that he found his true calling: decoding the complexities of digestive physiology. There, he unearthed the vital role of sodium absorption in gut function and its link to diarrheal diseases, working first with mouse and rabbit models and then with cells. He also helped apply human organoid systems—cell culture models made from normal human intestines—to advance the understanding of digestive physiology and pathophysiology (and potential treatments).

"That led us to a new understanding of the diseases," says Donowitz, professor emeritus of medicine and physiology at Johns Hopkins School of Medicine and past president of the American Gastroenterological Association. "We were able to suggest that you could have more success in developing drugs if you took what was known from the cancer cell lines and animal models and then showed in the humanoid models that there was similar safety and efficacy."

His research not only advanced the collective understanding of digestive physiology but led to the development of two promising therapies for diarrhea: a drug now beginning human trials and a peptide that may help treat a broad spectrum of diarrheal diseases by enhancing sodium absorption.

Translational physiology is a multidisciplinary field dedicated to improving human health. Physiologists are well-positioned to translate lab discoveries into practical interventions that improve individual and public health. From diagnostics to therapeutics, their work bridges the gap between research and real-world application.

Illustration by Alexandra Gallagher

THE HEART OF TRANSLATIONAL RESEARCH

Lara do Amaral-Silva, PhD, assistant professor of biology at Wake Forest University, doesn't work with humans (or human cells) at all. Her current research features birds; past subjects have included American bullfrogs and Tegu lizards. But her work with animals is grounded solidly in a desire to find solutions to problems that plague human health.

"Animals have cool adaptations that allow them to overcome stressors that otherwise cause major human health issues," Amaral-Silva says. "So, if we study and understand the mechanisms that help them avoid a disease state, we may find ways that humans can be treated."

Many well-known medical breakthroughs have resulted from careful study of animals. Angiotensin-converting enzyme (ACE) inhibitors, now commonly used to treat human hypertension and heart failure, sprung from research into the venom of the Brazilian Viper. Semglutide, the currently popular weight-loss drug and diabetes medication, was born from Gila monster saliva. Scientists identified a hormone-like molecule in the saliva that stimulated insulin secretion and realized it wasn't quickly metabolized by the body. The rest, as they say, is history.

Amaral-Silva has studied bullfrogs and birds because both animals have interesting metabolic adaptations to tolerate prolonged hypoxia, while such oxygen deprivation results in morbidity and mortality for humans. Her research pointing to the importance of NMDA receptors in maintaining brain health won the 2024 FaunaBio Translational Research Award from the APS Comparative & Evolutionary Physiology Section.

Besides studying mechanisms to avoid the neurotoxic cascade that arises from hypoxia, Amaral-Silva is also interested in birds because "they are physiologically comparable to a human that has type 2 diabetes," she says. "They have really high glucose and insulin resistance—traits that are related to cognitive diseases and declining cognitive performance in humans—so we would like to understand how they avoid that."

The desire to understand and improve human health is the commonality that links translational researchers, regardless of the site or focus of their work. For some researchers, that desire is based on clinical experience. Viswanathan Rajagopalan, PhD, is associate professor of biomedical sciences at the New York Institute of Technology and vice chair of the APS Translational Physiology Interest Group and a member of its steering committee. He began his career as a physician's assistant at India's premier tertiary care cardiovascular institute. He enjoyed working with patients in both inpatient and outpatient settings but saw so many challenging and unanswered questions in cardiovascular care.

That experience led him to study cardiomyopathy, right ventricular function and failure, anticancer chemotherapy-induced cardiotoxicity, and the interplay of endocrine hormones on cardiac physiology. Currently, he's researching the roles of noncoding RNAs in cardiovascular, thyroid and associated disorders.

Although clinical experience inspires and informs his daily research and actively remains in his background, clinical questions aren't always top of mind, Rajagopalan says.

"If we constantly ask clinical questions, we may not be able to answer key questions at the molecular, cellular and organ levels. So, when I study molecular physiology, including the use of human cells and tissues, I ask directly relevant mechanistic questions and, incrementally, the physiology helps us get to the patient. Physiologists are uniquely positioned to bridge molecules, humans and public health," he says.

FINDING QUESTIONS

Toggling focus between patients and physiologic discoveries is key to translational research. Clinical experience is not necessary but can be helpful. A physiologist's personal experiences with health and health care may also inform their research. Amanda Jo LeBlanc, PhD, also studies the cardiovascular system with an eye toward improving human health, but unlike Rajagopalan, she does not have clinical experience. Her focus instead grew out of a personal desire to better understand how sex and aging affect cardiovascular health.

"It was a very selfishly motivated line of research; I am a woman, I'm going to get older," says LeBlanc, professor in the Department of Cardiovascular and Thoracic Surgery at the University of Louisville and programming chair of the APS Translational Physiology Interest Group. So, she seized the opportunity to work with Judy Delp, PhD, a pioneer in the study of women's heart health.

LeBlanc encourages other physiologists to include understudied populations in their research. "If you have not previously used female mice or a female model, add a few extra groups to your study," she says. "Whether you find something that's different or not, we're still learning. If it turns out that there's no difference between the male and female model, that's absolutely information we need to know."

As LeBlanc's research revealed more about the function of cardiac

microvessels, she turned her attention toward interventions that "may make those small vessels of the heart look more like a young heart." She is currently studying the impact of diet, genetic modifications and cell therapies on the microvessels of aging rats.

COLLABORATING TO FIND ANSWERS

Because there are so many steps between the bench and the bedside, connecting with clinicians and scientists in other fields is helpful. To facilitate collaboration, the University of Louisville has started research interest groups that pull together people working in related but distinct fields.

"That's helped tremendously," LeBlanc says. "I can give a short talk about what I'm currently working on and a kidney researcher in the audience may ask, 'Does that work the same way in the blood vessels of the kidney as in the heart?'" Such questions may sharpen research questions, suggest previously unconsidered ideas and spark productive multidisciplinary collaborations.

