LEWIS KATZ SCHOOL OF MEDICINE AT TEMPLE UNIVERSITY | TEMPLE UNIVERSITY HEALTH SYSTEM

Temple Health Magazine

WINTER 2021

CONQUERING THE CLOT

Tackling Thrombosis with Technology and Tenacity

COVID-19 AT TEMPLE: STORIES UNMASKED

SEPSIS: INSIGHTS, INNOVATIONS

TEMPLE HEALTH

JOSEPH V. LABOLITO

Practical Wisdom

In the spring of 2020, when the City of Philadelphia needed a large indoor space to convert to a field hospital during the COVID-19 pandemic, any number of complexes in town could have sufficed — but Temple was the only organization to answer that call, lending the City its 340,000-square-foot Liacouras Center (page 18).

In 2017, a Temple physician named Riyaz Bashir, MD, was frustrated. Not a single catheter on the market could do what he needed a catheter to do, so he designed one himself. Now the unique tool — designed to instantly restore blood flow through blood clots — is poised for worldwide use (pages 12 and 44). There's been lots of practical Temple thinking about blood clots: the namesake of the university's Thrombosis Research Center — Sol Sherry, MD (1916-1993) — basically invented the field of using enzymes to melt clots (pages 12 and 46). Another field, colorectal surgery (page 32), owes much about its development to another wise and sensible Temple doc: Harry Bacon, MD '25 (1900-1981).

Examples abound.

Practical wisdom — a Temple trademark — has made its mark on many fields. Even the actual fields of Valley Forge National Park. When the 3,500-acre tract was nearly sold for development in 1970, a Temple alumnus named Kenneth Gordon, MD '48 (1924-2005), mounted the campaign to save it (page 53).

Were these people seeking fortune and fame? No. They simply saw what needed to be done and did it.

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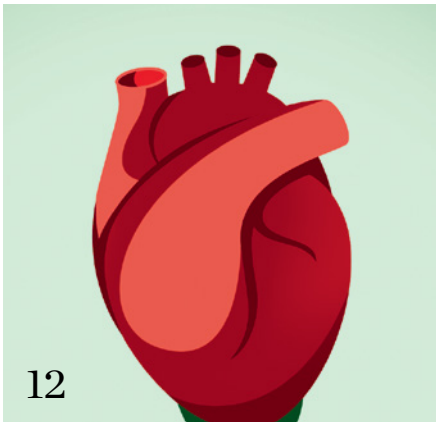


ON THE COVER: Blood clots take a huge toll on public health. Photo illustration by MMJ Studio.

OPPOSITE: ED CUNICELLI; TOP RIGHT: YUKO SHIMIZU; BOTTOM RIGHT: DARIA KIRPACH

CURRENTS

Teen Vaping

Within just months of its initial recognition in the summer of 2019, more than 2,700 cases (including 60 deaths) of E-cigarette or vaping product use-associated lung injury (EVALI) had already been reported to the Centers for Disease Control and Prevention. And nearly 80 percent of the patients were under the age of 35. "The surge in youth vaping is alarming," says Jamie Garfield, MD, Associate Professor of Thoracic Medicine and Surgery at Temple.

Between 2017 and 2019, the percentage of high school students who reported using E-cigarettes more than doubled (from 11.7 to 27.5 percent). And it more than tripled among middle school students (from 3.3 to 10.5 percent).

At the request of the Pennsylvania Department of Health, Garfield, who is also a spokesperson for the American Lung Association, developed a vaping education outreach program for Philadelphia-area schools — and recruited Temple medical student volunteers to help. "Medical students are excellent ambassadors to deliver this message since they are closer in age to our audience," Garfield says. "A lot can be lost when information is presented to teens by older authority figures."

Photograph by CLINT BLOWERS

Lay off the Brakes

Researchers at the Lewis Katz School of Medicine and Fox Chase Cancer Center have shown, for the first time, that a molecule called EGR4 — known mainly for its role in male fertility — serves as a critical brake on immune system activation. The study, published online in *EMBO Reports*, shows that taking EGR4 away — effectively releasing the brake — promotes the activation of killer T cells, which infiltrate and attack tumors, thereby boosting anticancer immunity. This strategy could open the door to a new mode of anticancer therapy.

The research was led by Jonathan Soboloff, PhD, Professor of Medical Genetics and Molecular Biochemistry at Temple, and Dietmar J. Kappes, PhD, Professor of Blood Cell Development and Cancer at Fox Chase Cancer Center, and was supported by the National Institutes of Health.

RAUL ARIAS

TEMPLE HEALTH MADE

FORBES' BEST EMPLOYERS

IN PENNSYLVANIA LIST FOR THE SECOND YEAR IN A ROW

$12 Million for Heart Research

Four Temple research programs focused on molecular mechanisms of heart injury and repair are now supported by a $12 million Program Project Grant (PPG) from the National Heart, Lung, and Blood Institute.

One relates to the role of G protein-coupled receptor kinases in heart function and disease; another on the influence of gender on bone marrow stem cells in heart-tissue repair; the third on cardiorenal syndrome; and the fourth on mitochondrial calcium exchange to reduce tissue injury associated with heart attack.

"All four aim to identify new therapeutic avenues," says principal investigator Walter J. Koch, PhD, FAHA, the W.W. Smith Endowed Chair in Cardiovascular Medicine and Director of the Center for Translational Medicine.

This is the Center for Translational Medicine's second PPG — prestigious federal grants awarded to pre-eminent research groups with track records of significant scientific impact. Two honors given for similar reasons were likewise recently bestowed on Koch himself: the 2020 Research Achievement Award of the International Society for Heart Research and the 2020 Distinguished Achievement Award of the American Heart Association Basic Sciences Council.

Chink in the Armor

Biofilms are dense communities of harmful bacteria that grow on tissues and implanted medical devices.

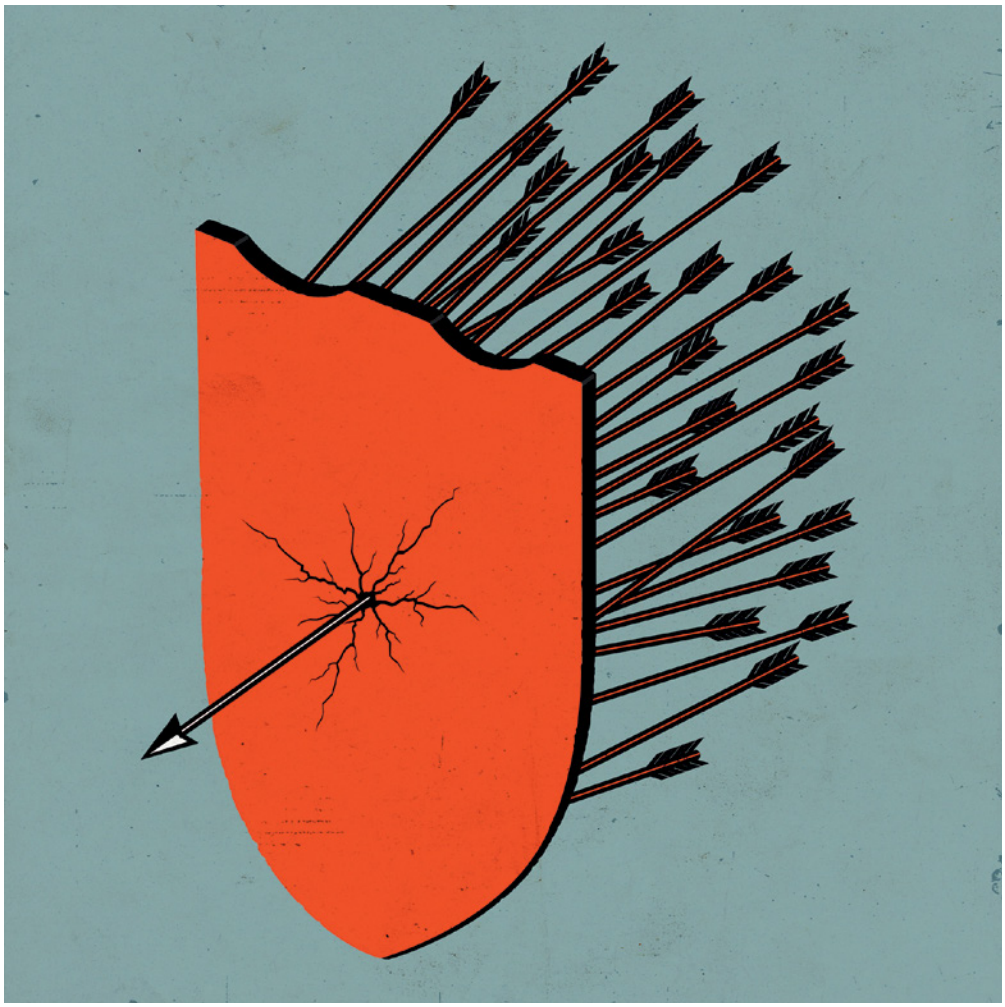
According to Çagla Tükel, PhD, Associate Professor of Microbiology and Immunology at Temple, "Biofilms are notoriously difficult to eradicate, because they secrete a tough protein called curli, which protects them like a shield."

But Tükel's team has made a breakthrough — literally — with an antibody called 3H3. It creates chinks in the curli armor — letting antibiotics flow in.

"We are very excited about 3H3," Tükel says. "There is great need for an immunotherapy to use alongside lower-dose antibiotics or antimicrobials to safely eradicate biofilms before bacteria enter the circulation where they could lead to deadly sepsis infection."

As reported in *Nature Communications*, 3H3 is a first-of-its-kind therapeutic molecule that was isolated by Scott Dessain, MD, of the Lankenau Institute for Medical Research, which supported the study, along with the NIH.

In other biofilms research, Roberto Caricchio, MD, Chief of Rheumatology, along with Tükel and Stefania Gallucci, MD, of the Department of Microbiology and Immunology, was the first to show that biofilms in the urinary tract can trigger autoimmune flareups in lupus patients (*Arthritis & Rheumatology*).



RICHARD MIA

Neuron Regeneration

New research at Temple shows that when present above its usual level, a molecule in the body called Lin28 stimulated long-distance axon regeneration in laboratory models of spinal cord and optic nerve injury.

Shuxin Li, MD, PhD, Professor of Anatomy and Cell Biology, based in the Shriners Hospitals Pediatric Research Center at Temple, was senior investigator on the study, which was published online in *Molecular Therapy*.

"Our findings show Lin28 as a promising therapeutic target for central nervous system injuries. This could be very significant clinically, since there currently are no regenerative treatments for spinal cord injury or optic nerve injury," says Li.

Other scientists in Temple's Department of Anatomy and Cell Biology participated in the study, along with researchers at Johns Hopkins University School of Medicine. The study was supported in part by the NIH and the Shriners Research Foundation.

Temple Health CEO Honored

Michael A. Young, MHA, FACHE, President and CEO of Temple University Health System, has been named one of *Becker's Hospital Review*'s "100 Academic Medical Center CEOs to Know." He was also honored for exemplary leadership, listed among the *Philadelphia Business Journal*'s "Most Admired CEOs," 2020.

AIDS Cure: Closer Yet

On November 27, 2020, *Nature Communications* published a major research milestone in the battle against HIV and AIDS: success in using CRISPR gene-editing technology to remove SIV, a virus closely related to HIV (the cause of AIDS), from the genomes of non-human primates. Human subjects will be the focus of the next phase of the research.

Kamel Khalili, PhD, Chair of Temple's Department of Neuroscience, and **Tricia Burdo, PhD**, Associate Chair of Education in the Department of Neuroscience, led the ground-breaking research, part of a long-term quest that continues to move ever closer to a cure for HIV infection, which affects more than 36 million people worldwide.

Collaborators on this NIH-supported research include researchers from Tulane University School of Medicine, the Texas Biomedical Research Institute, and the University of North Texas Health Science Center, along with Jennifer Doudna, PhD, of the University of California, who, with Emmanuelle Charpentier, PhD, won the 2020 Nobel Prize in Chemistry for developing the CRISPR gene-editing system.

Editor's Note: Khalili, Burdo, and another Temple scientist hold equity in Excision Biotherapeutics, which licensed the viral gene-editing technology from Temple University. Temple also holds equity in Excision Biotherapeutics.

ANNA GODEASSI

Spray-On Skin™

Temple is using a new technology to treat patients with acute thermal second- and third-degree burns: the RECELL® System, a Spray-On Skin™ Cells treatment, which was approved for use in adults by the FDA last year.

The RECELL® System, manufactured by AVITA Medical, requires far less donor skin than traditional grafting to achieve healing of burn wounds — and in less time. A skin sample the size of a credit card can be used to treat a wound up to 80 times larger, and the entire process can take as little as 30 minutes.

"This technology can reduce pain and scarring, improve joint mobility, speed healing, and produce better long-term cosmetic results compared to traditional skin grafting," says Lisa Rae, MD, FACS, Director of the Temple Burn Center.

The Philadelphia Award Goes to Goldberg

In recognition of her original, nationally acclaimed efforts to curb gun violence in Philadelphia, Amy Goldberg, MD, FACS, Temple Health's Surgeon-in-Chief, was recently honored with a Philadelphia Award — a coveted accolade recognizing "extraordinary service to the Philadelphia community." The homicide mortality rate in Temple's service area is 700 percent higher than the national rate — making Goldberg's work imperative. A Temple trauma surgeon for 30 years, Goldberg knows "the catastrophic damage a single bullet can inflict on an entire community. I'm honored to see Temple recognized for these efforts," she says.

Honored

Mary Abood, PhD, Professor, Anatomy and Cell Biology, made *The Cannabis Scientist*'s inaugural "Power List," recognizing the nation's most influential scientists in cannabis research.

Richard Bleicher, MD, FACS, is winner of the Susan G. Komen® Philadelphia 2020 Jamie Brooke Lieberman Remembrance Award for his work in the breast cancer community. Bleicher leads the Breast Cancer Program at Fox Chase.

Denise Connolly, PhD, Associate Professor in the Molecular Therapeutics Program at Fox Chase, is winner of the 2020 Sandy Rollman Ovarian Cancer Foundation's Teal Trailblazer Award.

Deborah L. Crabbe, MD, FACC, FAHA, Professor of Medicine, has been selected for the American Heart Association's 2021 Edward S. Cooper Award for her dedication to eradicating heart disease in women.

Edna Cukierman, PhD, Co-Director of the Marvin & Concetta Greenberg Pancreatic Cancer Institute, has been named a Fellow of the American Gastroenterological Association.

Jeffrey Farma, MD, FACS, Chief of General Surgery at Fox Chase, has been admitted to the American College of Surgeons Academy of Master Surgeon Educators.

Thomas Fekete, MD, MACP, Chair of Medicine, has won the 2020 Laureate Award of the American College of Physicians Southeastern Pennsylvania Chapter.

Glenn S. Gerhard, MD, Chair of Medical Genetics, has received the National Academy of Medicine's 2020 Healthy Longevity Catalyst Award.

Eric Gokcen, MD, Associate Professor of Orthopaedic Surgery and Sports Medicine, received the Pennsylvania Medical Society's 2020 Physician Award for International Voluntary Service.

Erica Golemis, PhD, Deputy Chief Science Officer at Fox Chase, has been named a Fellow of the American Association for the Advancement of Science.

Sergei Grivennikov, PhD, Associate Professor in the Cancer Prevention and Control Program at Fox Chase, was recently named one of the world's most highly cited researchers, according to the Web of Science Group.

Elizabeth Plimack, MD, MS, Chief of Genitourinary Medical Oncology at Fox Chase, has been elected to the American Society of Clinical Oncology Board of Directors.

Howard Ross, MD, FACS, FASCRS, Chief of the Division of Colon and Rectal Surgery at Temple, is President of the Pennsylvania Society of Colon and Rectal Surgeons.

Maura Sammon, MD, Assistant Professor of Clinical Emergency Medicine, has been named Medical Director of Global Response Management, which provides medical care at Matamoros, the largest refugee camp along the U.S.-Mexico border.

Christoph Seeger, PhD, Professor at Fox Chase, recently received the Hepatitis B Foundation's Baruch S. Blumberg Prize for excellence in hepatitis B research, the Foundation's highest honor.

Mark Sobczak, MD, FACR, Clinical Director of Radiation Oncology at Fox Chase, has been named a Fellow of the American College of Radiology. He was one of only eight radiation oncologists in the nation so honored in 2019.

Delana Wardlaw, MD, a family practice clinician with Temple Physicians, Inc., was named 2020 Family Physician of the Year by the Pennsylvania Academy of Family Physicians.

Edna Cukierman, PhD

COLIN LENTON

Milestone Findings

Fox Chase researchers have uncovered a fundamental mechanism that detects the influenza virus and rapidly destroys infected cells. The findings "have exciting implications for a variety of fields," says **Siddharth Balachandran, PhD**, Professor in the Blood Cell Development and Function program, lead author of the research, published in *Cell*.

