special report

MEDICINE AND THE MUSE

Dancin’ feat
Music and movement for Parkinson’s

Ow
Kids depict their pain

Seeing color
An ophthalmologist looks at art

Photographer, MD
A conversation with Max Aguilera-Hellweg

Multitalented
Medical students’ artistic pursuits

plus

The curious case of the mosaic heart
What was wrong with baby Astrea?

More than mutation
A new model helps explain cancer
This past fall, I took a break from my studies in medical school at Stanford to visit my grandparents and pick up my haul of vegetables from their garden. Grammy didn’t rise to greet me like usual. At my prompting, she said she had a terrible heat rash along her underwear line, but I wasn’t to worry, she was fine. I could feel my training kicking in. “Can you describe your rash for me?” I started gathering a history of the present illness. Onset — three days ago. Palliation — Gold Bond applied 2x daily (I made a mental note: Figure out what “Gold Bond” is). Quality — burning. Patient’s perspective — “fine, really.” Do you want to look at it?” she asked. We were in the kitchen.

I suggested moving to the bathroom, and when Grammy tugged down part of her underwear she revealed an ugly red rash and some crusty white powder. The Gold Bond. “It’s looking better today,” she said apologetically.

I stalled. “I haven’t done my dermatology block yet” (as if that would help), “but I’d take off your underwear for a few days and try hydrocortisone cream on a small portion to see if that area gets better.”

When I called the next day, Grammy sounded more like herself. I called a week later and Grammy was effusive. “The rash is gone. I don’t know what I would have done without you. You’re my doctor now.”

I sidestepped her thanks uncomfortably. “How did the hydrocortisone trial go?”

“I’ve been putting it all over the rash,” she said blithely. I resisted the urge to tell her that my instructions had been to try it on only part of the rash. I asked if she’d found different underwear.

She was suddenly defensive. “I haven’t worn underwear since you told me to stop wearing it. I’ve been doing everything you told me to do.”

I was shocked at her willingness to trust me.

I recounted this tale at the storytelling retreat I co-led this fall with Laurel Braitman, writer-in-residence at Stanford’s Medicine and the Muse program. We gathered at a farm in Vacaville with writers, physicians and 25 medical students to explore how storytelling can influence the learning and practice of medicine.

After hearing my story, my peers described their own role reversals with family members, fears of causing unintended harm, and surprise at how seriously their medical advice is taken. The physicians told us that, to some extent, these feelings never go away. Even the most experienced described being surprised by moments of intimacy with patients.

Rebecca Skloot, author of The Immortal Life of Henrietta Lacks, joined us on the retreat. She advised us to keep a journal while we’re in medical school. Remember how quickly patients have to trust their health care team with their bodies and their stories, she told us. Don’t underestimate how much you’ll learn about people when you take care of their bodies.

While I treated her rash, I saw a side of my Grammy I’d never seen before and, as I’ve told her story, I’ve learned things about myself I’d never known before. While not every patient interaction may have as large an impact on my journey to becoming a physician, I’ll take the advice to keep writing them down. You never know what can you learn when treating a rash. — RUTH MARKS
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DEPARTMENTS

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Sometimes my daughter and I engage each other in a thought experiment: What if you could listen to composers from only one half of the alphabet? Would you choose A to L or M to Z?

With the former, you get Bach and Beethoven. Not to mention Bartok, Brahms and Debussy. But with the latter, you get Mahler, Mozart, Schubert, Stravinsky, Verdi and Wagner. The game usually ends predictably: An impossible choice!

It’s hard to imagine a world without the transcendent beauty of a Bach cantata or a Mozart concerto. When I listen to music, especially during a performance at Stanford’s Bing Concert Hall, I am often reminded of the reason why: Music has a way of speaking to us and for us, conveying thoughts and emotions when words fail short. Music also brings us together, allowing us to share experiences across time and space.

Music has been an important part of my life since I was a child and began learning to play the cello. My musical training taught me valuable lessons about creativity — as Einstein said, artistic creativity is not so different from scientific creativity — and the power of teamwork. It’s still amazing to hear in a symphony how many separate notes and individual instruments can come together to create a whole that is so much more than the sum of the parts.

Now, as dean, I have found that my background in music — and my deep appreciation for the arts and humanities — is more important than ever. Stanford Medicine’s vision of the future of health care allows us, for the first time, to imagine a world without disease, fueled by astonishing scientific breakthroughs and incredible advances in technology. It’s an inspiring vision, and yet while we all want to live a long and healthy life, we also yearn to live a good and meaningful life.

Disciplines like philosophy and poetry can help us get there.