"Singularly focused projects with one main principal investigator are increasingly rare today. What's more common—and getting more funding—are multidisciplinary teams," LeBlanc says. Her most recent R01 grant includes cell culture work and human clinical trials, in large part because she's found collaborators who do clinical trials and can recruit patients.

Working with experts in other fields can be tricky, however, as each field has its own jargon and body of knowledge. Additionally, clinicians are often busy with patients and may not have dedicated research time. Use simple, straightforward language when working with collaborators and check for understanding. Clarify as needed.

"Be patient, persistent and perseverant in trying to find the right collaborator—someone who also has time and interest in your research," Rajagopalan says. "It's also important to remember that they don't have to know all the nitty-gritty things that we do and vice versa."

PLAYING THE LONG GAME

It takes time—an average of 17 years, according to some research—to translate scientific discoveries into clinical practice. And more often than not, researchers experience unexpected findings and significant frustration along the way. Maintaining forward motion can be challenging.

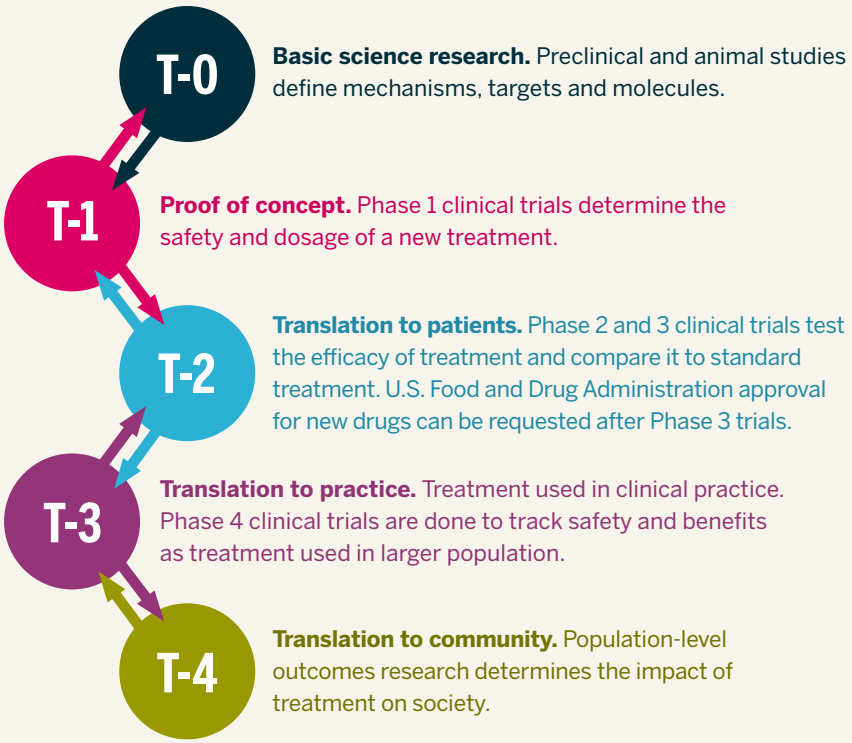
"In the lab, we're faced with 'Am I going to stop this project here or can I take it to the next level?'" Rajagopalan says. He encourages scientists to think about what they can keep doing on the side to advance their research, even if funding falls through, so that when a fitting grant opportunity eventually arises, they'll be prepared to seize it.

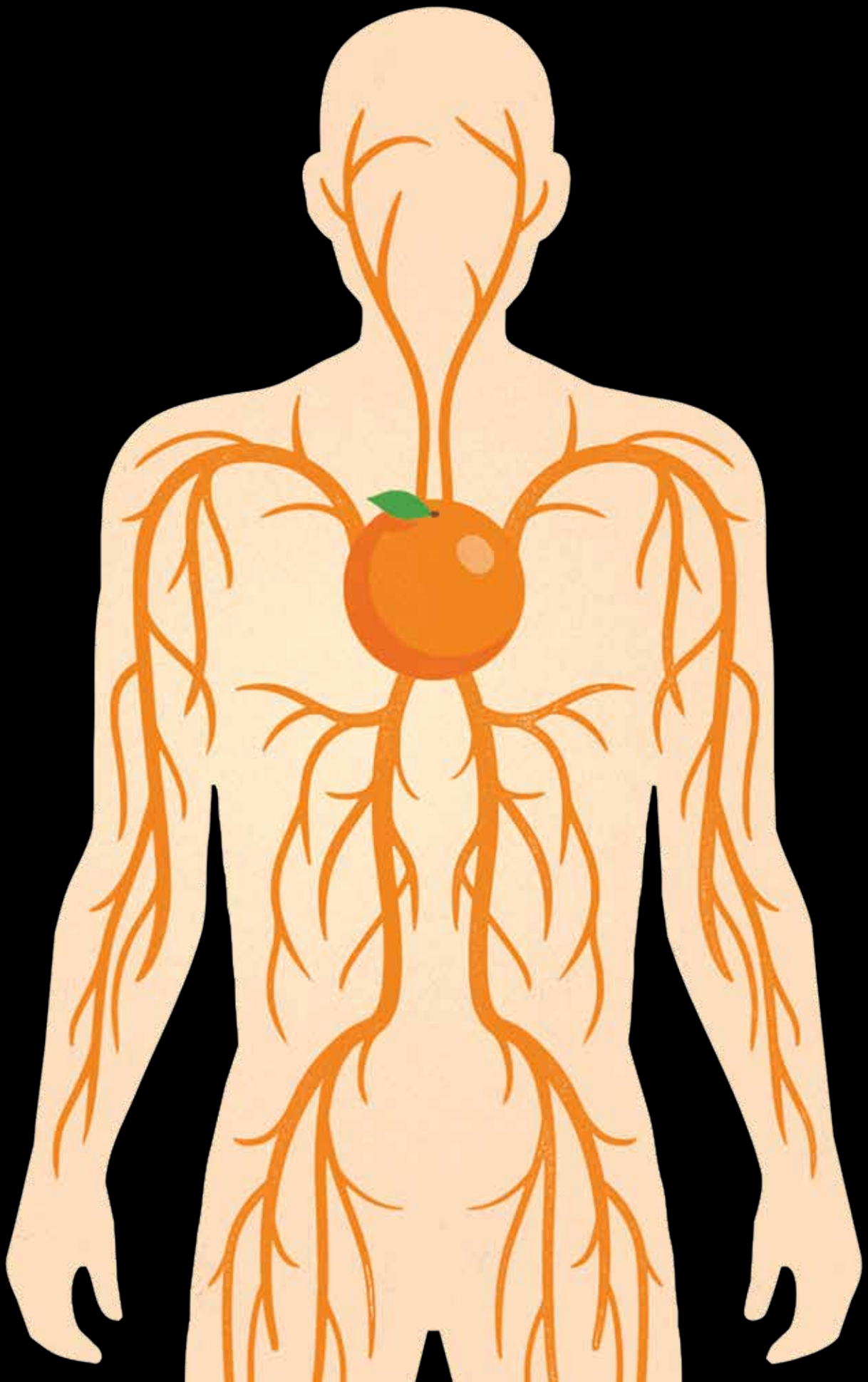
Celebrating successes is helpful, as is remembering your why. "There's still a half a million kids dying of diarrhea every year. Having that as motivation prevents me from really feeling discouraged about what we're doing," Donowitz says. "I'm also tremendously interested in the scientific questions. I get a high when I figure something out, and that's kept me going."