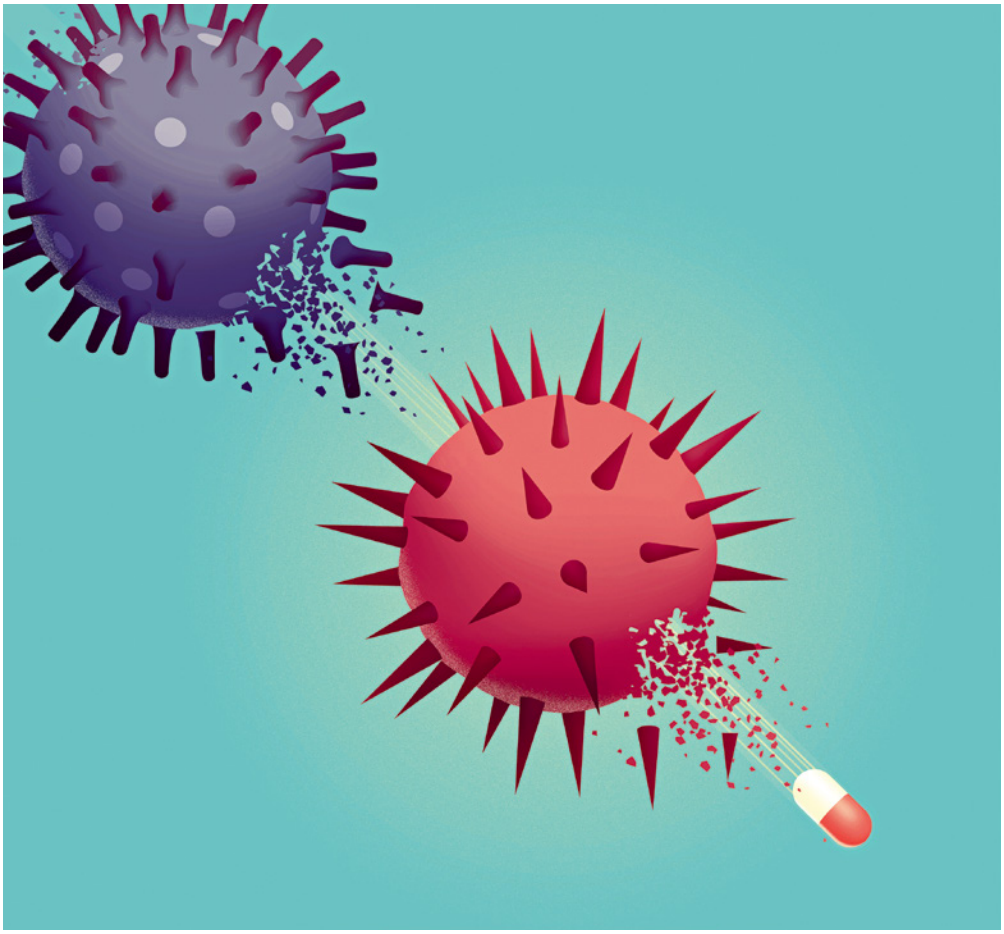
"We knew that a protein called ZBP1 detects the presence of influenza virus in lung cells — but did not know how," Balachandran says.

It turns out that ZBP1 "sees" Z-RNA, a new form of RNA produced by influenza virus.

"Z-RNA is made by the flu virus as it replicates. ZBP1 senses the foreign Z-RNA, then pushes an autodestruct button that kills the infected cell and alerts the immune system to the the virus," Balachandran says. "Scientists have been looking for Z-RNA for decades — and now we know that it follows a pathogen-associated molecular pattern, a new pattern. To discover a new pattern is a major milestone," he says.

LEAPFROG GRADED ALL 3 TEMPLE HOSPITAL CAMPUSES **"A"** FOR PATIENT SAFETY

JOEY GUIDONE



Old Drug, New Purpose

A cancer drug to treat heart failure? An AIDS drug to treat other viral diseases? Two research teams at Temple have identified promising new uses for drugs that are already on the market.

One team used a cancer drug to treat a common form of heart failure called heart failure with preserved ejection fraction (HFpEF). As reported in *Science Translational Medicine*, in laboratory studies the drug, Zolinza, reversed HFpEF symptoms, improving the heart's ability to pump.

"There are currently no FDA-approved therapies for HFpEF, although many people suffer from the problem," says Steven Houser, PhD, FAHA, Senior Associate Dean for Research, senior investigator on the study, a collaboration with the University of Colorado. Zolinza is currently approved for treating cutaneous T-cell lymphoma.

Another team used a drug currently approved for HIV-AIDS to treat Zika infection. In AIDS, rilpivirine works by suppressing viral replication. As reported in *Molecular Therapy*, in laboratory studies it suppressed Zika viral replication as well — "and is likely to do the same for the viruses that cause dengue, yellow fever, West Nile fever, Ebola, and hepatitis C — all flaviviral diseases — which could help prevent thousands of deaths each year," says Kamel Khalili, PhD, a senior investigator on the study, Chair of the Department of Neuroscience and Director of the Center for Neurovirology.

Collaborators on the virus study — which was supported by the National Science Foundation, the U.S. Army Research Laboratory, and the NIH — included Temple's College of Science and Technology, the NIH, the Monell Chemical Senses Center, and Cornell University. The Medical University of Graz (Austria) contributed to the heart study, which was funded in part by the NIH, the Department of Defense of the Office of Naval Research, and the American Heart Association.

Partners of Heart

Temple and the Guthrie Cardiac and Vascular Center, a nationally recognized program with 14 locations in north central Pennsylvania and upstate New York, have developed an affiliation that gives Guthrie patients streamlined access to Temple's heart transplant and advanced heart-failure services.

"We've created a unified approach to the care of heart-failure patients, with defined patient pathways between Guthrie and Temple," says Michael Young, MHA, FACHE, President and CEO of Temple University Hospital and Health System.

One of the most experienced in the world, Temple's Advanced Heart Failure and Transplant team offers the most advanced mechanical circulatory support solutions available — including a transplant program with one of the fastest "list-to-transplant" rates in the U.S. and the region's best one-year survival rate. The team has performed well over 1,000 heart transplants. It is highly experienced in complex dual transplants as well (heart-lung, heart-kidney, heart-liver, and heart-kidney-pancreas).

"We are also home to a robust research program that is pioneering methods to improve patient outcomes," Young says.

In 2020, Guthrie was named one of the nation's Top 50 Cardiovascular Hospitals by IBM Watson Health™. It's the 11th time Guthrie has received the distinguished honor.

DARIA KIRPACH

A Toxic Mystery Solved

Diabetes medications called dual PPα/γ agonists are effective in treating two major complications of the disease: excess lipids and excess glucose in the blood. But they can also be toxic to the heart. No one knew why until Temple scientists solved the mystery.

"We discovered that these drugs negatively impact mitochondria, the energy factories of the cell," says senior investigator **Konstantinos Drosatos, PhD**, Associate Professor of Pharmacology in the Centers for Translational Medicine, Metabolic Disease Research, and Alzheimer's Research.

"Now that we have a much clearer idea of how heart toxicity arises from treatment with dual PPα/γ agonists, we can more effectively guide the development of future drugs," Drosatos says.

The research, published in *JCI Insight*, was supported in part by the National Institutes of Health and the W.W. Smith Charitable Trust.

TEMPLE IS PENNSYLVANIA'S **1ST** TO PERFORM A "BREATHING LUNG" TRANSPLANT USING THE OCS LUNG™

Promoted and Appointed

Nicholas Barcellona has been named Executive Vice President and Chief Financial Officer of Temple University Health System.

Deborah Cancilla has joined Temple Health as Senior Vice President of Data Strategy and Chief Information Officer.

Roberto Caricchio, MD, FACR, has been named Chief of Rheumatology at Temple.

Heather Clauss, MD, has been named Senior Associate Dean of Faculty Affairs at the Lewis Katz School of Medicine.

Amir Emamifar, PharmD, MBA, has been named Chief Pharmacy Officer for Temple Health.

Henry Chi Hang Fung, MD, FACP, FRCPE, has been named Chair of the Department of Bone Marrow Transplant and Cellular Therapies at Fox Chase.

Michael Hall, MD, MS, has been named Chair of the Department of Clinical Genetics at Fox Chase.

Claire Raab, MD, has been promoted to Senior Vice President and Chief Clinical Officer for Temple University Hospital.

Abhi Rastogi, MBA, MIS, has been promoted to Executive Vice President and Chief Operating Officer of Temple University Hospital.

Tony Reed, MD, MBA, CPE, has been promoted to Executive Vice President and Chief Medical Officer of Temple Health.

Doug Tilley, PhD, FAHA, has been named Assistant Dean of Faculty Affairs at Temple's Lewis Katz School of Medicine.

Angelo Venditti, DNP, MBA, RN, FACHE, NEA-BC, has been named Chief Nursing Executive for Temple Health.

Sam S. H. Wu, MD, MA, MPH, MBA, has been named Chair of Physical Medicine and Rehabilitation and Professor of Clinical Physical Medicine and Rehabilitation at Temple.

JOSEPH V. LABOLITO

Ten Chairs

Ten faculty leaders have been honored with endowed chair appointments:

Hossein Borghaei, DO, MS, Chief of Thoracic Medical Oncology, Fox Chase: The Gloria and Edmund M. Dunn Chair in Thoracic Oncology.

Margie Clapper, PhD, Deputy Scientific Director, Fox Chase: The Samuel M.V. Hamilton Chair in Cancer Prevention.

Gary Cohen, MD, FSIR, Chair of Radiology, Temple Health: The Herbert M. Stauffer Chair in Diagnostic Imaging.

Thomas Fekete, MD, MACP, Chair of Medicine: The Thomas Durant Chair in Medicine.

Erica Golemis, PhD, Deputy Chief Science Officer, Fox Chase: The William Wikoff Smith Chair in Cancer Research.

Enrique Hernandez, MD, FACOG, FACS, Chair of Obstetrics/Gynecology and Reproductive Sciences: The J. Robert Willson Chair in Obstetrics and Gynecology.

Karen Lin, MD, MPH, FACP, DABMA, DABIHM, Section Chief, General Internal Medicine: The Abraham Roth Chair in Preventative Medicine.

Henry Parkman, MD, FACG, Professor of Medicine, Section of Gastroenterology: The Stanley H. Lorber Research Endowment Fund and Chair in Gastroenterology.

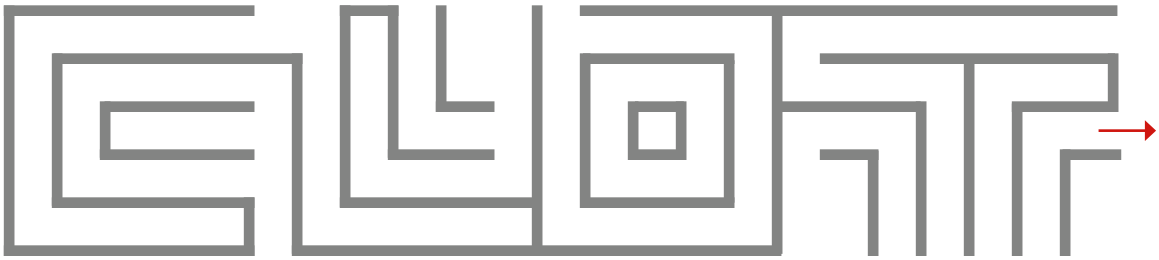
Mariusz Wasik, MD, Chair of Pathology, Fox Chase: The Donald E. and Shirley C. Morel, Stanley and Stella Bayster Chair in Molecular Diagnostics.

Johnathan Whetstine, PhD, Program Leader, Epigenetics, Fox Chase: The Jack Schultz Chair in Basic Science.

Heather Clauss, MD

Tackling Thrombosis with Technology and Tenacity

Conquering the Clot



Blood clots as big as carrots, roots and all, nearly killed Ted Exley and Michael Fischbach.

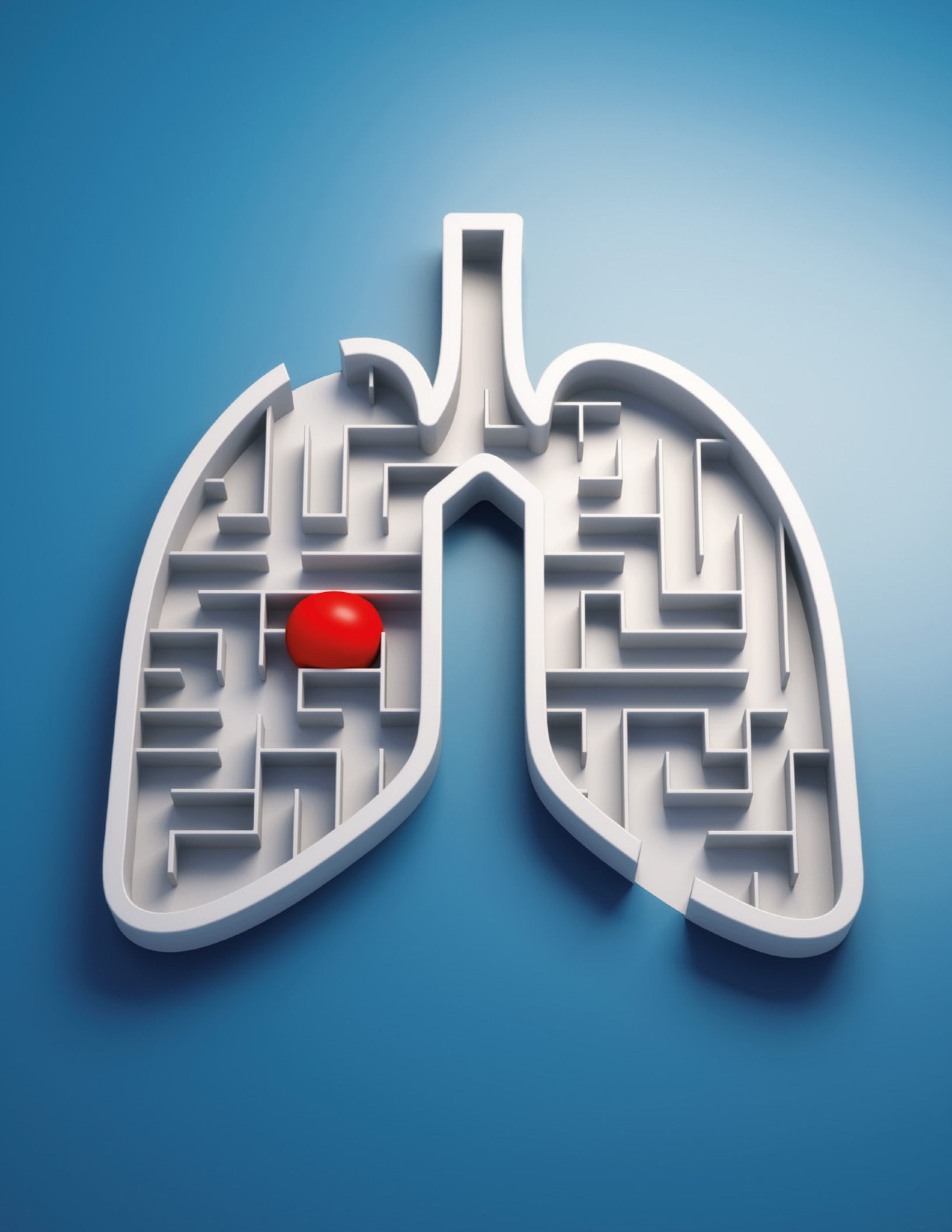
Exley's saga started with a terrible fall in an icy parking lot. He spent a week in the ICU with skull fractures and bleeding in his brain, but was eventually transferred to a rehabilitation center. He was doing well, all considered — until the night he suddenly had trouble breathing.

"Massive clots were found in Dad's lungs — so large, the physicians were surprised he was still alive. We were told he'd have the best chance of survival at Temple," Exley's daughter Ellyn recalls.

By the time he got there — transferred from another tertiary care center in the region — he was in heart and respiratory failure.

Parth Rali, MD, Assistant Professor of Thoracic Medicine and Surgery, remembers "looking at a 100 percent chance of mortality for Mr. Exley if the clots were not removed right away. The problem was, we couldn't use clot-busting drugs because they could increase bleeding in his brain. And he wasn't strong enough for open surgery."

By GISELLE ZAYON
Photo illustrations by MMJ STUDIO



The solution was percutaneous embolectomy, a procedure performed with the Inari FlowTriever® — a device designed to remove clots exactly like Exley's — large "central" clots in the main pulmonary arteries.

The effect was almost immediate. Within hours, Exley was awake and breathing more easily.

A few days later, he celebrated his 74th birthday in the hospital, with a party thrown by Temple staff — cake and singing included. As a joke, his family bought him a helmet, warning, "Don't break your head again."

LUNG CLOTS: ACUTE OR CHRONIC

The clots in Exley's lungs were acute. They formed quickly, posing immediate danger. But clots in the lung can be chronic, too, building slowly over time — like the ones that winded 34-year-old Michael Fischbach so badly he could barely tie his shoes.

The Florida resident's troubles started in 2018 with a clot in the femoral vein of his left leg that required emergency surgery. Then came shortness of breath. A CT scan showed clots in his lungs. Blood thinners helped for a while, but Fischbach was still developing clots. And one of them caused a stroke. It was quite a run for an active young father who remembers having "a clean bill of health until all this."

Fischbach was diagnosed with a condition called chronic thromboembolic pulmonary hypertension (CTEPH), which affects about 5,000 Americans every year.

In CTEPH, clots build up in the lung, starting a boatload of trouble. Pulmonary blood pressure shoots up to the sky. The heart must strain against resistance to get blood to the lungs — working so hard it can begin to fail.

"CTEPH is a debilitating, potentially life-threatening condition — but help is available," says pulmonary hypertension and CTEPH expert Paul Forfia, MD, Professor of Medicine and Co-Director of the CTEPH Program at Temple, a Pulmonary Hypertension Association Center of Excellence and Comprehensive Care Center.

Fischbach's doctors in Florida knew that only a handful of hospitals in the nation have the expertise to treat CTEPH — including Temple. So to Philadelphia he went for a thorough evaluation by the team. And on June 21, 2019, he became the 200th patient at Temple to undergo a specialized surgery called pulmonary thromboendarterectomy (PTE).

The goal of PTE is to surgically remove the clots. It entails placing the patient on a heart-lung machine to keep the blood circulating, cutting through the sternum to expose the heart and lungs, and cooling the blood to 65 degrees. Why cooling? To slow the metabolism, protecting the brain while the surgical team puts the patient into circulatory arrest.

"We periodically turn off the heart-lung machine — halting movement of the chest — so we can safely open the pulmonary arteries to clear them of clots and scar tissue," says Yoshiya Toyoda, MD, PhD, Chief of Cardiovascular Surgery. The patient's blood is then rewarmed, and the heart and lungs are returned to normal function. Fischbach came through it well.

Although PTE is unsurpassed for immediate, complete clot removal (and Temple's success rate is fantastic, with a 100 percent survival rate this past year), it's a risky, complex procedure. It is not appropriate for everyone with CTEPH.

"That's why it's imperative to have alternatives," says Riyaz Bashir, MD, FACC, Professor of Medicine and Director of Vascular and Endovascular Medicine. For some patients, the best approach is balloon pulmonary angioplasty (BPA), an endovascular procedure performed with catheters using X-ray image guidance.

"BPA is a minimally invasive treatment with a much lower risk profile," says Bashir. "Rather than removing the clots, we inflate small balloons inside the blocked pulmonary blood vessels to widen them. This restores blood flow, decreases pressure in the lungs, and eases strain on the heart."