In the arts and the humanities, we find a unique window into both ourselves and the human condition. As medical research and technology transform our lives, we will continue to attend concerts, visit art galleries and read literature to help us explore age-old questions about who we are, why we’re here and what it all means. Through science, we may be able to understand the fundamental workings of the human body and mind, but we still need to look beyond science to help make sense of things like suffering, love, hate and hope.

And within the practice of medicine, we physicians must bring the arts and humanities to bear — to ensure that high-tech medical treatment is paired with high-touch health care. In this way, we can approach each patient with empathy and compassion — with the understanding that a disease is not the same as the experience of illness, and that a patient is more than an ill person.

Keep reading to learn about some of the ways that Stanford Medicine is bringing this humanistic medicine to our patients and joining the arts and the sciences to create the future of health care. May it be music to your ears.

Sincerely,

Lloyd Minor, MD
Carl and Elizabeth Naumann Dean of the School of Medicine
Professor of Otolaryngology-Head & Neck Surgery
BIO POWER

STANFORD HAS OPENED its Laboratory for Cell and Gene Medicine, which is devoted to making biological materials for use in phase-1 and phase-2 clinical trials. “Stanford has a vast pipeline of potential cell and gene therapies that can now be realized without having to go off-site to make materials for testing,” says laboratory director David DiGiusto, PhD. Among the materials the facility plans to manufacture: purified blood stem cells to treat genetic diseases; immune cells engineered to attack cancers; and viruses equipped to replace faulty genes with healthy, functional copies.

Saving skin

A TEAM OF STANFORD researchers has demonstrated that grafting sheets of genetically corrected skin improves wound healing for patients with one of the most painful of diseases, recessive dystrophic epidermolysis bullosa. The phase-1 clinical trial marks the first time that skin-based gene therapy has been shown to be safe and effective in patients.

People with the disease don’t properly produce type-7 collagen, which anchors the upper and lower layers of the skin together. As a result, the layers slide across one another upon the slightest friction, creating blisters and open wounds.

The skin grafts do not cure the disease, but may be able to head off complications such as scarring that can result in fused fingers or inflammation that can lead to squamous-cell carcinoma. “Even a small improvement in wound healing is a huge benefit to the health of these patients,” says Jean Tang, MD, PhD, who shares senior authorship of the study with fellow Stanford associate professor of dermatology Peter Marinkovich, MD.

Four adult patients each received six grafts grown in the lab from their own skin cells, into which a corrected version of the type-7 collagen gene had been inserted. At three months, 21 of the 24 skin grafts were intact, and 12 remained so at 12 months. The researchers detected expression of the type-7 collagen protein in nine of 10 tissue biopsies at three months, and five of 12 at one year.

The study was published in November in JAMA.
Heart stopping?

Want to know whether a drug will damage a patient’s heart? Turns out you may be able to test that in a lab dish.

A team of Stanford researchers demonstrated that adult stem cells can be transformed into heart muscle cells that faithfully mirror the pattern of gene expression of a person’s native heart tissue. The stem cells studied were induced pluripotent stem cells — cells isolated from adult tissues such as skin and blood and enabled to differentiate into a variety of cell types.

The team investigated how the iPS cells responded to two drugs known to cause adverse cardiac effects in some people, but physicians can’t currently predict whom. The cells of one research participant responded differently to rosiglitazone, a drug sometimes used to treat diabetes. That person “exhibited a very abnormal expression of genes in a key metabolic pathway,” says cardiovascular medicine instructor Elena Matsa, PhD, who is the lead author of the study.

The study, which was published in August in Cell Stem Cell, validates the use of iPS cells to test the potential cardiotoxicity of certain drugs and to devise new therapies for conditions like cardiomyopathy.

Too short

MANY PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY, the most common of the heritable muscular dystrophies, die from heart failure. Stanford researchers are beginning to understand why their hearts become weakened and enlarged in the first place.

Telomeres, the protective caps on the ends of chromosomes, shorten with each cell division, measuring out a cell’s life span. But telomere length is usually stable in healthy tissues that don’t divide, like heart muscle cells.

Telomeres do shorten, however, in the heart muscle cells of lab mice bred to model Duchenne, which is caused by mutations in the gene that produces dystrophin, a protein that stabilizes muscle. The shortening triggers a DNA damage response that compromises the cells’ energy generators, or mitochondria, resulting in the inability of the heart muscle cells to efficiently pump blood throughout the body.

“This is the first time that telomere shortening has been directly linked to mitochondrial function via a DNA damage response in nondividing cells,” says Helen Blau, PhD, professor of microbiology and immunology and the senior author of the recent study. “We’ve outlined the molecular steps in this process that lead to death, giving novel insights into the condition and identifying alternative strategies for heading off heart failure in human patients with Duchenne.”