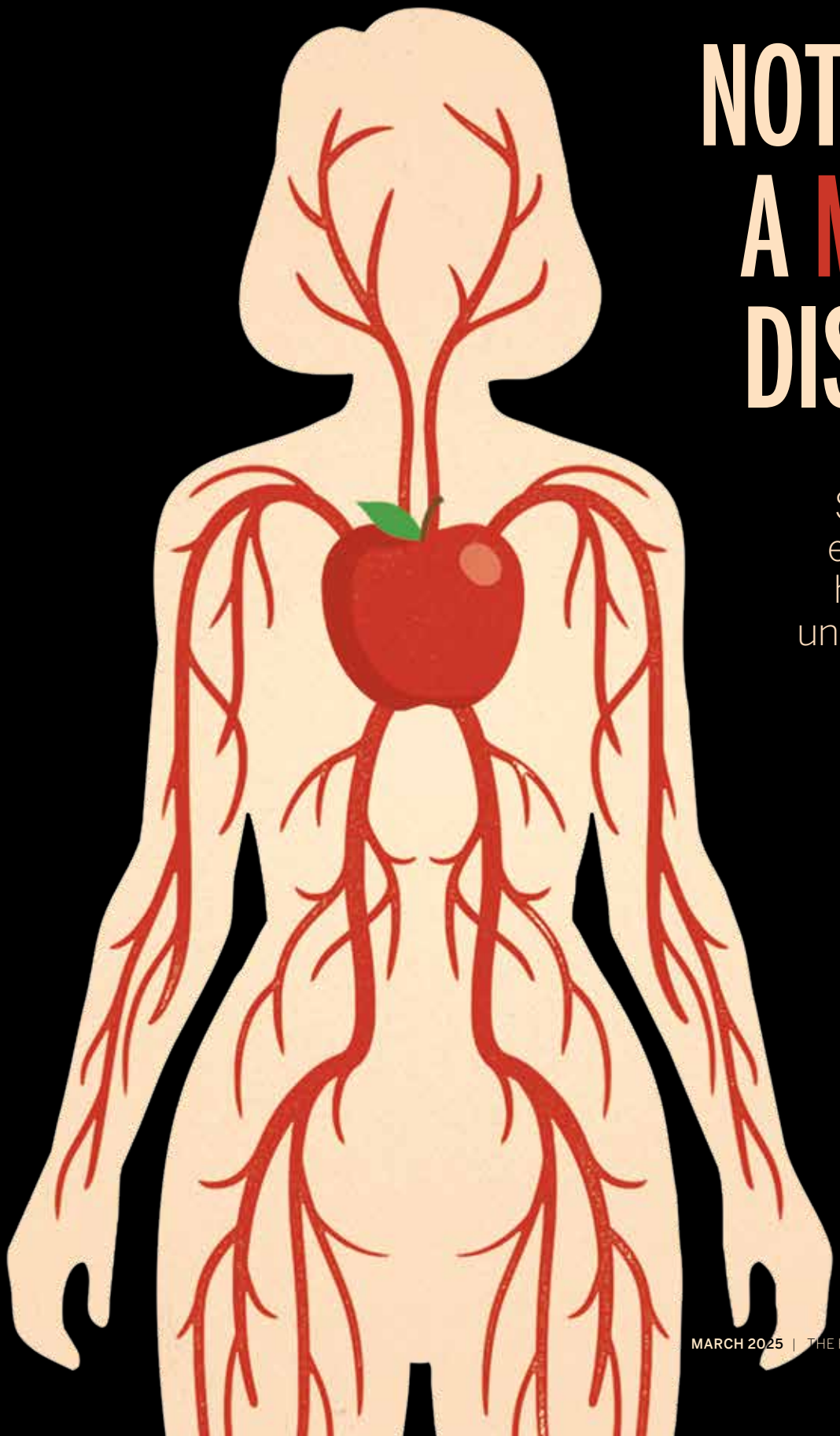
AT A GLANCE

The Spectrum of Research

Translational research is categorized by its stage in the progression from initial discovery to societal application and impact. The T Spectrum (Translational Spectrum) highlights these distinct stages of the research process.