BPA is performed only by a small handful of medical centers. Temple is the second-largest BPA center in the country.

"We offer exceptional, high-tech options for patients with life-threatening lung clots," Forfia says.

And *experience*. A founding member of the national Pulmonary Embolism Response Team (PERT) consortium, Temple has treated more than 500 patients with acute pulmonary embolism (PE) during the past three years alone.

"PERTs are rapid response teams, specialists in multiple disciplines who assemble quickly to expedite diagnosis and treatment. With prompt risk evaluation and treatment, PE survival rates can be significantly improved," says Parth Rali, MD, Temple's PERT Director.

"It's all about attaining excellent outcomes through comprehensive care — from diagnosis to treatment and follow-up. That's why physicians from all over the country send us patients like Mr. Fischbach and Mr. Exley," Forfia says.

> "You don't want 'tissue factor' and blood to meet, because it sets off a cascade of reactions that lead to the formation of a blood clot," Kunapuli says.

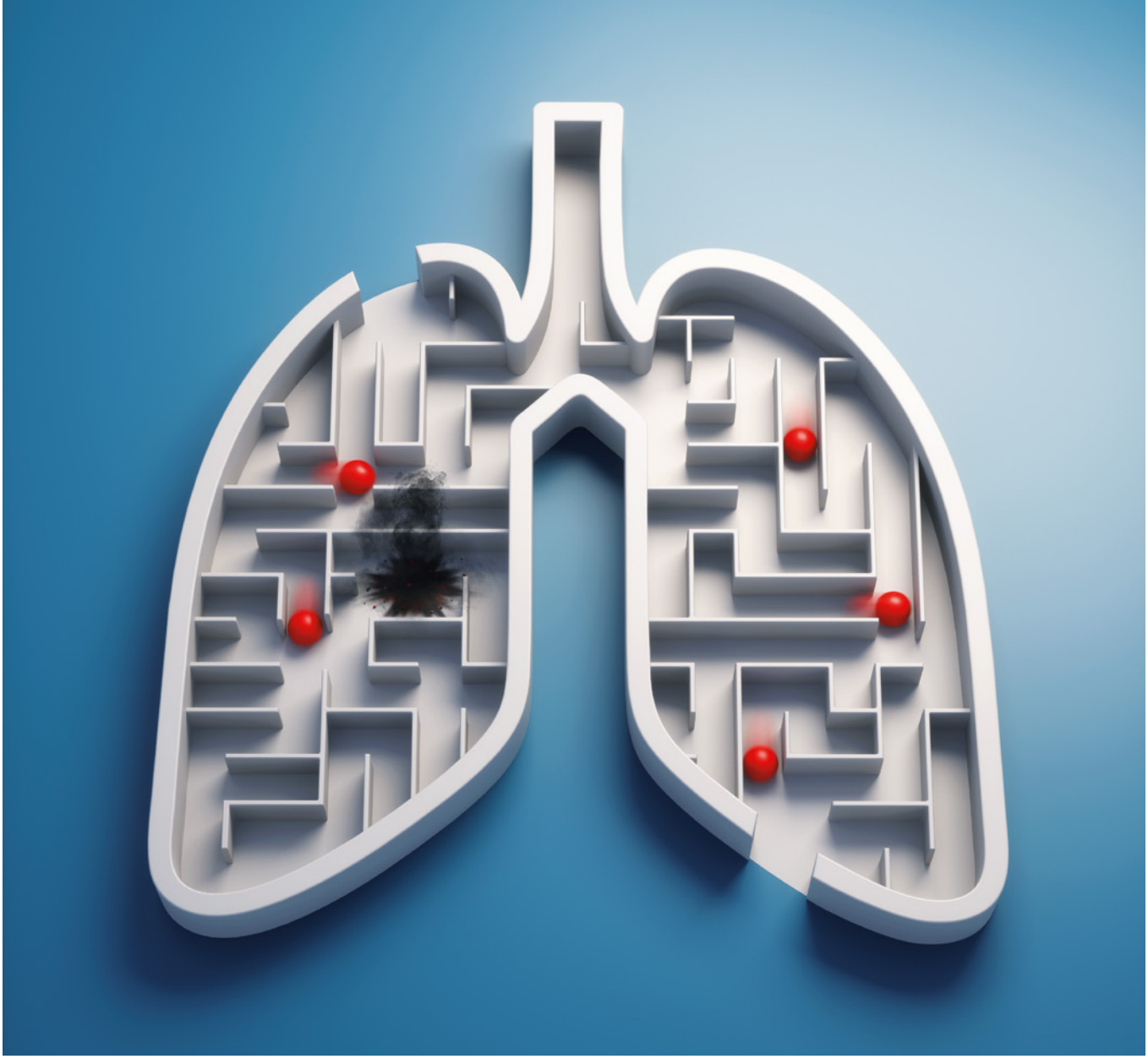
CLOT DIVERSITY

Chronic or acute. Tiny or giant. Different types, different locations. Every clot is unique — but all are threats. They can cause stroke or heart attack, compromise the kidney or liver, imperil limb and life.

"There are many different types of clotting disorders — some involving insufficient clotting, others too much. Thrombosis, clot formation, is a complex process that Temple's been studying for 50 years," says Satya Kunapuli, PhD, Director of the NIH-supported Sol Sherry Thrombosis Research Center.

The Center was founded in 1970 by Sol Sherry, MD (1916-1993), who helped introduce the original clot-busting drugs, streptokinase and urokinase, to the world (see page 46).

"We study all things clotting," says Kunapuli. "Inflammatory proteins; platelets; plasma coagulation factors; protease inhibitors; and the fibrinolytic, complement, and kinin-forming systems. We also study the vascular system, because clots are made



in partnership between blood and blood vessels."

Atherosclerosis, the buildup of cholesterol and calcium plaque within the vessel wall, plays a big role in clot formation. That's because these plaques are covered with "caps" that can shear off, with the constant motion of blood around them. Now a substance called "tissue factor," previously concealed by the cap, is exposed to the blood. "And you don't want tissue factor and blood to meet," Kunapuli says, "because when they do, it sets off a cascade of reactions that lead to the formation of a blood clot."

Clots can form almost anywhere in the body. A clot can even form at one point, break away from the vessel wall, and travel through the bloodstream to lodge in another.

HEADY STUFF

When a runaway clot lodges in the brain, it's called cerebral embolism. When a clot develops directly *in* the brain, it is called cerebral thrombosis. Both types cause ischemic strokes, strokes that block blood supply to part of the brain.

"Ischemic strokes represent about 87 percent of all strokes," says Paul Katz, MD, Interim Chair of Neurology and Director of Temple's nationally recognized Comprehensive Stroke Program.

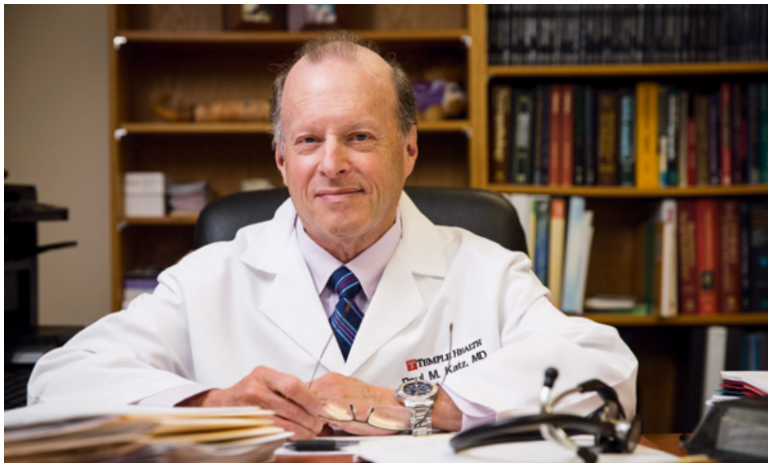
"In stroke, the treatment goal is to dissolve or remove the clot as quickly and safely as possible. The faster blood flow is restored to the affected area of the brain, the lower the chance of disability and death, and the better the chance for recovery," Katz says.

Temple has exceptional expertise in stroke care. It's one of just four Comprehensive Stroke Centers in the greater Philadelphia region. This Joint Commission endorsement goes to hospitals that provide the highest level of care for the most complex strokes — with speed, efficiency, and effectiveness.

"As a Comprehensive Stroke Center, we provide state-of-the-art stroke care 24/7 with advanced neuro-imaging and endovascular neuro-interventional capabilities," says Katz. "We also emphasize stroke prevention — medically and through patient education."

If ever a city needed stroke prevention, it's Philadelphia — where the stroke rate is 20 times the national average — due to so many citizens with unmanaged chronic diseases, difficulty accessing health care, poor nutrition, and other factors.

Against all odds, stroke care at Temple leads to nationally recognized outcomes.



"In 2020, for the eighth year in a row, Temple earned the American Heart Association/American Stroke Association's Get With the Guidelines® Gold Plus and Target Stroke Elite Plus Quality Awards. We were also the only hospital in Philadelphia to achieve Target Stroke Elite Plus status," says Katz, crediting the neurologists, neurosurgeons, nurses, and specialists in emergency medicine, radiology, pharmacy, and laboratory medicine who act fast to characterize strokes and initiate life-saving treatment.

"Through our participation in the National Institutes of Health's Stroke Net clinical trials network, we have access to emerging treatments," says Katz. "We also manage acute stroke care for neighboring community and rural hospitals through a telestroke/telemedicine network."

Kadir Erkmen, MD, FAANS, Director of Cerebrovascular Neurosurgery at Temple, is surgical director of the Stroke Program. "Many patients who would have been killed by stroke now walk out of the hospital a couple days later, totally neurologically intact," he says. "The sooner we can remove the blockage and reperfuse the brain — and we're successful in about 90 percent of cases — the better the improvement in functional outcomes."

What Erkmen is talking about is mechanical thrombectomy. The basic idea is to thread a catheter through an artery in the groin up to the blocked artery in the brain and grab the clot, restoring blood flow to that area. Several devices designed to do this have been tested and approved within the past decade. In 2014 Erkman led Temple's participation in a clinical trial affirming the safety and efficacy of one of the first to gain FDA approval: The Stentriever®.

Before the advent of mechanical thrombectomy, stroke treatment relied exclusively on clot-busting drugs to reduce blockage in the brain. "Now we use both approaches," says Erkmen, who, in addition to operating on patients who've already had a stroke, performs stroke *prevention* procedures to open blocked or narrowed arteries.

There's only one type of stroke-prevention surgery Erkmen doesn't do. His colleagues in cardiology manage it, because it's surgery of the heart — for patients with atrial fibrillation (AFib), a heart rhythm disorder that poses stroke risk.

"In AFib, blood can pool in a small pocket in the heart called the left atrial appendage, forming clots that can travel to the brain," explains Vladimir Lakhter, DO, Assistant Professor of Medicine.

Blood-thinning medications can keep clots from forming, but not everyone can take them.

"That's why we have other ways to treat AFib — including The WATCHMAN™. It's a dime-sized device we implant in the heart that keeps clots from developing — and also eliminates the need for patients to take blood-thinning medication," Lakhter says.

HEARTY MATTERS

When it comes to clots and the heart, the big kahuna is heart attack (myocardial infarction), a clot impeding or blocking blood supply to heart muscle.

The most serious heart attacks are called ST segment elevation myocardial infarctions (STEMIs). These are life-threatening, time-sensitive emergencies requiring immediate diagnosis and treatment. "The goal is prompt restoration of blood flow to the heart, which then improves blood flow throughout the whole body," Lakhter says.

One device to do this is the Impella pump®, a tiny, powerful device delivered to the heart via catheter. Other options include intra-aortic balloon pump (IABP), the Tandem Heart™, ventricular assist devices (VADs), and extra corporeal membrane oxygenation (ECMO).

"New devices and procedures have transformed the treatment of acute heart attack — and the management of heart

JOSEPH V. LABOLITO

Far left, top: Kadir Erkmen, MD, and Paul Katz, MD. Far left, bottom: Vladimir Lakhter, DO. This page: Riyaz Bashir, MD, and the BASHIR™ Endovascular Catheter.

disease as well," Lakhter says. "New medications, too, like PCSK9 inhibitors, a new class of drugs to reduce cholesterol."

There are many cholesterol-lowering drugs on the market, but PCSK9 inhibitors work in a whole new way.

"They enable LDL receptors to bind to more LDL — the bad cholesterol — and clear it from the circulation," says Michael Autieri, PhD, Director of the Lemole Center for Integrated Lymphatics Research at Temple, founded last year with a major gift from Gerald Lemole, MD '62, a well-known heart surgeon, and his wife, Emily Jane (page 48).

Another approach — the goal of many current therapies — is to promote reverse cholesterol transport, to move cholesterol from arterial tissue to the liver for clearance. "The lymphatic system plays an essential role in the reverse cholesterol transport process," Autieri says.

Clots create a public health impact — and medical challenge — of planetary proportion. But we're gaining more traction every day.

UNDAUNTED

To get ahead of clots, we must get ahead of atherosclerosis. Which means getting ahead of diabetes, too, because diabetes fast-tracks atherosclerosis by driving vascular inflammation. Nearly 80 percent of people with diabetes eventually die of clot-related causes.

"Clots, in some form or another, disable and kill thousands of Americans every day," says Eric Choi, MD, FACS, Temple's Chief of Vascular and Endovascular Surgery.

"Also, hundreds of people with vascular disease undergo foot and leg amputations every day. But with revascularization techniques and comprehensive care, we have ways to save nearly all of those limbs," says Choi, co-founding Director of Temple's Limb Salvage Center.

Diabetes. Vascular disease. Obesity. High blood pressure. Deep vein thrombosis. Amputation, stroke, pulmonary embolism, heart attack. It all adds up to a public health impact — and medical challenge — of planetary proportion.

"But look at the big picture," says Tony S. Reed, MD, MBA, CPE, Temple Health's Executive Vice President and Chief Medical Officer. "We have population health programs that reach patients with risk factors for all these conditions.

"We have tools like the EKOS EndoWave Infusion Catheter System®, which uses sound waves to accelerate clot breakdown. We even have tools invented by our own faculty, like the BASHIR™ Endovascular Catheter (page 44).

"We have specialized programs for difficult conditions, like post-thrombotic syndrome (PTS), a long-term complication of deep vein thrombosis that affects about half a million patients a year. There are only a few centers of excellence in the nation for PTS, and Temple is one of them.

"We have imaging techniques that help us differentiate thick, thin, and ruptured caps in plaque — which helps us identify patients who will respond to intravenous thrombolysis versus those who need more aggressive treatment," Reed says.

Robust research programs are also driving clinical advancement. "Our scientists are learning more about thrombosis every day — and our clinical studies mean we can give patients access to emerging tools, techniques, and medications they would otherwise never have," says John Daly, MD '73, FACS, FRCSI (Hon), FRCSG (Hon), Interim Dean and Emeritus Dean of Temple's Lewis Katz School of Medicine.

"It all comes down to patient benefit. To options. To delivering the right treatment to the right patient at the right time — with full consideration for benefits and risks a patient will experience. To multimodal care based on protocols endorsed by the NIH, the CDC, and leading specialty associations for safety, quality, and effectiveness," Daly says.

Lakhter, one of the younger clinicians in the "clot business" at Temple, is motivated, not daunted. "It's a privilege to be part of a distinctive team of professionals delivering complex care to patients with all categories of clot-related disease, both common and rare," he says.

"We cannot save everyone. But every day, patients with serious strokes and STEMI are walking out of here intact, on their own steam. Ditto for patients with pulmonary embolism and other thrombosis-related crises," he says. "How can you not be optimistic? How can you not be?"

To make an appointment with a Temple physician, call 1-800-TEMPLEMED.

COVID-19 AT TEMPLE

Behind the Mask

"When the pandemic infiltrated Philadelphia, Temple University Hospital was hit harder and faster than any other hospital in the region. But we were ready," said Michael Young, MHA, FACHE, President and CEO of Temple Health. The pandemic pushed caregivers everywhere close to their emotional and physical breaking points — but it also inspired them to new heights, unmasking what people and places are really made of. "Temple is a stronger, more agile, more capable organization in its wake," Young said.

By Michael Vitez and Giselle Zayon + *Photography by* ED CUNICELLI


EXIT
stryker

From *Creed 2* to COVID-19

In 2018, the Boyer Pavilion of Temple University Hospital was used as a movie set in the film *Creed 2*. Two years later, it was ground zero in a pandemic.

Gerard Criner, MD '79, FACP, FACCP, head of the Temple Lung Center, had been in frequent contact with his colleagues in Wuhan, China, where the coronavirus pandemic began. Create "two hospitals," they urged: one for COVID-19 patients and one for non-COVID-19 patients. They said this is the best way to protect patients and staff.

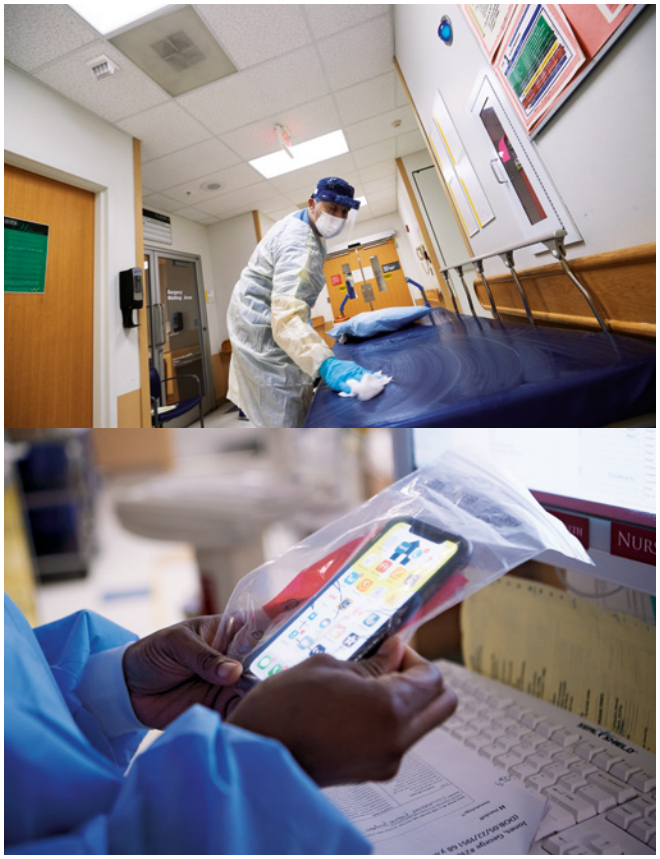
This became Temple's plan of action. Create a massive isolation ward. The *Creed 2* building was ideal because of its separation from other parts of the busy hospital. But since it was never designed for such a purpose, it required a massive overhaul.