The study was published online Oct. 31 in Proceedings of the National Academies of Science.

Stress test

ADOLESCENT GIRLS WHO experience trauma are more likely to develop post-traumatic stress disorder than boys, and a new study may help explain why.

A team of Stanford researchers found sex differences in the anterior circular sulcus, a portion of the brain’s insula, which contributes to the awareness of one’s feelings and to empathy. The region was larger in traumatized boys compared with nontraumatized boys in the control group, and smaller in traumatized girls than in girls in the control group.

“It is possible that boys and girls could exhibit different trauma symptoms and that they might benefit from different approaches to treatment,” says Megan Klabunde, PhD, instructor of psychiatry and behavioral sciences. She is the lead author of the study, published in November in Depression and Anxiety.

TERRY ALLEN
Hidden transmission

More than a year after the Ebola epidemic in West Africa ended, researchers have identified 14 people who tested positive for the virus but had not been identified previously as having the infection. Twelve of them said they were asymptomatic; the other two recalled having a fever.

“The study corroborates previous evidence that Ebola is like most other viruses in that it causes a spectrum of manifestations, including minimally symptomatic infection,” says lead author Gene Richardson, MD, a former fellow in Stanford’s Division of Infectious Diseases and Geographic Medicine who is now a PhD candidate in anthropology at the university. “This shows there was a lot more human-to-human transmission than we thought.” It is unclear whether asymptomatic individuals can transmit the virus.

In the Sierra Leone village where they conducted the study — an Ebola “hot spot” — researchers calculated the prevalence of minimally symptomatic infection at 25 percent. They say the results demonstrate the need for better public health efforts to contain the virus.

The study was published in November in PLOS Neglected Tropical Diseases.

A SAFER CURE

Bone marrow transplants could be widely used to treat autoimmune and metabolic disorders as well as many types of cancer, and to enable safer organ transplants. But before one is performed, physicians have to kill the patient’s own blood stem cells. Current methods — chemotherapy or radiation — are toxic. So bone marrow transplants are a last resort.

A team led by Stanford professor of medicine Judith Shizuru, MD, PhD, published a much less toxic method in August in Science Translational Medicine. The team targeted two proteins on surfaces of blood stem cells in mice: c-kit, a marker of blood stem cells, and CD47, which sends a don’t-eat-me signal to immune cells called macrophages. They attached antibody to c-kit and blocked CD47, which liberated the macrophages to “eat” the cells covered with c-kit antibody.

TERRY ALLEN

High and mighty

When it comes to taking statins for atherosclerotic cardiovascular disease, aim high, says a new study by Stanford Medicine researchers.

In a large, nationwide study of patients’ medical records, those who took high-intensity statins — medications that reduce cholesterol by 50 percent or more, on average — had a 9 percent increased chance of survival over those taking medium-intensity statins. The results held true for patients between the ages of 75 and 85, a group not well-studied in clinical trials. The study also showed a benefit to taking the highest dose tolerated.

Professor of cardiovascular medicine Paul Heidenreich, MD, is the senior author and cardiology fellow Fatima Rodriguez, MD, is the lead author of the study, which was published in November in JAMA Cardiology.
I WITNESS MANY GOODBYES. My job as an anesthesiologist is to care for people at their most vulnerable in the journey from goodbye to hello. Working at the Veterans Affairs Palo Alto Health Care System, I meet my patient and his family shortly before the time of surgery. We are all strangers. My patient, in a lavender, disposable gown, lies on a wheeled gurney, tucked under a hospital-issue blanket. He has already removed his wedding band and talismans. He still has his hearing aids, but he may be reluctant to talk without his dentures. Nonetheless, we talk. I ask questions, have him open his mouth and move his neck so I may examine his airway. I also ask questions of his family. My final question is to ask for their questions.

I unlock the gurney and wheel my patient away from the row of pre-op holding bays of fellow veterans (male and female), and from family, from consciousness. My patient gifts me with absolute trust: I will render him incapable of fending for himself. He will not be able to blink or breathe on his own. I have become my patient's guide and protector.

My awareness of the privilege of doctoring is heightened by my exposure to and immersion in the humanities and arts. My sister and I grew up as daughters of a costume designer and a playwright. There was no money, at times no telephone or electricity, but the advantages we had to be backstage during dress rehearsals, to attend poetry readings, to wander through the art museum on free day and to choose our own books in the sanctuary of the public library were extraordinarily rich. With full respect for the sacrifices and passions of artists, my sister and I both became physicians.