NOT JUST A MAN'S DISEASE

Scientists are exploring how heart disease uniquely affects women.

BY ISOBEL WHITCOMB

Illustration by Chris Gash

A man's disease: Until just a few decades ago, that was how the majority of the medical world viewed heart disease. Cardiovascular research overwhelmingly focused on men, and treatment guidelines—from blood pressure medication to diagnostic criteria—were simply extrapolated to women.

This lack of research into the effects of gender and sex on heart health hid a grim reality: Heart disease is the leading cause of death for women, as it is for men. Women experiencing heart disease and heart attacks were going undiagnosed, receiving inappropriate treatment, or having their symptoms dismissed as anxiety.

Thanks to advocacy and federal policy changes requiring research to include women in their analyses, the medical world and the public have become more aware of the prevalence and presentation of heart disease in women. We now know, for instance, that the symptoms of a heart attack can look very different in women than the crushing chest pain that men often experience. Women are more likely to experience pain in other parts of the body, lightheadedness and flu-like symptoms. Campaigns by the American Heart Association and others teaching patients and providers to recognize these symptoms have helped double awareness of heart disease in women and may have played a role in declining death rates.

Despite these forward strides in research and communications, worrying trends persist: Young women are being hospitalized for heart attacks at increasing rates, according to a 2018 study published in the journal *Circulation*. Meanwhile, women die from heart attacks at twice the rate of men, according to a 2023 study published in the *Journal of the American College of Cardiology*. On top of that, women are still underdiagnosed, undertreated and under-researched, says Glen Pyle, PhD, professor of molecular cardiology and a member of the IMPART Network at Dalhousie Medicine. "Pretty much across the board, women have worse outcomes," Pyle says. "That's really a result of a failure of the system from beginning to end."

Physiologists are working to close that gap. The questions they're exploring range from sex differences in cardiovascular physiology to the role of menopause and hormonal changes in heart health. For physiologists, it's crucial to stay up to date in what we know—and what we're still learning—about the leading killer of women.

THE PROTECTIVE ROLE OF HORMONES

For years, one of the reasons researchers gave for excluding women from studies was the unfounded belief that fluctuating hormones would confound results and make the population hard to study. As it turns out, those hormones are one of the most important reasons scientists studying the cardiovascular system should have been studying women all along—they play a key role in explaining the unique patterns and risk factors of heart disease in women.

There's a kernel of truth to the idea that heart disease is more prevalent in men. At younger ages, men do have a four- to five-fold higher risk of developing heart disease compared to women, according to an international 2017 study published in *BMJ Global Health*. Around midlife, however, that changes.

"We see this dramatic increase in women," says Megan Wenner, PhD, an associate professor in the Department of Kinesiology and Applied Physiology at the University of Delaware. In a recent study presented at the 2024 American College of Cardiology's Annual Scientific Session, researchers measured plaque buildup in the heart arteries of 579 postmenopausal women taking statins. Over the course of a year, average scores measuring plaque buildup increased twice as quickly in these women than they do in men.

Researchers have long attributed this pattern to menopause and the dramatic drop-off in estrogen that occurs during this transition, Wenner says. Sudden drops in estrogen are correlated with increased risk of heart disease in other groups of people, independent of age. For instance, young women who have their ovaries removed have a higher risk of heart disease than their peers.

Researchers are still working to understand the mechanisms for how estrogen boosts cardiovascular health—and why a drop-off in this hormone has such deleterious consequences for women. Wenner's research focuses on the role of sex hormones, including estrogen, on the cells in blood vessels. This focus is particularly important because heart disease in women tends to manifest as dysfunction in the microvasculature as opposed to larger heart arteries, which is more common in men, Wenner says.

"Estrogen has receptors in almost every tissue within the body, so it does have direct effects on the vasculature," she says. Estrogen plays an important role in blood vessel dilation; it stimulates the production of nitric oxide, which helps blood vessels relax. Some of Wenner's research shows that estrogen can decrease activity in the sympathetic nervous system. It also regulates the constricting and dilating effects of a receptor involved in blood vessel function.

Of course, estrogen isn't the only hormone that declines after menopause. Research from Wenner's lab suggests that other sex hormones may play an important role in heart disease. In a 2024 study, Wenner's lab looked at the health of blood vessels outside the heart in a group of healthy women between the ages of 18 and 70. They found that the biggest predictor of age-related declines in vascular function wasn't estrogen but two other sex hormones: progesterone and follicle-stimulating hormone.

"There has been a lot of focus and attention on estrogen, and that's for obvious reasons," Wenner says. "We think that there could be some important roles for other hormones that have just been understudied."

REMODELING THE HEART

If estrogen has such a strong protective effect for the heart, why don't we see clear benefits from hormone replacement therapy (HRT)? That question has intrigued Pyle for most of his career.

When Pyle first began his graduate training in physiology, it was assumed that HRT could only be beneficial to heart health. It was in the early 2000s that the groundbreaking longitudinal Women's Health Study began to unravel that assumption. Rather than protecting women from heart disease, HRT appeared to increase risk. "We've spent the last 15 years trying to look at why the study came to this conclusion," he says.

More recent data have shown that HRT is unlikely to increase the risk of heart disease, but there's still no strong evidence that it's protective, Pyle says. His research supports a theory that after menopause, it's not just that estrogen levels drop off but that the heart itself undergoes a radical transformation, a phenomenon researchers call "cardiac remodeling." That transformation might include a change in the heart's responsiveness to estrogen.