Within weeks, an operating room floor became an intensive care unit. Outpatient exam rooms and staff offices were converted into hospital rooms. The expansive lobby where Sylvester Stallone had staged a fight scene was now a hospital ward for COVID-19 patients.

The tsunami that had overwhelmed New York City hospitals was about to hit Philadelphia — and Temple Health was determined to be ready.

"There's an anxiety to an oncoming storm," said Claire Raab, MD, Chief Clinical Officer at Temple University Hospital. "But at least when you're prepared, you know you can handle it."

During the first surge, Temple's 24/7 COVID hotline responded to **65,000+** calls.



Believe

Raab worked with Amy Goldberg, MD, FACS, Chair of Surgery, and Shane McDevitt, Vice President of Facilities, to convert the building.

From February through April, the trio walked the floors, figuring out where to put up walls, remove doors, set up nursing stations, store equipment. They worked day and night, seven days a week.

Can't fit a hospital bed through a doorway? Put a stretcher in. No time to rewire the floor for telemetry? Use baby monitors. No call bells? Give patients flip phones preprogrammed to call the nurse's desk. No bathroom? Get commodes.

"Every single person steps up beyond belief, no questions asked. We make things happen out of the blue. We 'MacGyver' things, that's what we're best at," said Felicia Nemick, RN.

Monitors, air scrubbers, HEPA filters. Code carts, pharmacy carts, radiology equipment. Get them, fast. Everyone pitched in: carpenters, environmental services workers, transporters, security guards, biomedical engineers, infection control specialists, dietary staff.

Every day it seemed Goldberg and Raab would ask McDevitt to do something more extreme.

"Every day I thought, 'No way we can do this.' But out of my mouth was, 'We'll do it.' And when it was done, I thought, 'I can't believe we did this,'" McDevitt said.

Ultimately, the building was readied for 220 inpatients.

"Don't think something can't be done. It can," McDevitt said.

Sobering

"I've worked here 19 years and I've seen a lot," McDevitt added. "But when you see things you've never seen in 19 years, it's sobering."

One day he saw a Temple colleague in one of the COVID ICU beds. "She was my friend. And she died," McDevitt said.

Count Us In

Marissa Pietrolungo, RN, a nurse who normally works in the Cardiac Intensive Care Unit, remembers the day she volunteered to work full-time in the COVID-19 Intensive Care Unit.

"It was March 28. My manager said to me and another nurse, 'I don't know what they're going to do for tomorrow. They need 14 more nurses.' She wasn't asking us to work, but we both said, 'Tell them to put us on the schedule.'"

Foresight

At the peak of the surge, mid-April 2020, staff were burning through more than 12,000 surgical masks, 1,500 N95 masks, and 9,000 isolation gowns per day — five to six times the normal rate.

"Abhi Rastogi, Chief Operating Officer of the hospital, is the supply chain guy. He's like a godsend. Way back in January he was preparing for masks and gowns and gloves. He made it so we always had enough," Goldberg said.


Positive
Chart
784


5 North
5B09

Sprint

Normally, nurses care for one ICU patient, sometimes two. But now, to limit exposure to staff, they are truly *all* in. It was a full sprint, morning to night. Take vitals, give meds, mop the floor, empty trash, deliver food trays and carry them away. On Easter Sunday, Rosie Orr, RN, worked so hard and long she limped to her car after her shift ended.

Hug

Late one afternoon, Pietrolungo had a patient who was dying.

"I was hugging her, gently telling her she was not alone. And I look up and see the patient in the next bed staring at us. She's intubated, so she can't speak, but I know she's thinking 'Is this my fate, too?'"

Pietrolungo wanted to go to her and comfort her, but couldn't.

"I give the first patient some morphine to settle her, make her comfortable. When she's calm, I go over to the second patient and tell her it's okay. Then go to a third patient, whose dialysis alarm is beeping, and take care of her.

"The first patient died an hour later," Pietrolungo said. "But she didn't die alone. We're their family now."

200+
nursing homes in southeastern Pennsylvania were educated and coached by Temple during the first surge.

Spur

"To say that you were educated in a crucible of change would be an understatement," John Daly, MD '73, Interim Dean and Dean Emeritus, told the medical school Class of 2020 at their commencement ceremony, an online event.

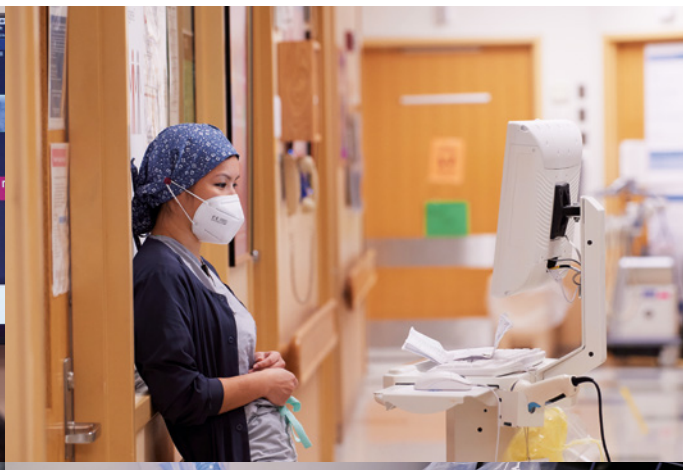
Who knew that Zoom would become a tool as critical as a stethoscope? That modes and methods of medical education and medical research would have to be reinvented practically overnight?

"World-altering events like this pandemic will long be remembered not just for the damage they inflict, but also for the innovations they spur," Daly said.

Rise

In March, the Liacouras Center, Temple University's sports and entertainment arena, was converted into a field hospital, readied to accept patients should Philadelphia's hospitals exceed capacity. Temple medical students helped with the transformation — working with City, military, and various agencies, with speed and high purpose.

"We teach teamwork in medical school," said Larry Kaplan, MD '86, Associate Dean for Interprofessional Education. "but didn't envision our students actually working in a scenario quite like this."

With personal protective equipment in short supply, the risk of infection too enormous, and no time for veteran doctors to teach and instruct in a pandemic, students were not allowed in the hospital. So they found other ways to contribute. Delivered groceries to local families. Started a phone-a-friend program to ease the loneliness of quarantined patients. Did online tutoring for low-income school kids. Made 9,000 masks.

"It's been an amazing opportunity and we're happy to see such impactful results," said Kurt Koehler, a fourth-year medical student involved in the mask project.

Swab

Christopher Goodwin, MD, ABFM, is one of the people you call at Temple when you are an employee and fear you're sick with COVID-19. He's an occupational health physician — tasked with caring for Temple workers yet still maintaining an adequate workforce to keep the hospital running. It's an impossible position to be in.

"Who to quarantine," he said, "who to send back to the beast.

Despite poor baseline health in Temple's service area — one of America's poorest urban communities — Temple's COVID mortality rate was **5.25%**, while New York City's was above **10%**.

The cleaners, nurses, doctors, cooks, pharmacists, therapists. Quarantine, test, wait, hope. So small, so huge, that swab at the back of the nose."

Me

Like everyone else, McDevitt took extra care not to bring the virus home with him. "My work shoes don't come inside. I shower as soon as I get home. I wash my clothes separately."

Raab has four children at home, ages 9, 7, 5, and 1. She worked 15-hour days at Temple — then tried to follow home-schooling instructions. She decided against asking her parents for help, even though they live nearby. "The biggest risk to them would have been me," she said.

Lost

A man had been found in his house, hugging his wife's corpse. She died from COVID-19. Now he was sick, too. He was a teacher. He made his living by talking. "But when I met him, he could barely speak. He lost his place in the world," said Monica Busuioc, MD.


STOP
ROOM 19
6 North
6B19
Facing Prostate Cancer?
EXIT TO LOBBY


EXIT

Low

Asked to describe a low moment, Goldberg responded this way: "You can't have it. You can't. You must see the positive. You must move forward. You must have a plan, the thing you're going to do next. The more patients we got, the more organized we got. We outran it. We did. We outran it."

Vitriol

At first, COVID-19 was described as flu- or pneumonia-like. But it turned out to be more insidious, complex, unpredictable. Some patients experienced mild to moderate symptoms and recovered.

"You can usually look at someone and say with relative predictability that they may or may not make it," said Duwayne Dixon, RN. "But we learned that you can't do that with COVID."

Pronto, Temple stepped into the global scramble to find the best treatment for the virus, taking part in 32 clinical treatment trials.

"In two of them, we enrolled the first patients in the United States. One is a Phase 2 study evaluating intravenous treatment with gimsilumab. The other is a Phase I trial using CPI-006, an immunostimulatory monoclonal antibody," Criner said.

Temple was part of a COVID-19 vaccine trial, too. The only hospital in Pennsylvania selected for the ENSEMBLE trial of an investigational vaccine made by Janssen Pharmaceuticals. "It's an important study because it's the only vaccine designed to work with one dose rather than two, and because the technology used to develop the vaccine candidate has a long safety record in vaccines for other diseases," says Nina Gentile, MD, Associate Chair and Professor of Emergency Medicine.

Divide

Far from being a great equalizer, the virus was quick to exploit patients with underlying health conditions such as hypertension, chronic lung disease, cardiovascular disease, and diabetes. Exactly like the population in Temple's surrounding neighborhoods. "We see up close how this disease really illustrates the social determinants of health — divides right down racial disparity and socioeconomic lines," Goodwin said.

Every day, staff burned through **13,500+** masks and **9,000+** isolation gowns, **5x's** the normal rate.

Groundswell

Pop star Pink donated a half million dollars. Football player Jullian Taylor made a generous gift. R&B icon Patti Labelle sent 3,600 sweet potato pies — to cap off 25,000+ meals donated for hospital staff. Nearly 350,000 donated masks came in. Temple's Pharmacy school made bucketloads of hand sanitizer. Medical students delivered more than 8,000 bags of groceries to local low-income families.

"Whatever challenges Temple faced, we did not face them alone," said Nina Weisbord, Chief Advancement Officer.

People donated more than $3 million to Temple's COVID emergency fund. A groundswell of giving.

Honor

"I had never seen teamwork like this," said Tiffany Denson, RN, a Respiratory Intensive Care Unit nurse who switched her schedule to work in Boyer every shift.

"Someone was constantly checking on you. 'Are you okay?' they'd ask. I was amazed by the ways everyone chipped in and helped out. It was like we formed this bond and felt thankful — honored — to work together."

Yo, Philly

By August 2020, Temple had administered nearly 40,000 COVID tests, cared for more than 1,500 outpatients with milder cases of the disease, and admitted more than 2,000 patients suffering extreme symptoms.

Staff played the *Rocky* theme song whenever a patient recovered and went home.

Every discharge was a victory.

For more information, visit templehealth.org/2019-novel-coronavirus

Slaying Sepsis

It started like upper respiratory illnesses he'd had before: nasal congestion, body aches, a low-grade fever. The otherwise healthy 50-year-old man initially dismissed the symptoms, but went to the emergency room when they intensified. He was diagnosed with the flu on Monday. By Friday, he was dead.

Technically, influenza didn't kill him. It was that the flu led to sepsis, a phenomenon in which an infection — often bacterial, sometimes viral or fungal — triggers an out-of-control immune response that ravages healthy tissues and organs in addition to attacking the infection itself.

While many types of infections that can "turn septic" are preventable, sepsis nevertheless remains the leading cause of death worldwide, killing one out of every five people. That totals 11 million deaths every year, according to a January 2020 study in *The Lancet*. In the U.S., more than 1.7 million adults develop sepsis annually, and 270,000 die as a result — more than opioid overdoses, breast cancer, and prostate cancer combined.

Despite skyrocketing diagnoses, confusion about the disease process, and a dearth of treatments, Temple clinicians and scientists are steadily gaining traction against this formidable threat — reducing mortality rates in Temple's hospitals and uncovering potential new therapies with promise for better outcomes in the future.

"It's exciting. We've created a program that's saving lives — by educating clinicians, leveraging technology, improving communication, and expanding our knowledge base," says Tara White, MSN, RN, CIC, CNL, Temple's Senior Clinical Project Manager. "Because we know how to use all the tools in our toolbox, fewer patients at Temple are dying of sepsis."

By KAREN BROOKS
Illustration by YUKO SHIMIZU

White, a seasoned acute and critical care nurse with a background in infection prevention, joined Temple in late 2018 to manage its sepsis program exclusively. She supports and guides staff caring for patients with potential or actual sepsis diagnoses, spearheads sepsis education, and leads sepsis management protocols. Roles like hers are becoming more common as hospitals recognize the need to get a better handle on the condition.

RAPID RESPONSE

The term "sepsis" dates back more than 2,700 years to the ancient Greek poems of Homer, who used it as a derivative of the verb "sepo," meaning "I rot."

Today, we understand the condition as a systemic, dysregulated, life-threatening response to infection. Inflammation becomes widespread. Blood clots form. Blood vessels leak. Organs become oxygen-deprived. Once septic shock (marked by perilously low blood pressure) commences, the survival rate is 50 percent. Treating sepsis before it reaches this dire stage presents unique challenges for clinicians.

"A patient doesn't walk into the ER with a sign on their forehead announcing, 'I have sepsis,' and there's no test that identifies it," says Richard Martin, MD, Associate Professor of Emergency Medicine. "Presentation can be vague. Patients might not even have a fever. Many common signs — rapid heart rate, shortness of breath, confusion, just feeling terrible — look like other conditions, and we have to differentiate between those and sepsis."

Initial complaints can stem from seemingly benign issues — even a minor cut. "But sepsis can come on abruptly and catastrophically, striking people you would never expect. I remember a 16-year-old who came in feeling sick — and died of overwhelming sepsis that night," Martin says.

Sepsis requires intensive care involving antibiotics (provided the cause is bacterial), fluids, and medications that prevent blood pressure from dropping. Ventilators and dialysis come into play if the condition worsens. Its rapid progression means early detection is essential, and treatment needs to start in the emergency department — where the vast majority of Temple's sepsis patients enter the hospital.

"It's a common misconception that most cases of sepsis start with hospital-acquired infections. Only 15 percent of our sepsis patients develop the condition while in the hospital. The rest come in as emergencies," says Mark Meyers, DNP, MBA, RN, NEA-BC, Associate Vice President for Performance Improvement and Project Management.

Meyers says Temple follows the sepsis treatment protocols of the Centers for Medicare and Medicaid Services, which outline several steps — measuring the patient's serum lactate levels (which rise during infection), obtaining blood cultures, and administering antibiotics on a precise schedule. The guidelines require quick thinking and action by members of a multidisciplinary team beyond frontline clinicians; last year, U.S. hospitals adhered to them on average only 49 percent of the time.

Since the risk of sepsis death increases nearly eight percent with every hour that passes before intervention, Temple's team doesn't want to miss a beat.

SURE SIGNS

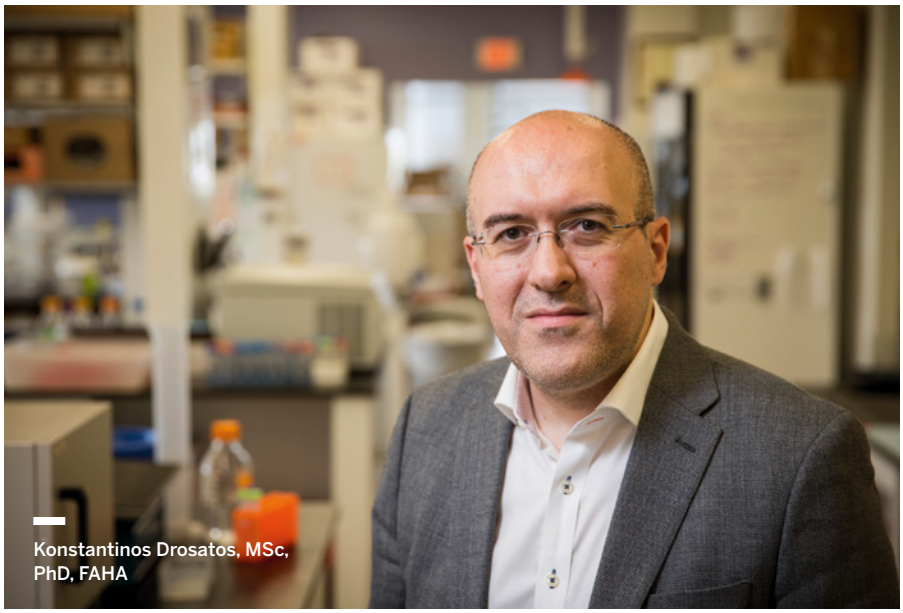
Temple's sepsis mortality ranking is among the best. In 2019, only seven U.S. academic medical centers did better than Temple, according to the rankings agency Vizient.

"Temple's sepsis-slaying work is really paying off," says Tony Reed, MD, Temple Health's Chief Medical Officer. "Since 2018, we've had a significant decrease in sepsis deaths, and there has been a substantial drop in the number of sepsis cases that have developed within hospital walls."

If sepsis is so difficult to identify early on, how is Temple making advances? White and Meyers point to multiple reasons. First, technology has made it easier to detect sepsis. Electronic health record systems — like EPIC, used at Temple — can calculate risk by collecting patients' vital signs and laboratory test results, then issuing an automated warning about patients in danger. But these systems use a "one-size-fits-all" algorithm — and while they provide information about sepsis risk, they don't tell anyone what to do about it.

"Standard predictive models use data from millions of patients, but not all populations are the same. Ours is actually very different from the so-called 'norm,'" Meyers says. "For example, we have a predominantly hypertensive patient population here. So when EPIC fires off a high blood pressure warning — well, most of our patients are already there on any given day. And when blood pressure goes down to what would be considered normal for most populations — for our patients, that would more likely be hypotensive."