In a 2019 study published in the journal *Acta Physilogica*, Pyle's team of researchers modeled menopause in mice by delivering a drug that caused their ovaries to stop producing estrogen. The researchers then compared the hearts of these "perimenopausal" mice to those of intact mice. They found that the hearts of the altered mice had changed on a cellular level even before menopause was complete: Protein complexes that regulate the contraction of the heart had become less active. And in response to drugs that stimulate estrogen receptors, the hearts of menopausal mice were less responsive to estrogen receptor activation—a finding that might explain why HRT is unable to recapture the benefits of estrogen.

"What we found is the heart didn't lose its responsiveness to estrogen—its response changed," Pyle says. "After menopause, the heart is fundamentally different than before the transition."

DIABETES AND THE HEART

While for the first half of their lives, women do generally have a lower risk of heart disease than men, that's not true for a substantial portion of the population. For the roughly 14% of U.S. women with diabetes, regardless of age or menopausal status, heart disease poses just as great a risk as it does in men, says Judith Regensteiner, PhD, director of the Ludeman Family Center for Women's Health Research and distinguished professor of medicine at Colorado University School of Medicine. "Diabetes eliminates the protection that people think is afforded by the hormones in premenopausal women."

And these women fare even worse compared to men with diabetes. "The consequences of type II diabetes on the [female] heart are more severe than in men—women have heart attacks more often, and those heart attacks more often kill them," Regensteiner says.

Regensteiner and her lab are looking at how diabetes changes the cardiovascular system and the impact those changes have on the ability

"Pretty much across the board, women have worse outcomes. That's really a result of a failure of the system from beginning to end."

—Glen Pyle, PhD

of men and women to function in both exercise and daily life. They found that the cardiovascular system appears to stiffen and lose functional capacity even before any other complications become obvious. "That is pretty startling," Regensteiner says.

While these changes occur across genders, they appear particularly pronounced in women. In one study, Regensteiner's lab compared the VO2max, or maximum oxygen consumption, of 29 young men and women with diabetes to 35 non-diabetic peers. VO2max was 16% lower in men with diabetes compared to their healthy peers, but among women, that difference rose to 24%. That's significant because VO2max isn't just a measure of athletic performance—it also indicates one's ability to function in daily life.

"It can mean the difference between being able to live a normal independent life and not being able to live a normal independent one," Regensteiner says.

THE FUTURE OF CLINICAL PRACTICE

Since the 1990s, cardiovascular research may have become sex- and gender- inclusive, but the decades-long focus on men has an important lasting consequence. Men and women are still, almost uniformly, diagnosed using the same tools and prescribed the same treatments. "It's just not based on evidence," Regensteiner says. While these therapies have been rigorously tested for safety and efficacy in men, the same can't be said for women.

Already, there is evidence that some long-established medical practices are much less effective in women than in men. For example, research suggests that women have lower levels of troponin, a protein that the heart releases into the bloodstream when it's damaged.

The future of women's heart health is personalized. Sex-specific therapies might be considered to promote healthy immune responses and minimize chronic inflammation.

For decades, troponin has been used as a diagnostic biomarker for heart attacks. Too often, however, women who experience heart attacks will release too little of this protein to meet diagnostic criteria.

"There aren't specific guidelines for treatment that take in this newer information," Pyle says. Meanwhile, mounting evidence suggests that women are more likely than men to have adverse reactions to ACE inhibitors, used since the early 1980s and one of the most prescribed antihypertensive drugs today.

But the future of women's heart health doesn't just involve testing already-established protocols to make sure they work for women, says Kristine DeLeon-Pennell, PhD, associate professor of cardiology at the Medical University of South Carolina.

Indeed, the future of women's heart health is personalized. For example, DeLeon-Pennell has identified that after a heart attack, male and female immune systems behave differently as they work to clear damaged heart tissues. In the future, sex-specific therapies might consider this information to promote healthy immune responses and minimize chronic inflammation.

"Historically, clinical trials don't stratify by sex," DeLeon-Pennell says. "In the clinic, we need to start being more cognizant of the therapies that are working best in women versus those that work best in men."

That's where basic science and physiology research comes in, Pyle says. His lab is conducting pre-clinical research on hormone replacement therapies better designed to interact with the post-menopausal heart.

"Until you understand how the physiology differs, you can't understand how the disease develops differently, and you certainly can't design therapies that are sex-specific," Pyle says. "Without that foundation of fundamental science, it's a weak case for any sort of therapy."

ON-DEMAND WEBINAR

Cardiovascular Risks in PCOS Explained

Learn more about the heightened cardiovascular risks in people with polycystic ovarian syndrome (PCOS). Topics include the mechanisms underlying these risks, current treatments available, potential new therapies and the existing knowledge gaps in women's health research. Learn more and watch the webinar recording at **physiology.org/pcos**.

center for physiology education
AN APS INITIATIVE

Elevate the way you teach.

Join us in the Center for Physiology Education, a home base for scientists who are passionate about inspiring the next generation of physiology researchers.

Discover new learning modules designed by experienced educators for your modern classroom.

Access 650+ expert educator-approved resources sorted by core themes.

Make inquiries, share your experiences, attend monthly events and find opportunities to get involved.

Upcoming Community Events

Journal Club—Alignment of Learning Objectives, Assessments and Active Learning to Promote Critical Thinking in a First-year Medical Physiology Course: Lessons Learned

March 11, 5 p.m. EDT

Career Development Hour—Developing Inclusive Assessment Strategies

March 19, 3 p.m. EDT

Register to attend at physiology.org/CPE.

Inspiring Keynote Speakers and Eight Game Changers

Celebrate and share breakthroughs, discoveries—and how even failed experiments advance our understanding of life and health. Top scientists from around the world will come together to present on **topics vital to the scientific community and the world around us**.

80 Foundational Science Sessions

Fill your days with foundational science on novel scientific topics. Dive deep into system-based basic research or zoom out and examine the **translational implications of basic research**.

Welcoming Community

Reunite and collaborate with old and new friends in your global physiology community. From a lively welcome festival at Camden Yards to group workouts and off-site meetups, the Summit is stacked with **opportunities to connect**.

A Program Designed to Propel You Forward

Access career development programming designed to help you fund your research, manage your teaching responsibilities, publish your work and more. Find the right people, resources and opportunities to **navigate an impactful career in science.**

Register by March 31 to save up to $110.

physiology.org/APS2025

Time	Thursday	Friday	Saturday	Sunday
6 a.m.		6 a.m. Runners Meetup		
6:30 a.m.		6:30–7:15 a.m. Bootcamp	6:30–7:15 a.m. Yoga; 6:30–7:15 a.m. Spin Class	
7 a.m.				
7:30 a.m.				
8 a.m.	8 a.m.–4 p.m. Pre-conference Programming			
8:30 a.m.		8:30–10 a.m. Game-changer Sessions *Four Concurrent Sessions*	8:30–10 a.m. Game-changer Sessions *Four Concurrent Sessions*	8:30–10 a.m. Foundational Science Sessions
9 a.m.				
9:30 a.m.				
10 a.m.		10 a.m.–7 p.m. PhysioHub Open	10 a.m.–7 p.m. PhysioHub Open	
10:30 a.m.		10:30 a.m.–12 p.m. Foundational Science Sessions	10:30 a.m.–12 p.m. Foundational Science Sessions	10:30 a.m.–12:30 p.m. Closing General Session with Keynote Speakers Holly Ingraham, PhD, and George Brooks, PhD, FAPS
11 a.m.				
11:30 a.m.				
12 p.m.				
12:30 p.m.				
1 p.m.				
1:30 p.m.		1:30–3 p.m. Foundational Science Sessions	1:30–3 p.m. Foundational Science Sessions	
2 p.m.				
2:30 p.m.				
3 p.m.				
3:30 p.m.		3:30–5 p.m. Foundational Science Sessions	3:30–5 p.m. Foundational Science Sessions	
4 p.m.				
4:30 p.m.	4:15–5:45 p.m. Opening General Session with Keynote Speaker James Rothman, PhD			
5 p.m.		5:15–7 p.m. Poster Reception	5:15–7 p.m. Poster Reception	
5:30 p.m.	5:45–7 p.m. Welcome Festival at Oriole Park at Camden Yards			
6 p.m.				
6:30 p.m.				
7 p.m.	7–9 p.m. Presidents' Reception *Invitation Only*; 7–9 p.m. Trainee Meetup	7–10 p.m. (or later) Special Events, Including Section Banquets	7–10 p.m. (or later) Special Events, Including Section Banquets	
7:30 p.m.				
8 p.m.				
8:30 p.m.				
9 p.m.	9–11 p.m. LGBTQIA+ Meetup			
9:30 p.m.				
10 p.m.				
10:30 p.m.				

american physiology summit

APRIL 24–27, 2025
BALTIMORE

LEGACY

Erlanger Family Donates Nobel Medal to APS

The family of Joseph Erlanger, MD, a renowned physiologist and Nobel laureate, has donated his Nobel Prize medal to APS, Erlanger's scientific home. This significant honor acknowledges Erlanger's groundbreaking contributions to science. The historic artifact, awarded to Erlanger for his work on the properties of nerve fibers, will now reside with APS.

During his career, Erlanger's research focused on electrophysiology and circulatory physiology. He studied sphygmomanometry, developing a recording sphygmomanometer to examine pulse pressure effects on kidney secretion and orthostatic albuminuria in humans. He later created a clamp to reversibly block the auriculo-ventricular bundle in the mammalian heart, allowing him to investigate its function.

Joseph Erlanger, MD, in his laboratory.

Erlanger, who served as APS president from 1926 to 1927, received the Nobel Prize in Physiology or Medicine alongside Herbert Gasser, MD, in 1944. Working together in the late 1920s, they used innovative electrophysiological techniques to demonstrate how the conduction velocity of nerve impulses varies with the fiber diameter. This discovery provided a fundamental understanding of how nerves transmit information, advancing both neuroscience and medical treatments for neurological conditions.

Erlanger earned a bachelor of science degree in chemistry from the University of California before obtaining his MD from Johns Hopkins University in 1899. After a year of hospital training, he became an assistant in the Department of Physiology at Johns Hopkins Medical School, rising to associate professor by 1906. He then became the first professor of physiology at the University of Wisconsin's new medical school, where he mentored Gasser. In 1910, Erlanger joined Washington University in St. Louis as a professor of physiology, retiring as chair in 1946.

Before being housed at APS headquarters, the Nobel medal will be featured at the upcoming American Physiology Summit, April 24–27, in Baltimore. The display will highlight the lasting impact of physiological research on society.

By donating the medal to APS, Erlanger's family ensures that his legacy continues to inspire both current scientists and the next generation of researchers. "Our family is honored to share Joseph's Nobel medal with the APS community. This is not only a tribute to his discoveries but also a way to inspire future generations of physiologists," says Dorothy Erlanger, Joseph's granddaughter. "We hope that seeing his medal and learning about his work will ignite the same curiosity and passion for discovery that drove him throughout his career."

Visit **journals.physiology.org/nobel-laureates.Joseph.Erlanger** to view a list of articles Erlanger published in APS journals.

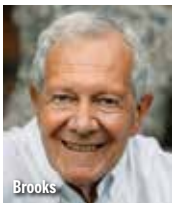
HONORS

Awards Recipients Announced

APS is honoring two member-researchers with the 2025 Physiology in Perspective: The Walter B. Cannon Award and the Henry Pickering Bowditch Award lectureships. These awards recognize the lifetime achievement of an established researcher and the physiological research excellence of an early-career researcher, respectively.