To devise an algorithm that better suits Temple patients, White — with programming support from Associate Professor of Emergency Medicine



Konstantinos Drosatos, MSc, PhD, FAHA

JOSEPH V. LABOLITO

Tara White, MSN, RN, CIC, CNL

Wayne Satz, MD — customized a "home-grown" alert system that accounts for chronic problems like the unmedicated hypertension, uncontrolled diabetes, and assorted pulmonary deficits that persist among patients in North Philadelphia.

"We built this system based on known health disparities in the areas we serve. Our model has nuances — lab-based, radiology specific, vital sign specific," White says.

Sepsis alerts go straight to White, who springs into action, checking a patient's records and heading to the bedside to consult with caregivers — to make sure protocols are followed without delay.

White credits the electronic alerts with expediting sepsis detection but believes Temple's sepsis successes are actually more reflective of the excellent knowledge of the staff.

Reed agrees. "Predictive algorithms have an increasingly important role in health care organizations — but only when organizations re-engineer processes and redefine roles in order to act on information. Temple has done that," he says.

White says everyone's learning to identify sepsis, even the most complicated cases. "We're not just teaching everyone to follow algorithms and check boxes — we're creating an army of independent clinicians with considerable know-how, with tools to draw on," she says.

One is a visual cascade, a flowchart that shows exactly what steps to take for management of sepsis, severe sepsis, and septic shock. Depending on where a patient's status falls, the cascade tells the clinical team what to do, and when to do it.

"When there are tough moments, we want to be able to say with certainty to a patient's family, 'we did everything we could, as fast as we could.' We want everyone here to be confident in their ability to treat sepsis in the best way possible," she says.

"We've created a program that's saving lives. Fewer patients at Temple are dying of sepsis," says White.

IMMUNE SYSTEM IN OVERDRIVE

Despite decades of trying, scientists have not developed a medication that targets the hostile immune response and wards off the organ damage that occurs with sepsis.

Because sepsis is not one identifiable organism or "thing," therapies must be multifaceted. In the past decade, more than 150 drugs have shown enough promise in laboratory settings — but all have failed in clinical testing in humans, prompting pharmaceutical companies to give up their quests for new treatments for sepsis.

Researchers at Temple, however, are not deterred. One of them is Laurie Kilpatrick, PhD, Professor of Physiology, Thrombosis Research, and Translational and Clinical Lung Research. She studies how sepsis harms the lungs.

Many sepsis patients develop acute lung injury or respiratory distress syndrome, because during infections, the vascular endothelial system — the barrier controlling the passage of materials in and out of organs — becomes permeable. This means white blood cells and fluid begin to enter the lungs. At this point, patients often require a ventilator.

"Trying to understand why in sepsis the immune system reacts the way it does to an infection, why it goes on to cause this kind of organ damage, is a fascinating challenge. It's hard to design therapeutics to impact the immune system without immunosuppressing a patient," says Kilpatrick, who is President Elect of the Shock Society, a national group focused on improving care for victims of trauma, shock, and sepsis.

According to Kilpatrick, most failed sepsis drugs have targeted single molecules, which is problematic since immune system pathways are redundant — if you thwart one of them, others will still perform the same function. Therefore, she began to zero in on an enzyme called Protein Kinase C-delta (PKCδ) because it represents a "hub" within the immune system — where several pathways join together — becoming activated in response to inflammation or stress.

In laboratory models, Kilpatrick has shown that inhibiting PKCδ helps preserve the integrity of the vascular endothelia, protecting the lungs by keeping white blood cells out.

White blood cells (neutrophils) have a job. They eat harmful bacteria. "But when there is no bacteria to phagocytize, you have 'innocent bystander injury' or 'friendly fire.' Tissue gets very damaged," Kilpatrick explains. "We're trying to corral the neutrophils without knocking them out altogether, because then the patient would die from overwhelming infection."

Kilpatrick has found that inhibiting PKCδ, in conjunction with standard care using antibiotics and fluids, results in septic shock survival rates jumping from 50 percent to 90 percent in the laboratory setting. "I am very pleased," she says. "But will this translate to patients in the hospital?"

She hopes her collaborative work with Mohammad Kiani, PhD, Professor of Mechanical Engineering at Temple, will help answer that question. Kiani is an expert in microfluidics, a field involving tiny, 3D devices that move liquid through miniature microchannels, some measured in submicrons (for comparison, a human hair is about 100 microns thick). Kiani has engineered a novel microfluidic system that Kilpatrick can use in her research.

"He mimicked the microvascular geography on a device that models the structure and function of microvessels. You can see all the bifurcations, the different vessel diameters, and so on. We can actually grow human endothelial cells in the vascular channels," Kilpatrick says.

Known as "organs on a chip," these devices offer unique tools for all kinds of research and provide a way to test therapeutics without relying on animals or humans. Kilpatrick can isolate neutrophils from healthy donors and patients with sepsis, put them in the microfluidics device, and watch how they move through endothelial cells. Then, she can observe whether therapeutics she develops affect that movement.

"This is exciting. We're beginning to have the tools to really look at the vascular endothelial cells and how the immune cells are interacting with them," she says. "We are really positioned to make organ-protective advances here."

> More than 150 drugs for sepsis failed clinical testing, prompting pharmaceutical companies to give up. Temple, however, is not deterred.

BUYING TIME

One might assume anti-inflammatory drugs have not worked against sepsis because they were inadequately designed, but Konstantinos Drosatos, MSc, PhD, FAHA, believes they just don't have enough time to do their job.

"I propose that by stimulating organs' energy production, which shuts down in sepsis, we can buy extra time for anti-inflammatory drugs to work," says Drosatos, Associate Professor of Pharmacology, who also holds appointments in the Centers for Translational Medicine, Metabolic Disease Research, and Alzheimer's Disease Research at Temple.

Drosatos looks at sepsis in relation to cardiovascular complications, which factor into most sepsis deaths. The heart muscle, weakened by systemic inflammation, cannot generate the energy it needs to contract, resulting in insufficient blood flow and oxygen delivery to the body. Drosatos and his team have improved sepsis survival rates in the lab by blocking the activation of enzymes such as cJunN-terminal kinase (JNK) and NADPH oxidase 2 (NOX2) in the heart, thereby returning cardiac energy production to near-normal levels.

"NOX2 drives oxidative stress, creating reactive oxygen species — which target mitochondria, the energy producers in cells. When we modified expression of NOX2, we were able to restore cardiac function within just a few hours," says Drosatos. These findings suggest that NOX2 inhibition could potentially keep a sepsis patient's heart from failing, giving traditional anti-inflammatory treatments time to take effect.

Drosatos and his team have discovered another way to restore energy production in the heart, using LGM2605, a synthetic version of an antioxidant in flaxseeds. A rich source of omega-3 fatty acids, flaxseeds have proved helpful in controlling cholesterol, regulating blood sugar, and fighting several types of cancer. Supporting heart function can now be added to the list. When Drosatos gave LGM2605 to septic mice, the mitochondria in their hearts worked better, cardiac function improved — and when the compound was given in conjunction with antibiotics, mortality rates fell.

Blood pressure control is another clinical aim in sepsis treatment. "When blood pressure becomes uncontrolled, that's it — the end," Drosatos says. But new work raises hope. As detailed in a recent study published online in *JCI Insight*, Drosatos identified that a protein secreted by the heart in various types of cardiac stress drives blood pressure down in sepsis. It's called B-type natriuretic peptide (BNP). And the more BNP, the worse.

Sepsis Rankings

In hospitals, patient death rates are conveyed by what's called a mortality index — a ratio created from two sets of numbers pertaining to a group with a particular illness or condition:

- Observed mortality, or the number of actual patient deaths in the hospital over a given time period.
- Expected mortality, or the number of patient deaths the hospital would have during the same time period if it performed identically to other hospitals for the same population.

Therefore, if a hospital's mortality index is:

- More than 1.0, then more patients died than expected;
- Equal to 1.0, then the hospital's mortality is equal to what is expected; and
- Below 1.0, then fewer patients died than expected.

In 2019, Temple's sepsis mortality index was 0.88. This statistic puts Temple in the top quartile of academic medical centers in the United States for low rates of sepsis mortality, as ranked by Vizient, the leading health care performance improvement rankings agency. The ranking made Temple 8th best out of 160.

Nina Gentile, MD

JOSEPH V. LABOLITO

"But BNP activity can be halted — to stabilize blood pressure and give other medications, such as antibiotics, time to work," Drosatos explains. "This strategy could be used alongside current supportive strategies, which attempt to slow or prevent fluid loss to stabilize blood pressure."

Drosatos is working with Nina Gentile, MD, Associate Chair and Professor of Emergency Medicine, to explore potential clinical applications of BNP inhibition to prevent septic shock. One is a monoclonal antibody that inhibits BNP.

"COVID-19 makes BNP inhibition very timely — because elevated BNP plasma levels are linked with COVID-related sepsis," Drosatos says.

COVID has exacerbated prevalence of sepsis worldwide in two ways. First, of course, the virus itself can spark sepsis by targeting multiple organs and causing systemic inflammation. Second, "The large numbers of people putting off getting medical care out of fear of acquiring COVID-19 means more patients arrive at the hospital very sick with infections that make them prone to sepsis," Gentile says.

In addition, Drosatos and Gentile were just awarded a new NIH grant to study the role of a cardiac stress protein in causing septic hypotension. "We are excited about the opportunity this study might give us to discover novel treatments for one of the most devastating complications of the disease," Drosatos says.

HUB AND SPOKES

"At Temple, scientists reach out to work with clinical teams and vice versa. This is translational research. It doesn't happen everywhere," Gentile says.

Gentile is lead physician for Temple's involvement in SIREN, the NIH's Strategies to Innovate Emergency Care Clinical Trials Network. The network spans institutions across the nation but only has 11 hubs, one of which is Temple. In her role, Gentile heads a regional network of community and academic medical center "spokes" in implementing emergency treatment clinical trials for various conditions, including sepsis.

"SIREN has marked Temple as a leader in acute care trials requiring rapid identification of patients to start on protocols very quickly," she says.

Temple investigators participate in several studies for sepsis patients. One study is called CLOVERS, Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis.

Clinicians on the front lines of sepsis care have deliberated on what works better to increase patients' blood pressure: generous administration of fluids or the use of early vasopressors — medicines that constrict blood vessels. "CLOVERS compares these two methods," says Gentile, who has joined forces with Nathaniel Marchetti, MD, Director of Temple's Respiratory Intensive Care Unit, to evaluate how much oxygen sepsis patients need during ventilation.

"There's evidence showing negative effects of hyperoxia, too much oxygen, so we're looking at tiers of oxygen delivery. We identify patients for the study in the emergency department, consent them, randomize them to a group, and start the study protocol — then Dr. Marchetti and his team take it from there," she says. "We are highly collaborative, and that makes a difference in figuring out the best ways to change outcomes."

BEFORE AND AFTER

Continuing to reduce sepsis mortality requires efforts in both hospital and laboratory settings, but there's work to be done off campus, as well. Tara White's next big push is for prehospital care — what happens to patients before they come through Temple's doors.

Since Temple owns and manages a critical care transport operation (called T3), White has access to EMS providers, flight nurses, and patient transporters — and she's helping them recognize sepsis and initiate treatment en route to the emergency department.

"I also work with City first responders," she says. "Unfortunately, though, nine times out of ten, our penetrating trauma victims — people who have been shot or stabbed — come in via police car, so prehospital care just doesn't happen. That can be challenging, because penetrating trauma can lead to severe sepsis."

That doesn't mean hope is lost for victims of violence who develop sepsis. White recalls a 24-year-old man who had come into Temple's trauma bay with gunshot wounds and ultimately went into septic shock. He was discharged from the hospital after a long stay in the ICU.

"To see him smile and get out of bed, and to get this big bear hug from his mom, who was so grateful — it is a gift to be a part of those moments, and that's what keeps our team going," White says.

"Sepsis is a very complicated puzzle, but everyone on our team knows how to pick up their piece and put it in the right place. That's why we have been as successful as we have."

Karen Brooks is a Philadelphia-based freelancer who specializes in higher education and health care.

By HOWARD ROSS, MD, FACS, FASCRS
Illustration by SOPHIE TOULOUSE

Harry E. Bacon, MD, ScD, FACS, FAPS

HARRY "TED" BACON, MD, SCD, FACS, FAPS, was a world leader in colon and rectal surgery, and an example to me of what can be accomplished by one person — at Temple — where he held the position that I fill today: Chief of Colorectal Surgery.

Dr. Bacon is a descendant, it's said, of Sir Francis Bacon (1561–1626), the statesman, scientist, and philosopher. His father, Augustus Bacon, MD (1868-1929), was a surgeon who was Professor of Operative Surgery at Temple for 22 years.

In the 1920s, when Dr. Ted Bacon went to college and medical school at Temple, his ambition and intellect were already apparent. He was President of the Applegate Obstetrical Society. He was President of the Hickey Physiology Society. He organized school banquets. He edited the school's very first yearbook, the Class of 1925 *Skull*.

For training, he conducted a seven-year world tour with master surgeons at University of Pennsylvania, St. Mark's Hospital (London), the Hospital St. Antoine (Paris), the Polyclinico (Rome), and Allgemeines Krankenhaus (Vienna). All of this predated residencies as we know them today. It also predated the recognition of colorectal surgery (or proctology, as it was initially called) as an official specialty.

After learning all he could, Dr. Bacon returned to the U.S. in 1932 and accepted a faculty position at Temple. In 1938, he was recruited by the University of Pennsylvania — then in 1942, was lured back to Temple again, where he remained Chief of Colon and Rectal Surgery for the remainder of his 50-year career.

BRAZEN

IN 1929, WHEN DR. BACON WAS A "RESIDENT" AT PENN, HE approached the Vice Dean and head of proctology with a plan to create a regional surgical society focused on diseases of the anal canal, rectum, and colon. How many trainees would dare approach the boss with a plan to advance his field?

Brazen or not, Dr. Bacon was focused on the "big" picture. He knew that we could decrease the number of patients requiring stomas, enhance quality of life for patients, and improve outcomes in many areas of colon and rectal disease. He believed in standardizing screening to detect colorectal cancer early. He believed in documenting findings, assessing results, and developing critical pathways for the care of patients with colorectal disease.

Like his ancestor Sir Francis, Ted Bacon was an empiricist. Temple had been teaching colorectal surgery since 1906. But only about 30 of the nation's medical schools were teaching it in 1929 — and that had to change. Dr. Bacon knew that the nation needed more and better teaching programs. He didn't have all the answers personally, but he knew that if colorectal surgeons came together, they could re-engineer pretty much everything, through clinical conferences, educational programs, teaching, publishing, research, and goal-setting.

Thanks to Dr. Bacon, the Philadelphia Proctologic Society was born in 1932. And based on its success, 18 other regional societies followed. And he didn't stop there. He went on to become a principal organizer of other major organizations, including the American Board of Colon and Rectal Surgery — which helped to make colorectal surgery an official specialty, complete with board-certification requirements.

At one time or another, Dr. Bacon was president of all the major colorectal surgical societies. He wrote 15 textbooks, 21 chapters in other texts, and nearly 350 articles. He earned honorary membership in the Royal Society of Medicine, held 11 honorary degrees and 69 honorary surgical fellowships, was granted audiences with three popes, and was decorated by the governments of eight countries. In 1957, he became founding and longtime editor of *Diseases of the Colon and Rectum* — still the leading international journal in the field.

Ted Bacon, MD, as pictured in the 1925 medical school yearbook. In addition to making charming pen-and-ink drawings like those at right, he wrote music (and lyrics), and earned a PhD in literature, publishing three volumes of poetry.

THE BOSS

IN THE SURGICAL WORLD, DR. Bacon is known for perfecting an operation called the "Bacon pull-through," a procedure he developed in 1939 with W. Wayne Babcock, MD, Chair of Surgery at Temple.

This operation — which Dr. Bacon traveled the world to teach — prevented patients from having to live with stomas, surgically created openings in the abdomen, to expel waste. By the 1970s, the pull-through operation was the gold standard.

Indru Khubchandani, MD, MS, FRCS, FASCRS, FACS ("Dr. K"), was

a fellow of Dr. Bacon's from 1962 to 1965, one of more than 80 surgeons he trained personally.

"We called him 'the Boss,'" Dr. K says. "Everyone did. Except his son, who called him 'Dr. Bacon.' In addition to the pull-through operation, Dr. Bacon created a 'pouch surgery' for patients with ulcerative colitis. It was the number one surgery for this condition in the world."

According to Dr. K, the Boss wore sunglasses, extravagant suits, and two-toned shoes. He had a chauffeur-driven Cadillac. He was invited to all the best parties. Patients flew in from faraway countries just to see him.

"He treated presidents, premiers, and movie stars. He was a movie star himself," Dr. K says. The American College of Colon and Rectal Surgeons named a major lecture in his honor: The Harry E. Bacon Oration. It's delivered at the national congress every year — and Dr. K was the Bacon Orator in 1988. He was also the longtime Director General of an organization Dr. Bacon helped create, the International Society of University Colon and Rectal Surgeons.

Howard Ross, MD, with a portrait of Dr. Bacon over this right shoulder.

« HIGH IDEALS »

MUCH HAS CHANGED SINCE DR. BACON'S DEATH IN 1981.

Minimally invasive surgery to treat many colon and rectal diseases, performed with laparoscopic or robotic equipment, is now routine. We know many things about colorectal disease that were total mysteries in Dr. Bacon's day. Especially cancer. We have identified distinct phenotypes and the major genes involved. We can better predict treatment responses. We have immunotherapies and other new treatments. All of it would delight Dr. Bacon.

When he was young, he idealized medicine's potential. "In a world torn with uncertainties, conflicting ideologies and confusion, the medical profession will serve as a stabilizing influence . . . establishing good will and promoting understanding among all the peoples of the world," he said in a 1950 article in the *American Journal of Surgery*.

By the time Dr. K met him, Dr. Bacon had given up on obtaining world peace through medicine, but his demands on fellows and residents made his goals abundantly clear: optimize cure rates while maintaining optimal quality of life for patients.

"The Boss cared deeply about the impact of surgery and treatment on patients in terms of digestive, sexual, and urologic function," Dr. K says. That's what everything came down to. Doing the best for the patient. Yet Dr. K recalls that on post-op rounds with residents and fellows, the Boss was so preoccupied with so many things that sometimes he forgot patients' names or the details of their cases. He was good at hiding it. But Dr. K knew what was going on.