George Brooks, PhD, FAPS, is the 2025 Physiology in Perspective Walter B. Cannon Award Lectureship recipient. This lectureship is the most prestigious award that APS bestows. Audrey J. Stone, PhD, was announced as the 2025 Henry Pickering Bowditch Award lecturer. The lectureship is awarded to a regular APS member who is 42 or younger or less than eight years from the start of their first faculty or staff research scientist position beyond postdoctoral training. The recipient is recognized for original and outstanding accomplishments in the field of physiology.

George Brooks, PhD, FAPS, is a professor in the Department of Integrative Biology at University of California, Berkley. He is a longtime APS member who has produced decades of exercise physiology research. Brooks' extensive body of research focuses on metabolic adjustments to exercise. His work has advanced the understanding of the pathways and controls of how lactate is produced and cleared before, during and after exercise, as well as after carbohydrate consumption. Lactate is a preferred fuel source, the major gluconeogenic precursor and a signaling molecule. This foundational research is valuable for improving health outcomes for patients with injuries and infections, including traumatic brain injury, heart failure and inflammatory conditions. Brooks previously presented the prestigious Adolph Distinguished Lecture for the Society's Environmental & Exercise Physiology Section.



Top left: Paramonov Alexander/Shutterstock; bottom left: © U.S National Library of Medicine

Audrey J. Stone, PhD, is an associate professor in the Department of Kinesiology and Health Education at the University of Texas at Austin. She became an APS student/trainee member in 2009 and a regular APS member in 2013. She is an exercise physiologist specializing in the autonomic control of circulation during exercise, with continuous funding from the


Stone

National Heart, Lung, and Blood Institute since 2019. Stone's primary research focuses on the effects of type 1 and type 2 diabetes on the exercise pressor reflex. Her research group was the first to determine the exercise pressor reflex is exaggerated in type 1 diabetic rats and that this response evolves as the disease progresses. They also determined that diabetes-induced inflammation contributes to exaggerated blood pressure responses during exercise in type 2 diabetes. Understanding the mechanisms behind these blood pressure spikes during exercise in individuals with compromised cardiovascular systems—who often use exercise as part of their treatment—is crucial for developing safe and effective therapeutic strategies for those with diabetes.

This year's awardees will each deliver a lecture at the American Physiology Summit in April 2025. Stone will speak at the Summit on April 24 at 2:30 p.m. Brooks will speak at 10:30 a.m. on April 27, at the closing session of the Summit.

2025 SUMMIT

Women's Health Researcher to Close out Summit

Holly A. Ingraham, PhD, an APS member and the 2024 recipient of the Federation of American Societies for Experimental


Ingraham

Biology (FASEB) Excellence in Science Lifetime Achievement Award, will deliver a closing keynote at the 2025 Summit. Her talk, "How Brain-body Crosstalk Sculpts Facets of Female Physiology," will be held on April 27. Ingraham's research focuses on sex differences and hormone-responsive nodes in the brain and peripheral tissues that maintain metabolic, skeletal and gut physiology in females to address the significant gaps in women's health.

MEMBER NEWS

Kim Barrett, PhD, FAPS, is the 2024 recipient of the John Snow Public Health Innovation Prize. The award is part of Applied Microbiology International's Horizon Awards and honors those whose work significantly improves public health and environmental sustainability. Barrett, a gastrointestinal physiologist and vice dean for research at the University of California, Davis, studies the transport and barrier properties of the gut lining in health and disease. Her research is relevant to the public health issues surrounding diarrheal diseases such as Salmonella. Barrett was the 86th president of APS.


Barrett

Michael Schumacher, PhD, received the 2024 FASEB BioArt award for fluorescence or electron microscopy for his image of crypt-villus architecture in the small intestine. The annual BioArt Awards "honor original, visually stunning photographs, illustrations, data visualizations or videos that effectively communicate an important aspect of 21st century biological research." An assistant professor at Children's Hospital Los Angeles and the University of Southern California, Schumacher studies immune and epithelial drivers of tissue remodeling and regeneration in the gut.


Schumacher

DATES & DEADLINES

CALLS FOR PAPERS

New! **Explore our ongoing cross-journal calls for papers on key women's health research topics:**

- Alzheimer's disease
- Autoimmune diseases
- Breast cancer
- Cardiovascular disease
- Hormone replacement therapy and menopause
- Migraines
- Novel perspectives on sex as an investigative variable
- Pregnancy and postnatal conditions:
  - Endometriosis
  - Gestational diabetes
  - Preeclampsia
  - Polycystic ovary syndrome

Join APS in advancing our mission to improve health care outcomes and promote greater scientific understanding of women's health. Learn more about this special call for papers at **journals.physiology.org/womens-health-research-initiative**.

American Journal of Physiology-Endocrinology and Metabolism

- Immunometabolism (March 1)
- Clinical Metabolism (April 30)
- Exercise Metabolism (April 30)
- Liver Metabolism (May 30)

American Journal of Physiology-Renal Physiology

- The Pathophysiology and Therapy of Polycystic Kidney Disease (March 31)

Journal of Applied Physiology

- Context-Dependent Mechanisms of Striated Muscle Dysfunction (March 1)

Physiological Reports

- Exercise and Diet (March 1)
- Interoception: Hidden Senses (April 30)

More details: journals.physiology.org/calls

AWARDS

Award deadlines vary and may be subject to change. For the latest information, including award descriptions, amounts, eligibility requirements and to apply, visit ***physiology.org/awards****.*

MARCH 15

Hugh Davson Distinguished Lectureship

MARCH 21

Environmental & Exercise Physiology Section Edward F. Adolph Distinguished Lectureship

Environmental & Exercise Physiology Section Impact Award

APRIL 22

Joseph Erlanger Distinguished Lectureship

MAY 17

Environmental & Exercise Physiology Section Honor Award

More details: physiology.org/awards

MEETINGS & EVENTS

American Physiology Summit
April 24–27, Baltimore

- Housing deadline: March 31
- Regular registration deadline: March 31
- On-site registration rates apply: April 1–27

More details: physiology.org/APS2025

WEBINARS

See the latest events at **physiology.org/webinars.**

APPLY FOR SOCIETY AWARDS

american physiological society®

The American Physiological Society (APS) offers more than $800,000 in awards and fellowships each year as part of our mission to encourage excellence in physiological research and education. These awards are a vital investment in our researchers and educators of all career levels.

Learn more about all the available opportunities and apply for the awards highlighted below at **physiology.org/awards**.

March **15**

Cell & Molecular Physiology Section Hugh Davson Distinguished Lectureship

$1,000 honorarium. Highest award bestowed to a scientist with meritorious contributions to the Cell & Molecular Physiology Section in honor of Hugh Davson, DSci.

March **21**

Environmental & Exercise Physiology Section Edward F. Adolph Distinguished Lectureship

$1,000 honorarium. Recognizes an eminent research scholar with meritorious contributions to the areas of environmental, exercise, thermal or applied physiology.

March **21**

Environmental & Exercise Physiology Section Impact Award

$1,000 honorarium. Recognizes a mid-career member who has established a line of impactful research or made a seminal discovery in physiology research.

April **22**

Joseph Erlanger Distinguished Lectureship of the APS Central Nervous System Section

$1,000 honorarium. Highest award bestowed to a scientist with meritorious contributions to the Central Nervous System Section in honor of Joseph Erlanger, MD.

Ongoing

Local Undergraduate Research Awards in Physiology

Established to foster interest and encourage undergraduates in physiological research. Recognizes APS members at their home institution.

Research, Life and the Open Road

BY CHRISTOPHER BANEK, PHD

As I settle in after our recent move to my home state of Minnesota with a new career chapter and our first child, I find myself reflecting on the influences that guided me toward this wild career in academic research. Among them, Robert M. Pirsig's "Zen and the Art of Motorcycle Maintenance" left an indelible mark on my teenage brain—that and Anthony Bourdain's "Kitchen Confidential," but that book report is for another time. Pirsig's writings clearly shaped not just my yearning for cross-country motorcycle touring but my approach to scientific inquiry. Here are a few key lessons I have learned on the road and in the lab:

FINDING PEACE IN THE PROCESS. While a PhD signals mastery of a specific subject, I've come to view it more as evidence of one's capacity to troubleshoot and have an unquenchable drive for improvement. Whether we are diagnosing a stubborn engine's death rattle under the desert sun or identifying the precise reason why our Western blot image looks like a Jackson Pollock painting, we scientists are driven by our methodical minds and devotion to the scientific method.

As Pirsig understood, there is profound peace in this technical approach that transcends mere problem-solving. When meticulous experimental design is unified with genuine scientific curiosity, we create what Pirsig labeled as quality [research]—work that bridges the gap between mechanical execution and deeper understanding.

THE ART OF THE MENTAL PITSTOP. Early in my training, I made the rookie mistake of racing from one milestone to the next, never pausing for a proper vacation and much-needed R&R. While I inexplicably managed to avoid a complete burnout, this relentless pace likely limited both my creativity in experimental design and my insight in interpreting results. I've since learned the value of strategic breaks—let's call them "micro-vacations" because it sounds markedly better than "running away from my problems temporarily." Motorcycling effectively provides this escape, offering focus and meditation aided by the perfect cocktail of wind noise, engine rumble and open road. Plus, it is remarkably difficult and hazardous to check your email and eRA Commons at 60 mph.

THE POWER OF SCIENTIFIC FELLOWSHIP. Science and motorcycling share a crucial truth: Both improve exponentially when you stop pretending you are a lone wolf and embrace the community around you. Just as motorcyclists instinctively share their ideas on the best design lines or exhaust cam configurations, we scientists share an inherent and deep desire to expand our understanding, build on previous work and seriously geek out. Quality work demands the integration and collaboration of our diverse expertise to understand mechanisms at a systems-wide level.

The APS community, and physiology as a whole, exemplify this collaborative and integrative spirit, offering countless opportunities to exchange ideas, build on or challenge our shared knowledge, and blur the boundaries of our fields to move the area forward.

The road, like science, rewards those who remain curious, methodical and ready to pretend their unexpected detours were part of the plan all along. I know there is a parenting metaphor in here as well, but I am just too sleep-deprived to see it.

Christopher Banek, PhD, is an associate professor in the Division of Autonomic Neuromodulation in the Department of Surgery at the University of Minnesota Medical School. His research focuses on the neural control of the kidney and application of neuromodulation interventions in models of cardiovascular or renal disease.

Do you have a life lesson to share or insights on a pressing topic in physiology? Share your thoughts and you could be featured in an upcoming issue of *The Physiologist Magazine*. Email us at tphysmag@physiology.org.

Illustration by Brett Affrunti

Renew Your APS Membership

and Empower Your Community

With the support of a diverse professional network, American Physiological Society members like you are driving groundbreaking discoveries and advancing the field of physiology and related disciplines. Your dedication strengthens our community and inspires progress.

Renew your APS membership today and continue to lead innovation, empower others and enjoy the valuable benefits that fuel success. Together, we thrive!

physiology.org/renew

New Trends in Sex Differences and Women's Health Research

October 2025

New Orleans, Louisiana

Abstract Submissions and Registration Open May 5

Join us for this biennial event gathering leading experts in sex differences and women's health. Engage with renowned scientists, expand your network and discover cutting-edge research. Don't miss this chance to be part of groundbreaking discussions shaping the future of sex and gender medicine.

Learn more at physiology.org/SexGenderConf25.

american physiological society®

aps
women's health research initiative