> "Everyone called him 'the Boss.' Except his son, who called him 'Dr. Bacon.'"

Was the Boss embarrassed? Was he indicting himself in the piece he contributed to the *Journal of the American Medical Association* in 1963 called "Science is Not Enough"?

"It is shocking to hear a physician speak of the hemorrhage in bed 10 or the rectal cancer on Ward B," Dr. Bacon wrote. "In this impersonalization lies the seed of loss of compassion and empathy for the infirm."

Was the Boss lecturing everyone? Yes, himself included. "Let us not permit compassion and humanity to be brushed aside by the frenzied pace of our time," he went on. Dr. Bacon's prescription? It was time to look at oneself. "Reflect on the full meaning of the inscription on a temple of the Greeks: 'Know thyself.' If we have lessened our insight into ourselves, it is sure to be reflected in an equally diminished insight into the patient," he continued.

As Dr. K says, the Boss was not perfect — and he knew it. Which is one tiny reason he was so perfectly amazing.

Every specialty has its rock stars. Sir William Arbuthnot Lane (1856-1943) might be the headliner in colorectal surgery. But take a closer look: Ted Bacon's name is also on the marquee.

About the Author: *An internationally recognized surgical educator, Howard Ross, MD, FACS, FASCRS, is Professor and Chief of the Division of Colon and Rectal Surgery at Temple, where he serves as Program Director of the General Surgery Residency, Professor of Clinical Surgery, Surgical Director of the Digestive Disease Center, and Vice Chair for Clinical Affairs. He is President of the Pennsylvania Society of Colon and Rectal Surgeons.*

JOSEPH V. LABOLITO

Stories of the Human Side of Medicine

"ALONG WITH THE HEALER'S TOUCH, stories are at the core of a patient's relationship with caregivers," says Michael Vitez, Pulitzer Prize-winning author and Director of Temple University's Narrative Medicine Program. "Stories like these, written by faculty, students, and staff at Temple Health, have the power to heal, inspire, build relationships, and change the world," Vitez says.

Post-Op Weight Chart

For years I have told all my friends that my dad was pretty much Liam Neeson from the movie *Taken*. It's about a girl who travels to Europe with her friends and is kidnapped. Her father does *everything* to get his baby girl home safe. That was my dad.

He would do anything for me. He would send me "Good morning, bunny honey, Daddy loves you!" texts every morning and call me every night just to hear what I learned that day in med school. He'd cry at birthday and Father's Day cards.

He didn't ask for help because he didn't believe he needed it. On the rarest occasion that he did ask, if you hesitated an instant, he'd get angry. I think that's because it was just so hard for him to ask.

And then my dad was diagnosed with esophageal cancer. Prior to his diagnosis, he'd lost over 60 pounds. He couldn't swallow due to the obstruction in his esophagus. After he was diagnosed, he needed to go through chemo and radiation, which could lead to more weight loss, so his doctors gave him a feeding tube.

On top of chemo and radiation each day, every week brought on more feeding tube issues and new infections. Despite all of these difficulties, he never let anyone know how much he was suffering.

My dad had esophageal resection surgery on January 21, 2019. He was released from the hospital on January 28. He died on February 4, just two weeks after the surgery.

Here's the thing. His death was totally unnecessary.

My parents had been divorced since I was three, but my mom helped him more than anyone else. But with all of us living separately, my mom and I didn't know that the nurses were only coming every third day.

I was studying for an exam. And I wasn't checking on him like I should have.

The last time I saw my dad, he was walking towards me, proud that he was on his fourth lap around the step-down unit, smiling and joking with the nurses that he was starting bids to be the next "Bachelor."

He sent me a text after he was released: "Good morning, bunny honey. This exam? Chew it up raw and spit it out. You're the best! I love you! XOXO."

After the test, the night of the Super Bowl, the night before he died, I texted him. My dad was a huge sports fan, and his text back was just two words, "Was asleep." I should have known.

The next day, worried that we hadn't heard from him, my mom went to check in and found him on the floor, clearly having suffered from excessive fluid and blood loss. It was horrible. There was blood and diarrhea everywhere.

At first, I couldn't react like a daughter, only as a medical student. It was way too painful otherwise. When he died, I had to think of him as if he were a patient vignette: "A 63 y/o male diagnosed with esophageal cancer presents to the clinic with complaints of pain in his abdomen around his J-tube and severe diarrhea and bleeding." Okay, so, severe fluid loss . . . that can lead to decreased cardiac output, hypotension, hypovolemic shock, and death.

It wasn't until a few weeks later that I built up the courage to look through my dad's phone. His last note was titled "Post-Operation Weight Chart." From his release on January 28 up until February 4, he'd logged his weight, every day.

In five days, he'd lost 7 pounds, down to 115 pounds.

After his surgery, he gained back some of the weight he had previously lost. He was so proud of himself. But, as it turns out, the feeding directions he was given were not correct — and he quickly lost weight again. He didn't complain. Nobody noticed.

How could he have not known something was wrong? Why didn't he have the right feeding? Why didn't he have a nurse coming more often? Why didn't he call me or my mom or 911?

He must've been scared. I would've been. But it was always just too hard for him to ask for help.

It's hard to admit that I'm angry at my dad, but it's true. How did he let himself get to this point? Why didn't he just ask for help? I'm also angry at his medical team. They must not have really known my dad. If they had, they wouldn't have let him push them away. They would have known he was too proud to ask for help.

Illustrations by LEONOR GARCIA DEL VALLE

But I'm also mad at myself. I should've done more. Why didn't I force him to go to the doctor months beforehand?

I don't have all the answers, and that's okay. But I do know that I want to make sure that no one else's daughter has to ask the questions that I'm asking now.

Sharing this now helps me deal with my own grief. But I also hope sharing this with all of you, my peers and colleagues, can help us learn to become better doctors, nurses, and family members. We can perform the fanciest procedures and provide the best medications, but that's not enough. Medicine is as much an art as it is a science. It's not just about a patient's creatinine or glucose levels, it's also about truly understanding your patients.

I want truly to know my patients and ask myself — can I do more to help them? I also want my patients to feel comfortable asking me for help. As doctors, we have to connect with patients, care for them and follow up with them. And if our patients aren't going to advocate for themselves, we must advocate for them.

So as I continue to study microbiology, cardiopulmonology, and the science of medicine, I'm also going to learn the art of medicine. I'll continue to grieve about my dad's death, but I hope I can learn from it, too, and become a better physician because of him.

— RACHAEL SMITH
MD Candidate, 2022

The Whitest White Coat

I keep my white coat white. I'm talking Mr. Clean white. Sensodyne White. White-on-rice white. New Balance sneakers on a middle-aged suburban dad white. In fact, some classmates make fun of me for getting my white coat dry-cleaned, but what can I say? It's my favorite piece of clothing.

Every time we put on that Temple white coat, we are ready to learn, we are ready to teach, we are ready to make a difference. But we are also ready to make mistakes. And that's okay. This year we are likely to be the most inexperienced members of the health care team. And just as these last two years have flown by, so too will the next two. Regardless of the impending challenges, we are ready for what's next.

While I doubt I will be able to maintain my coat's bleached-white color, there is also pride in wearing an "aged" white coat. Every stain, every scuff, and every accidental pen mark will forever be linked to a memory. After all, a white coat is not meant to spend its life hanging in a locker.

This coat will travel with me. And no matter how worn it gets, one thing will never change: this will always be my first white coat. And regardless of how "un-white" it may get, it will always be my favorite.

— AZAM HUSAIN
MD Candidate, 2021

What Does it Mean to be a Good Doctor

A few years ago, I shadowed a neurologist at a hospital near my family home in Connecticut. It was a relatively slow day for the doctor, full of chart reviews and sifting through brain images for abnormalities. As she went about her paperwork, she shared her insights with me, especially when something "exciting" popped up.

I learned what an ischemic stroke looked like on a CT scan. I saw what electronic health records looked like across an assortment of patients and health statuses, annotated by various health care providers. I read what doctors considered to be objective truths about their patients, data points and test results. I read the things that mattered to insurance companies and provided the doctors their paychecks. I saw a complicated system of documentation that put the medical record and provider reimbursement at the heart of "patient-centered" care.

And as I read phrases like "patient insists [x]" or "seems convinced of [y]" or "comes in frequently, seeking attention," it was as if a person's own lived experience was not trustworthy enough for science — or at least not relevant within our fee-for-service model. There is no place for a patient to be the first author in their own story, a role reserved for the educated, objective clinician.

When no data exist to explain particular illnesses — when science has no answers for patients — they are judged, labeled attention-seekers. When time is money, it's easier to view the patient as hypochondriacal, noncompliant, or attention-seeking. While looking through the charts that day, I could almost hear the authors scoff in judgment.

One might be inclined to believe that electronic health records bring more benefit than harm to health care. But, in reality, it means patients get significantly less time with doctors and feel more neglected. It means people are living longer but with more chronic conditions. It means patient-centered care is being swapped for patient-centered charts. Little wonder that a 2018 Physicians Foundation survey found that six out of every 10 doctors surveyed were either very or somewhat pessimistic about the future of the medical profession.

Fortunately, however, some physicians, like the neurologist I was shadowing, take time to know their patients. Because it can be difficult to mentally construct patients' lives and narratives from the medical lingo of their charts, the doctor filled in the gaps for me that day. She gave life and meaning to abridged notes and apathetic paperwork. She told me about a young man who was likely taking his last breaths following a combined alcohol/cocaine/narcotics overdose. And while I was there, she was called to the ICU to examine him for the nth time in as many days.

On the elevator ride up, she told me he was an Ivy League college student who had been doing careless college student things. Her disappointment was laced with a hint of sadness. It was humbling to see — especially since I didn't know what I was walking into that day. I wondered what it meant to be an overdose patient in a culture rife with overmedicating, over-testing, and over-charting — none of which offers an iota of compassion to a patient on the verge of death or a family nearing an irreplaceable loss.

She led me to her patient's room in the ICU. He was no more than a year or two older than I was at the time. As I watched the ventilator help his limp body inhale and then exhale, I imagined he might have had a bright future ahead. I wondered about the college party that allegedly landed him in this place. I wondered if he had been addicted or could've been helped. I wondered who he would be leaving behind. I said a silent prayer for him as the doctor examined him, again confirming a poor prognosis.

Quick footsteps approached. The doctor stepped into the hall to greet her patient's mother. It became clear that his mother was just as much in need of the doctor's warmth and care as he was. And the neurologist recognized it. I listened as the doctor relayed a difficult prognosis. I watched the mother clutch her prayer beads so tightly her knuckles turned white. "I know he'll be okay," the mother argued. She had seen him move. I remembered learning that overdose-related comas can result in elevated levels of motor activity due to the drugs' effects on the brain stem. Contrary to what a hopeful mother might believe, this was not a reflection of consciousness or active motor reflexes.

The doctor delivered her opinion with patience and kindness. She was present for the mother. She understood that the young man was someone with a family, a life worth living. She saw a grieving mother who would soon have to make peace with this tragedy. Observing their interaction, I could see that most of the medical information the doctor shared flew past the woman's ears. She knew what she had seen; she fully believed that her son was on the cusp of waking up. But the neurologist knew the damage was done.

That day, I saw that the language of evidence-based medicine cannot console human beings facing loss. That the objective medical gaze or microscopic view of the body cannot provide comfort or reassurance. That the empathy we are taught to show patient-actors in our clinical skills courses cannot build trust between real doctors and real patients. A scripted "Oh, I'm sorry to hear that" only goes so far.

In the end, it's about the impulse of being human, the vulnerability of being ill, and the process of healing, all of which we share in but often forget in the process of becoming "professionals."

But that day, I saw what it meant to look beyond a patient's chart and to deviate from the script of a medical school doctoring course. I saw a young man with his own story; a mother in sorrow, no less a patient in that moment; and a doctor with oodles of knowledge standing quietly in solidarity with her. The neurologist reached her hand out and the mother graciously accepted the comfort, genuine and uncontrived. That, to me, is patient-centered care. I'd be curious to see how an electronic health record or insurance company might capture it for reimbursement.

— KOMAL GULATI
MD/MA Candidate, 2023

Editor's Note: *A version of this essay was published in* Scientific American *on March 27, 2020.*

Wear, Tear, and Repair

"A condition called telegraphists' cramp, which affected the hand muscles required to operate a Morse code machine, was prevalent in the early 1900s. It was one of the first documented repetitive strain injuries," says **Mary F. Barbe, PhD, Professor of Anatomy and Cell Biology** at Temple.

Caused by repeated motion that damages tissues of the musculoskeletal and nervous systems, repetitive strain injuries (RSIs) spark persistent pain — usually in the neck, shoulders, forearms, wrists, and hands. "They can be debilitating," Barbe says.

RSIs are common among athletes. Computer and smartphone overuse can cause them, too. But Barbe studies "higher-load, higher-force tasks. Think construction workers, nurses moving patients, or hotel staff lifting mattresses and ending up with elbow tendinitis or a rotator cuff problem," she says.

High-force, high-repetition movements create microinjuries in muscle fibers. Muscle tissue responds by making small repairs. But over time, with repetition of the activity causing the injury, muscle tissue becomes replaced with connective tissue — weakening muscles and putting pressure on nerves, causing inflammation and pain. "With nerve injury, you develop hypersensitivity to normally innocuous stimuli," Barbe says.

"A lot of treatments fail. Rest doesn't work for everyone. Physical therapy doesn't work for everyone," says Barbe, who also holds an appointment as Professor in the Department of Physical Therapy. "Even surgery fails, because you can't just go in and pick out all the fibrosis."

RSIs have long been thought to be irreversible, but Barbe's research shows, for the first time, that it may be possible to undo the damage caused by fibrosis and restore muscle strength — offering hope for people who have been unable to work due to overuse injury.

The findings, published online in 2019 in *The FASEB Journal*, detail the results she's achieved in preventing and reversing RSI-related fibrosis with a drug called pamrevlumab, a compound recently approved by the U.S. Food and Drug Administration for the treatment of Duchenne muscular dystrophy. Barbe and colleagues, including Steven Popoff, PhD, the John Franklin Huber Chair and Professor of Anatomy and Cell Biology, found that the drug can halt — even reverse — the scarring process. Pamrevlumab is an antibody that inhibits connective tissue growth factor, a protein that contributes to fibrotic disease progression.

Pamrevlumab for RSI is a novel application. "It's being fast-tracked by the FDA for patients with idiopathic pulmonary fibrosis and kidney fibrosis — but would also be a good drug for people with overuse injury whose other treatments are not working. If we can reverse muscle fibrosis, workers could eventually return to their jobs," Barbe says.

Last year, in the *Journal of Orthopedic Research*, Barbe reported that pamrevlumab also relieved the irritative, compressive effects of carpal tunnel syndrome, a common RSI associated with weakness and functional decline.

She's also found that manual therapy — techniques including massage, stretching, and chiropractic intervention — is helpful. It breaks down fibrotic tissue, promoting repair and recovery. "Bodies are amazing things — sometimes we just need to help them along," she says.

Barbe has authored many book chapters and has won numerous teaching and research honors, including the 2018 research prize of the International Society for the Study of the Lumbar Spine — recognizing her collaboration with David Klyne, PhD, and Paul Hodges, PhD (University of Queensland, Australia), for findings regarding contributors to low back pain.

Barbe also collaborates with Michael Ruggieri, PhD, Professor of Anatomy and Cell Biology at Temple, to develop techniques to reinnervate the bladder and urethral sphincters. "Functional reinnervation of the bladder is possible — and would be a great boon to patients who've suffered spinal root injury," she says.

Barbe's research has been supported by the National Institutes of Health for 18 years. A native of Virginia and North Carolina, she is a fellow of the American Association of Anatomists and the American Society for Bone and Mineral Research — and is currently Vice President of Advances in Mineral Metabolism, an international association.

Photograph by CARDONI

Mary F. Barbe, PhD

Oneida Arosarena, MD, FACS

ASSOCIATE DEAN, DIVERSITY AND INCLUSION

Q & A

Diversity is part of accreditation criteria for medical schools, correct?

Yes. In 2009, the Liaison Committee on Medical Education (LCME) toughened diversity requirements for accreditation, mandating that medical schools enact "policies and practices ensuring the gender, racial, cultural, and economic diversity of its students." The LCME has called for schools to diversify faculty as well.

Q: *Latinx and African Americans make up 31 percent of the U.S. population — but only 10 percent of its doctors. That said, if physicians are fair-minded and clinically excellent, does their race really matter?*
A: Let's look at things from the patient perspective. When patients receive care from physicians of their own cultural background, communication is enhanced and patients do better.

At medical schools, diverse teams are best able to flex, pivot, and adapt as they teach future generations of physicians to care for a wide spectrum of patients.

The Institute of Medicine endorses diversity in the medical profession as a strategy to improve public health. Cultural competence is a gateway to clinical competence.

Q: *Temple and other groups you work with, such as the Association of American Medical Colleges, endorse implicit bias training. What is implicit bias?*
A: Implicit bias is bias that we don't realize we have. And we all have it. It's part of the human legacy, based on the "norms" we grow up with in our families and communities.

Many organizations, including medical schools like Temple, conduct implicit bias training to help students and faculty identify bias that might negatively impact patients, families, and colleagues. The trainings can be a real eye-opener.

Q: *Systemic bias is bias that's baked into a system or process. Is that implicit, too?*
A: Absolutely. For example, imagine you're a faculty recruiter. You approach the process in a traditional way: getting leads on candidates from chairs at your school, advertising in major medical publications. While your school encourages minority applicants, rarely do any apply. Then someone suggests you advertise in publications read by minority physicians — and try asking faculty of color in your school if they have any candidates to recommend. When you do these things, you get wonderful minority applicants. Implicitly, systemically, the prior approach had been biased toward traditional applicants and away from minority applicants. You just didn't realize it.

Q: *What barriers do minority faculty encounter?*
A: They tend to feel isolated, not truly part of the larger academic community. They tend to experience more pressure to "prove" themselves by serving on committees, mentoring minority students, and other things that do not "count" among the criteria for being promoted. Minority faculty report lower career satisfaction, and leave academia sooner than other faculty. So recruiting is just for openers. If you want people to stay, you must make them feel welcome and wanted.

Q: *What can schools do to improve faculty diversity?*
A: Efforts to enhance faculty diversity require long-term commitment. For starters, we must get more people of color into the medical profession. Which means working with children. And if you have people of color on your faculty, you need to *keep* them by limiting obligations that do not contribute to promotion; supporting protected research time; setting clear goals; developing mentoring programs for junior faculty; and improving networking and leadership opportunities. You need strong institutional support — not just dollars, but advocacy from faculty leaders, support that affects the climate of the institution. It's not just about who gets a seat at the table, but whose voice is heard.

Q: *You are a highly respected head and neck surgeon. You do NIH-supported research. You teach. You've traveled the world on surgical missions. What means most to you?*
A: Seeing opportunity where once there were obstacles — and openness in minds and hearts once closed.

Photograph by PETER FREED

Oneida Arosarena, MD, FACS

A New Twist

The BASHIR™ Endovascular Catheter

Blood clots threaten the health and lives of 900,000 Americans every year. As detailed in the story on page 12, there are several ways to treat these circulation-blocking culprits. One rapidly evolving modality is catheter-directed therapy (CDT).

"The idea behind CDT is to get clot-dissolving medication right into the blood clot," says Riyaz Bashir, MD, FACC, RVT, Director of Vascular and Endovascular Medicine at Temple.

Conventional CDT usually works for clots in smaller blood vessels.

But for clots as big as carrots, its abilities are limited. "When clots completely obstruct the circulation, medications in the blood can only reach the small area of the clot exposed to blood flow. The interior of the clot remains impervious," Bashir explains.

Clot-dissolving medication can only reach the part of a clot exposed to blood. Hence Bashir's inspiration: to design a catheter that fissures the clot, getting blood to flow in, along with medication.

Hence his inspiration: to design a catheter that carves channels within a clot — increasing that exposed surface area.

"The other goal with this device is to get the blood to flow into the clot along with the natural clot-dissolving chemicals in the patient's own blood," explains Bashir, inventor of the BASHIR™ Endovascular Catheter (BEC) .

The BEC's magic is its expandable spiral-shaped "basket," composed of six hollow filaments that do two jobs. First, they work like scalpels, fissuring the clot. Next, they work as catheters, infusing clot-dissolving medication through 48 tiny laser-drilled holes.

Bashir had a punch list for designing the device: It must be easy to use. It must involve minimal procedural risk. It must reduce the amount of clot-dissolving medications needed (thus likewise decreasing the associated risks, like brain bleeds). It must also shorten patient length of stay, and with it, health care costs.

The BEC checks all these boxes. Bashir designed it in 2015 with help from an experienced engineer, Nicholas Green. Then Temple University and other investors founded a company called Thrombolex, Inc., to manufacture the BEC and other catheters designed by Bashir and team.

In an FDA-approved early feasibility study, the BEC was shown to be safe and highly effective for treating acute clots in the lungs. In this small study, the outcomes were significantly better than those of standard CDT and/or mechanical approaches to clot removal.

"Right now, an FDA-approved NIH-funded pivotal study called the RESCUE trial is underway. Twenty medical centers across the U.S. are evaluating the BEC for patients with large blood clots in the lungs," Bashir explains.

The BEC has even been used with success in COVID-19 patients.

THE BEC: HOW IT WORKS

After the patient is sedated, the physician inserts the BEC into the blood vessel where the clot is located using X-ray guidance over a wire. When its tip is in proper position within the clot, the physician expands the basket by sliding the red lever on the hand-held control. The basket is 2.3 mm wide when closed and can be expanded up to 45 mm.

As the basket opens, its six filaments twist and expand, creating spiral fissures in the clot, restoring blood flow. The filaments of the basket are nickel-titanium reinforced nylon tubes with 48 laser-drilled holes that deliver medication, which can be pulse-sprayed or infused at precisely controlled rates.

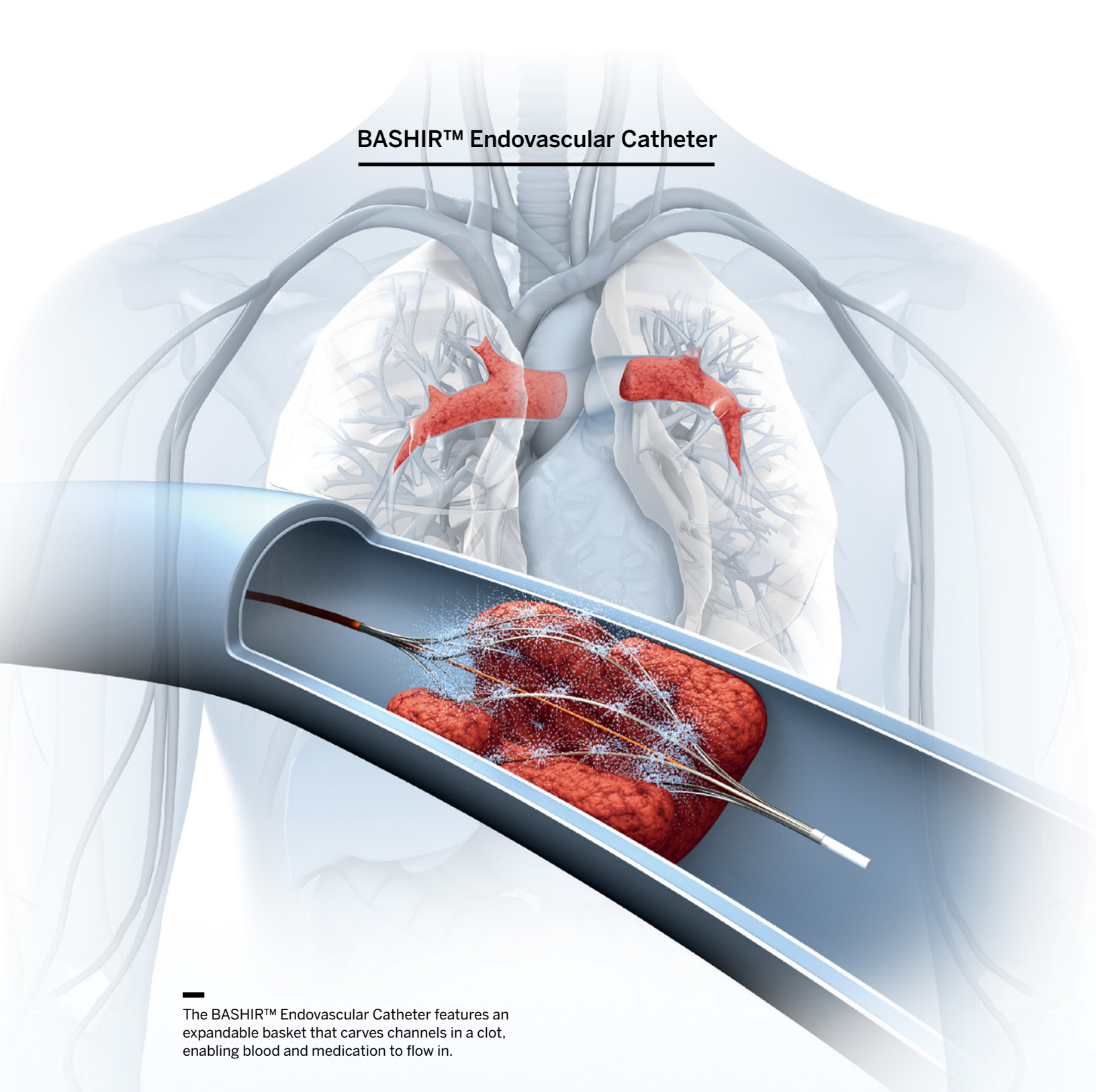
When the clot has dissolved and it's time to remove the catheter, the physician returns the basket to the closed position using the red lever on the hand-held control.

OTHER UNIQUE CATHETERS

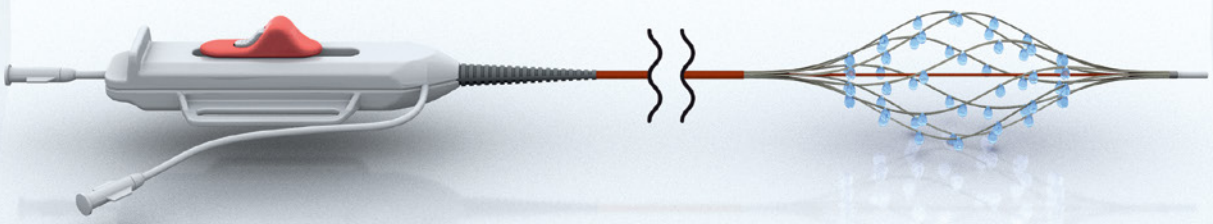
In addition to the BEC, the team has designed six other catheters for specialized functions: The BASHIR™ Endovascular Catheter NX, which creates one channel in a clot; the BASHIR™ Endovascular Catheter SB (Short Basket); and the BASHIR™ Plus Endovascular Catheter line, a series of catheters with two infusion pathways, one in the basket and one in the shaft. These come in four sizes: The BASHIR™ +10 (cm); +20; +30; and +40. All are easy-to-use tools that can be used quickly and safely in veins and arteries in the limbs, torso, and lungs.

Illustration by BRYAN CHRISTIE

BASHIR™ Endovascular Catheter



The BASHIR™ Endovascular Catheter features an expandable basket that carves channels in a clot, enabling blood and medication to flow in.



Titan of Medicine

Sol Sherry, MD, MACP (1916-1993)

After school and on weekends in the **1920s**, young Sol Sherry worked in his parents' New York grocery store, totaling customers' purchases in his head. He loved math problems and puzzles, the tougher the better. He certainly picked a challenging career: thrombosis. The field was practically a blank slate when he was introduced to it in the **1940s** — but that's probably what captivated him about it in the first place. Sherry devoted 50 years to developing it to the point of "a clinical payoff," he said, "so I could feel that my life has been fulfilled."

AGAINST THE ODDS

"Thrombosis is a clinical cosmos in its own right, and Sol Sherry deserves credit for making it so. He's the father of thrombolytic therapy," says A. Koneti Rao, MD, FACP, FHAA, the Sol Sherry Professor of Medicine and Co-Director of the Sol Sherry Thrombosis Research Center at Temple.

Sherry — who spent the last 20 years of his remarkable career at Temple (and recruited Rao) — basically created the life-saving field of clot-busting via the therapeutic use of enzymes. "His insights were amazing," says Rao. "He recognized early on that thrombosis was a primary cause of myocardial infarction — not a secondary or incidental aspect thereof."

In the **1950s** Sherry proposed that most heart attacks are caused by a blood clot in an artery. Few experts believed it until it was definitively proven in **1980**.

"Dr. Sherry had been right all along — that blood clots in heart vessels caused 90 percent of heart attacks. He reported on streptokinase for acute myocardial infarction at least 25 years before it became an established therapy," says Ronald Rubin, MD '72, Emeritus Professor of Hematology at Temple.

Sherry drove the development of a new approach to clotting-related pathologies — revolutionizing treatment not just for myocardial infarction but also for pulmonary embolism and deep vein thrombosis, common pathologies all over the world.

> "Everything he embraced turned to gold. Institutions prosper for years on the energy of great leaders like Sol Sherry," says Rubin.

FIRSTS

Sherry met his love/nemesis in **1946** when he got his first job, with William Tillett, MD, at New York University. About 12 years earlier, Tillett had discovered that beta-hemolytic streptococcal organisms — the bacteria that cause strep throat — can induce a proteolytic reaction that breaks down blood clots (*J. Exp. Med*, 1933). This "reaction" came to be known as streptokinase. Foreseeing its immense possibilities, Sherry was sold. He had to study the fibrinolytic system in human blood and the action of lysing enzymes.

In **1949**, he and Tillett became the first to use streptokinase to dissolve fibrinous collections of fluid in patients' lungs. "Back then, streptokinase was used in tissue spaces. It was too impure to be administered intravenously," Rao says, "but Sherry helped change that."

In the early **1950s**, at the University of Cincinnati, Sherry and Walter Troll, MD, became the first to use synthetic substrates and plasminogen activators to dissolve clots intravascularly. Then in **1954**, when Sherry was Chair of Medicine at Washington University, he became the first to use urokinase to treat pulmonary embolism and venous thrombosis. After that, things really picked up speed. In **1967**, Sherry led the famous Urokinase and Urokinase-Streptokinase Pulmonary Embolism Trials, funded by the National Institutes of Health.

"This study was a game-changer," Rao says. But what was truly amazing is that Sherry was hugely influential in making federal funding available for that study in the first place. He'd been leading a campaign at the highest echelons of medicine to draw attention to clotting pathology and the need to intervene. In **1965**, as part of this effort, Sherry persuaded the National Academy of Sciences to create

1954 IMAGE: COURTESY LILLIAN AND CLARENCE DE LA CHAPELLE MEDICAL ARCHIVES, NYU;
1990 IMAGE: TEMPLE UNIVERSITY LIBRARIES SPECIAL COLLECTIONS RESEARCH CENTER

a task force on thrombosis. It did, and named Sherry chair. In **1971** (while at Temple), he founded the American Heart Association Council on Thrombosis. He also became a founding organizer and Chair of the International Society of Thrombosis and Hemostasis.

"These organizations played a critical role in making the medical world aware of the enormous public health impact of thrombosis, in rallying for study and funding," says Rao.

"That was Dr. Sherry's genius in a nutshell — seeing the global picture and the molecular details — with clarity to change the world," Rubin says.

THE TEMPLE YEARS

Sherry was recruited to Temple in **1968** to chair the Department of Medicine. "He did so much for medicine and for Temple during his 20 years here — including making Temple's Internal Medicine residency one of the best in the country," Rubin says.

In **1970**, Sherry founded Temple's center for thrombosis research — one of the first to receive NIH funding as a Specialized Center of Research (SCOR) in thrombosis. He appointed and recruited outstanding researchers and faculty, including Alfred Bove, MD, PhD; Andrei Budzynski, MD, PhD; Robert Colman, MD; H. James Day, MD; Robert Fisher, MD; Holm Holmsen, PhD; Bennett Lorber, MD; Leon Malmud, MD; Victor Marder, MD; Stefan Niewiarowksy, MD, PhD; Gwendolyn Stuart, PhD; Peter Walsh, MD, PhD — and many more.

"He wasn't just the father of thrombolytic therapy; he was *our* father, and we revered him," says Rubin. "He was an astute judge of character. He could see what we were good at — and not so good at — and directed each of us accordingly. Respecting him like a father also meant that every summer when he brought in these nine-pound zucchinis he grew in his beloved garden, everybody would have to eat them."

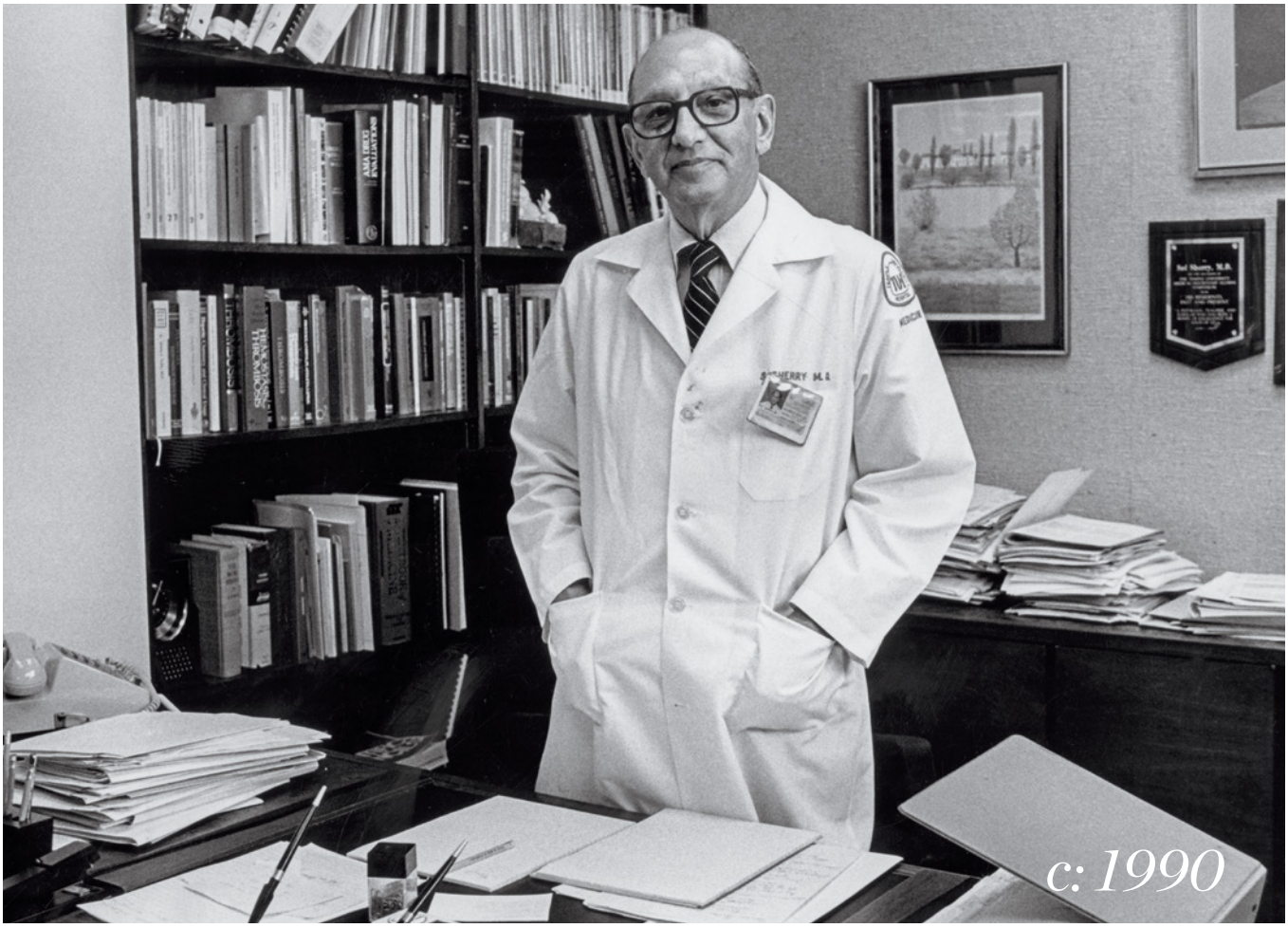
In **1983**, Temple University named Sherry its first Distinguished Professor. In **1984**, it appointed him Dean of Temple's medical school. In **1986**, Sherry established Temple's MD-PhD program. In **1987**, Temple presented an endowed chair in his name (currently held by Rao). And in **1991**, the Thrombosis Research Center was renamed in his honor.

Sherry was never nominated for the Nobel Prize that some say he deserved, but many honors came his way from high-status organizations like the Texas Heart Institute, the American Heart Institute, the American College of Physicians, and the American College of Cardiology.

Sherry died at Temple University Hospital on **January 28, 1993**. He had pancreatic cancer.

"Sol Sherry was an astounding scientist of great vision," says Rao.

"Everything he embraced turned to gold," Rubin adds. "He was extremely loyal to Temple, and we were loyal to him. Institutions prosper for years on the energy of great leaders like Sol Sherry."



IMPACT

Emphatic for Lymphatics

With a $5 million gift, Gerald M. Lemole, MD '62, and his wife, Emily Jane, have established the Lemole Center for Integrated Lymphatics Research at the Lewis Katz School of Medicine at Temple University. There are only a handful of research centers of its kind in the United States.

Lemole, an internationally known cardiovascular surgeon, has been fascinated with the lymphatic system since training under transplant pioneers Debakey and Cooley at the Texas Heart Institute in the 1960s. Today we know much more about the lymphatic system, but it's still a vastly understudied system of the body, with many mysteries to decrypt.

"Exciting discoveries await us at the Lemole Center that could alter our approach to human disease," says John M. Daly, MD '73, FACS, Interim Dean and Dean Emeritus of the medical school. "We're grateful to the Lemoles. Transformative philanthropy like this accelerates science."

As the following discussion reveals, the lymphatic system — and Lemole's appreciation for it — run deep.

Lemole on Lymphatics

Q: ***How did your interest in lymphatics begin?***
A: In my early days in Houston, I was puzzled by unexplained poor heart transplant outcomes and suspected lymphatics were somehow involved. So little was known about this system at the time that it was largely overlooked. Then, serendipitously, when I returned to Temple as Chief of Cardiovascular Surgery in 1969, I met two scientists who were studying lymphatics and immunology. We started looking into how the surgical team could handle the lymphatic system during transplant surgery. Temple was one of the first institutions to appreciate the significance of lymphatics research. For the most part, scientists tend to approach it tangentially as they study other things. Temple recognizes it as the integral system that it is.

Q: ***Integral?***
A: Yes, the lymph system is integral to every system and process in the body, to the health of all organs and tissues. It maintains organ homeostasis by returning excess interstitial fluid to the circulation. It clears the body of dietary fats, dead cells, cellular debris, and pathogens. It absorbs essential fatty acids — like vitamins A, D, and E — from the intestines and transports them to the blood. In addition, the lymphatic system is one of the most important components of the human immune system, with major roles in innate and adaptive immunity. The contributions of the lymphatic system to health, to every function of the body, cannot be overstated. Untreated lymph-related illness can be serious, even deadly.

SAMEER KHAN/FOTOBUDDY

Q: ***In 1981, with an article you wrote that was published in the*** Annals of Thoracic Surgery, ***you became the first to recognize lymphatic dysfunction in the origins of cardiac atherosclerosis. In 2016, you revisited the topic in the journal.***

A: Little was known in 1981 about lymphatic filtration in the clearance of lipids from the coronary wall, but I believed that deficiency in that process — lymphostasis — was a critical factor in the development of atherosclerosis, and now we know this to be true. There is a strong association between defects in cardiac lymphatic function and the progression of cardiovascular disease.

Therapies to improve lymphatic flow could advance the prevention and treatment of atherosclerotic disease. In fact, Michael Autieri, PhD, the director of our new research center, is looking into this. His lab is pinpointing the role of lymphatic vasculature in driving or resolving the atherosclerotic process. And he's identified a potential therapeutic agent: A cytokine called interleuken-19, which holds great promise as a therapeutic agent with potent anti-inflammatory, anti-atherosclerotic, and pro-angiogenic actions. About seven other lymphatics research projects are already underway at the Center related to the heart and brain. It's exciting.

Q: ***What is your vision for the Center?***

A: It's been my lifelong goal to see lymphatics gain greater attention and appreciation within the scientific and medical communities. The work that will be done in the Lemole Center will help get us there — positioning Temple to compete for NIH grant funding in lymphatics, forging scientific progress, educating seasoned professionals and students, publishing, raising awareness — and ultimately improving patient care.

The Lemole Center is multidisciplinary, yet integrated around a lymphatics focus. Clinicians and scientists will collaborate to seek out new insights into the lymphatic system and its roles in human health and disease. The goal is clinical impact. To advance approaches to detecting, preventing, and treating not just lymphatic system issues but many disease states, including edema, infarction, atherosclerosis, and neurodegeneration.

There are intimate connections between the lymphatic system and every system in the body that we've only just begun to identify and explore. I'm excited. We're entering a portal that just might alter our approaches to medicine in fundamental ways.

Michael Autieri, PhD, Director of the Lemole Center for Integrated Lymphatics Research, is a respected educator and research leader who has been on the Temple faculty since 1998. He's also Associate Director of the Cardiovascular Research Center and holds professorships in the Sol Sherry Thrombosis Research Center, Center for Metabolic Disease Research, and Department of Physiology.

JOSEPH V. LABOLITO

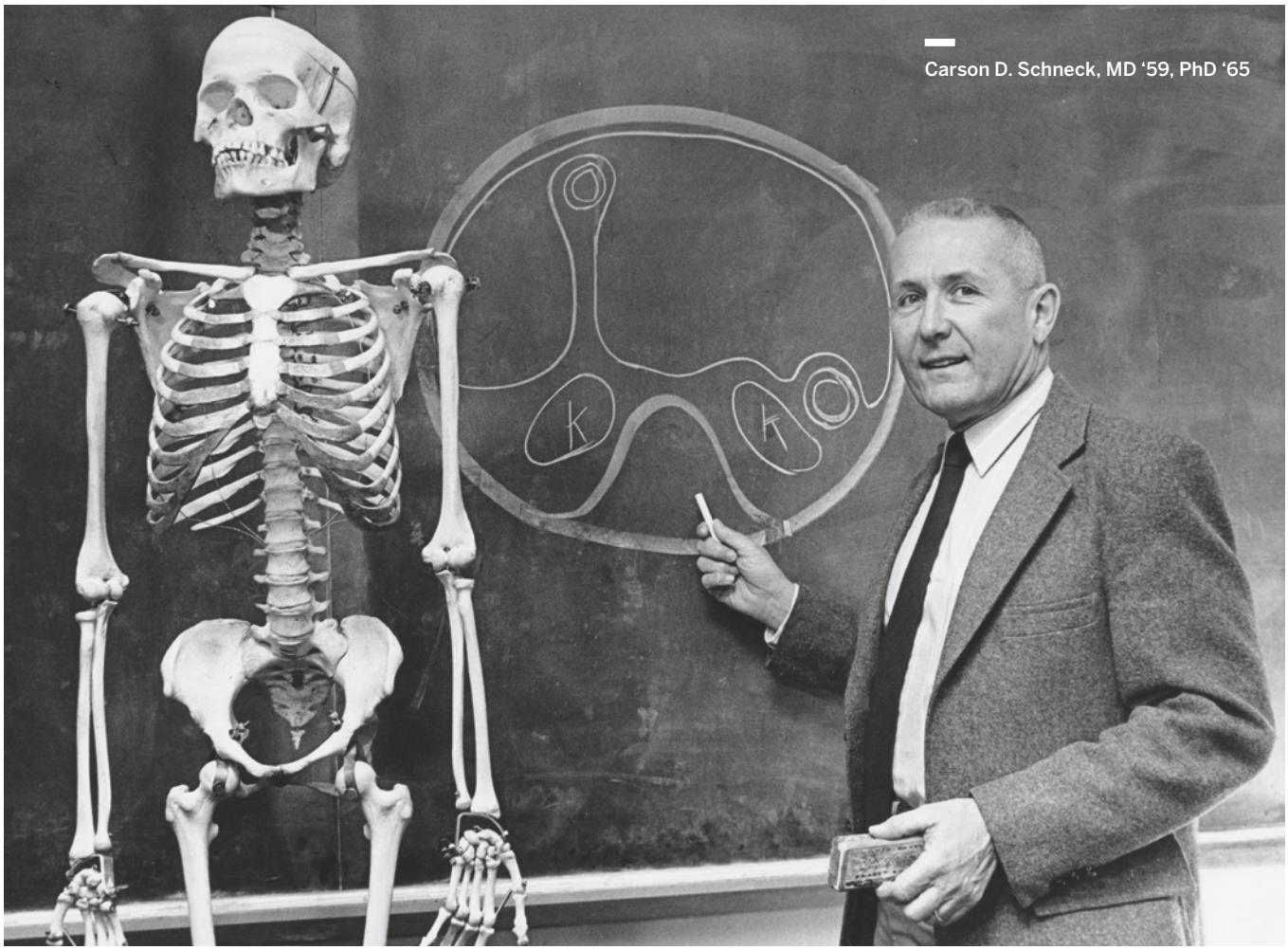
About Gerald Lemole, MD

A 1962 graduate of the Lewis Katz School of Medicine, Gerald Lemole, MD, has accrued many "firsts."

In 1968 he was part of the team that performed the first heart transplant in the U.S. In 1969 when he returned to Temple as Chief of Cardiothoracic Surgery, he performed the first coronary bypass surgery in the tristate region.

Lemole has had a distinguished career. His leadership contributions include roles as Chief of Surgery at Deborah Heart and Lung Center (New Jersey); Chief of Cardiovascular Surgery at the Medical Center of Delaware; and the W. L. Samuel Carpenter III Distinguished Chair of Cardiovascular Surgery at the Christiana Care Health System in Delaware.

Throughout, he's remained close to Temple as a major benefactor and leader. He chaired LKSOM's Board of Visitors from 2011 to 2014, established the Lemole Lecture Series in Integrative Medicine, and named a major conference center in the school's Medical Education and Research Building. Lemole is currently writing a book about the lymphatic system.



Carson D. Schneck, MD '59, PhD '65

Hirsh's Gift Expands Schneck's Legacy

"An excellent teacher can change a life and deepen a lifelong connection to the University where it all began — and for me, that teacher was Carson Schneck. He's an extremely brilliant man who taught anatomy at Temple for 50 years," says S. Jay Hirsh, MD, a 1970 graduate of Lewis Katz School of Medicine.

To honor his mentor — and benefit anatomy students of today and tomorrow — Hirsh donated $1 million to create the S. Jay Hirsh, MD Endowed Anatomy Lab Fund. It's dedicated to keeping the Carson D. Schneck Gross Anatomy lab outfitted with the latest tools and technologies.

"I remember working on cadavers like it was yesterday. It was a tough time, but the best of times, too," says Hirsh, a urologist in Chester County, PA.

"Dr. Schneck and the other faculty — all fantastic — taught us to respect the body and the wealth of information it imparts in life and after death.

"But it was really Dr. Schneck who showed me that I could become a doctor," Hirsh says.

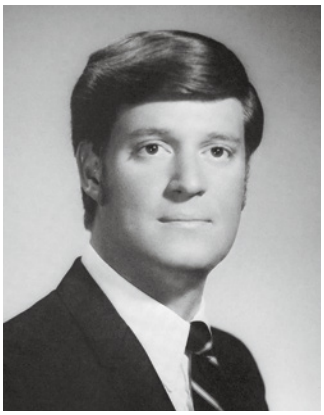
RITE OF PASSAGE

Medical students take several courses during their first semester of medical school, but Human Gross Anatomy is the standout — in Hirsh's words, "the portal into medicine, a rite of passage."

Hirsh commends Temple for still using cadavers to teach anatomy while an increasing number of medical schools are using virtual and digital resources as an alternative to cadaver-based dissection. Medical students at Temple still work their way across the human body, dissecting specific regions and identifying components of anatomy. This process has not changed much since Hirsh's student days — but the setting definitely has.

Hirsh's class — all classes between 1969 and 2008 — took Gross Anatomy in a windowless room in the Kresge Building. Then, in 2009, Temple opened a stunning new building featuring

MEDICAL SCHOOL ARCHIVAL MATERIAL



Above: S. Jay Hirsh, from the 1970 *Skull*. Opposite: Carson D. Schneck, MD '59, PhD '65, the beloved alumnus who taught at the Lewis Katz School of Medicine for five decades. He was the first Anatomy and Cell Biology faculty member to earn a second doctoral degree while working full time — a degree in Diagnostic Imaging — from Temple.

a high-tech, spacious gross anatomy suite bathed in natural light. Alumni mounted a campaign to name it for the enormously popular Schneck. Hirsh contributed, but "knew I had to do more, although I wasn't sure what at the time," he recalls.

IT COMES TOGETHER

According to Steven Popoff, PhD, the John F. Huber Professor and Chair of the department, in the Schneck suite, students get practical experience not just in anatomy but in diagnostic imaging.

"We use X-rays, CT, and MRI in tandem with dissection to teach students to identify normal and abnormal anatomy. It's all part of an approach to teaching called clinical correlation," he explains.

Clinical correlation puts anatomy in context, Popoff says, drawing on multiple sources of information — physical exam findings, blood and imaging study results, a patient's symptoms and medical history — to create a full clinical picture. For example, when students study cranial nerves, they learn about diseases and injuries that affect nerve function.

"It's a far more practical approach than memorizing structure without gaining an understanding of their clinical relevance — and Carson Schneck was masterful at it," Popoff says.

Hirsh concurs. He remembers Schneck illuminating clinical scenarios that students were likely to encounter in practice someday.

"Gross anatomy is an immersive experience that draws not just on superior teachers but also on superior technology — and that's where I come in — with a donation to help keep the Schneck lab at the cutting edge for years," says Hirsh.

Popoff calls the fund "a perfect way to amplify Carson Schneck's legacy."

> "That feeling of belonging is why I succeeded in becoming a doctor — and also why I became a donor," Hirsh says.

FOR THE FAMILY

Hirsh says he'd wanted to make a significant gift to the Katz School for a long time; it just took some brainstorming with Popoff and the medical school's Advancement staff to pinpoint the opportunity.

"My days in the Temple anatomy lab taught me a great deal besides anatomy," he says. "I learned that I was part of a group on a long journey to becoming a doctor, to joining the medical family.

"Dr. Schneck knew how to teach and what to teach," says Hirsh. "His heart was big, his knowledge encyclopedic. Temple was the first institution to make me feel that I really belonged — and Dr. Schneck was a big part of that.

"That feeling of belonging really got me through medical school. It's why I succeeded in becoming a doctor — and it's also why I became a donor," he says.

HIRSH AND SCHNECK: MEDICAL SCHOOL ARCHIVAL MATERIAL; STUDENT: RYAN S. BRANDENBERG

"It is a true blessing to learn medicine in a community that encourages us to prioritize the human aspect in everything we do."

— DANIEL ELCHEDIAK, CANDIDATE, MD CLASS OF 2023

For the 3rd consecutive year, Temple University Hospital earned the designation of "LGBTQ Healthcare Equality Leader," scoring 100 out of 100 in the 13th edition of the Human Rights Campaign Foundation's Healthcare Equality Index report.

"WHERE THERE ARE OPTIONS — AND TEMPLE GAVE ME MANY — THERE IS HOPE."

— ROBERT SWEETIN, TEMPLE LUNG TRANSPLANT PATIENT

DURING THE 2020 FISCAL YEAR, TEMPLE HEALTH SUPPORTERS DONATED NEARLY **$42 MILLION** IN GIFTS AND NEW PLEDGES — A SUM REPRESENTING ROUGHLY **40 PERCENT** OF TEMPLE UNIVERSITY'S RECORD-BREAKING **$107.7 MILLION** FUNDRAISING YEAR.

DURING THE FIRST 3 MONTHS OF THE COVID-19 PANDEMIC, **91** MEDIA OUTLETS — INCLUDING *THE NEW YORK TIMES*, *ROLLING STONE*, *PEOPLE*, AND *TIME* — FEATURED **96** TEMPLE HEALTH FACULTY, STAFF, AND STUDENTS IN **300+** ARTICLES AND BROADCASTS.

Temple University Hospital Stats, 2019

$93.5 M
Professional Education Investment

$40.2 M
Charity Care Investment

$19.5 M
Subsidized Health Services

$12.5 M
Community Improvement Investment

$520 M
Salaries & Benefits

"Providing high-quality health care to underserved communities has been a hallmark of Temple University for more than a century."

— RICHARD ENGLERT, PRESIDENT, TEMPLE UNIVERSITY

"What counts most in the long arc of adult life is not brilliance or charisma or panache, but rather the quality the Romans called 'gravitas': patience, stamina, and weight of judgment."

— PAUL MATHER, MD, PROFESSOR, UNIVERSITY OF PENNSYLVANIA; LKSOM ALUMNUS, 1988

148 TEMPLE FACULTY PHYSICIANS representing 42 SPECIALTIES were named TOP DOCTORS by *Philadelphia* magazine in 2020.

PHOTO COURTESY OF THE WOODMERE ART MUSEUM

Gordon Gave a Hoot

This patinated bronze owl, part of the Woodmere Art Museum collection in Philadelphia, is the Temple University mascot as interpreted by Kenneth H. Gordon Jr., MD '48.

A child psychiatrist and sculptor, Gordon (1924-2005) was President of Temple's medical alumni association from 1995 to 1997 and for a time also served on the school's faculty.

But more than just a loyal Temple Owl, Gordon is to credit for preserving a national historic treasure: Valley Forge National Park.

In the early 1970s, upon learning that the land (then state-owned) was slated for commercial development, Gordon mounted the campaign to save it. He lobbied Congress, created petitions signed by thousands of voters, and presented testimony to three separate congressional committees in Washington, D.C.

Gordon devoted five years to saving the land symbolic of the American struggle for independence. In 1975, his efforts finally paid off. Every year, the park attracts well over a million visitors.

Temple Health
Magazine

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Together we care for patients, educate the next generation of medical leaders, assist our neighbors, and pursue groundbreaking research.

To donate to our emergency funds, visit:
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templehealth.org/2019-novel-coronavirus/support