The arts and health have been intertwined for millennia: Recall Apollo as the god of both healing and music, or the creation of fertility statues such as the Woman of Willendorf. Physician-writers trace back to François Rabelais and earlier. Medical humanities as an academic discipline originated about half a century ago, not uncoincidentally with the steep slope of scientific and technologic progress in medicine that can alter who or what is human.

THE SYNERGY of medicine and the humanities

BY AUDREY SHAFER, MD

ILLUSTRATION BY JEFFREY FISHER

PHOTOGRAPH BY TIMOTHY ARCHIBALD
MEDICAL HUMANITIES began as a study of literature and medicine, as an inquiry not only into the many ways medicine and the human condition are represented in literature, but also to investigate the parallels between the close reading of texts and the data interpretation and diagnostics of medicine. Furthermore, scholars began using literary theory to situate illness and health care in the context of society and history.

In the past 30 years, medical humanities blossomed into a diverse multidisciplinary field that encompasses the arts, humanities and qualitative social sciences. It goes by many names, including health humanities, narrative medicine, social medicine and bio-humanities. The Stanford program I founded and direct, Medicine and the Muse, uses the term “medical humanities and the arts.” In a dynamic, intimately related field of practice and research, arts and health, artists and arts therapists work directly with patients and research therapeutic benefits.

Medical humanities can be seen as ancillary, a nice-to-have rather than a must-have. Modern medicine, with its focus on evidence-based practice guidelines, technological advances, genomic precision and big data, may seem too demanding of our attention to warrant the inclusion of arts and humanities, with their inquiries into philosophy of mind, postmodernism and conceptual art.

But the field of medical humanities is growing in tandem with the explosion of information and of scientific and technological discovery in medicine, and that’s the crux of why medical humanities should be viewed as a must-have. The arts, humanities and social sciences teach us both to look outside of ourselves and to look within: to explore, examine and record what it means to be human. What do health, illness, suffering and healing mean? What is caring? What is the experience of exhaustion, loss and grief? Such inquiries enable us to think critically about what we do, what we say, how we affect others, how our relationships are tied to our choices and perspectives, and, ultimately, how we live. This is precision health at its most nuanced, contextual and intimate level.

Furthermore, creativity is germane to all forms of inquiry, and the study of creativity in the arts can open pathways for studying perception, translation and innovation in additional contexts. Medical humanities and the arts provide entrée for nonphysician scholars into the protected guilds of medical care, thus allowing explorations of mortality, embodiment, frailty and resilience. These collaborations can even lead to medical advances, such as the development of the “brain stethoscope,” a device that transforms brain waves into music to detect seizures, by Chris Chafe, DMA, and Josef Parvizi, MD, PhD, professors of music and of neurology, respectively.

Lastly, the clinical encounter is not a robot-to-robot interaction — medical humanities and the arts are critical for both sides of the interaction, for patient and physician well-being. Metaphor and storytelling illuminate our connections. Art weaves us into the fabric of humanity.

As a poet, I assess the tone and arc of what my patient says. I wait through the pauses and listen for what is unsaid. As a

‘what do health, illness, suffering and healing mean? What is caring? What is the experience of exhaustion, loss and grief?’
music lover, reflecting on musical structure helps me examine how I may be led astray by assumptions of what comes next and the dynamics of team member discourse. As a participant in observation skills training at Stanford’s Cantor Arts Center and Anderson Collection, I better understand my trainees’ fresh perspectives, which I have suppressed due to immersion and habit. Medical humanities and the arts inform every aspect of my doctoring.

I witness many hellos. They come as my patients emerge from anesthesia, having completed one important leg of their health care journey. I explore these hellos in my poetry. My poem “The Anesthesiologist and the Patient,” from the anthology *Grit, Gravity, & Grace: Poems about Medicine and Healthcare*, concludes:

> You are both here and elsewhere until I welcome all of you back, onto the shore where people ask you questions check your bandage. Tell you sad or happy news.

> You will not remember your kindness that you thanked me.

> Maybe once more I shall see you at the far end of the hall, bathed in light from the atrium windows pushing your IV stand poling your way towards recovery.

Due to the growth of perioperative medicine, anesthesiologists engage in even more hellos as postoperative patients progress under team-based care.

Hellos in my work in medical humanities are diverse and plentiful. The hello of a medical student reawakening a deep-seated passion for writing and literature. The hello of an anthropologist and a psychiatrist as they collaborate on a study of hallucinations. The hello of a patient and nurse listening to a concert in the hospital. These hellos are the heart of academic inquiry and form the connection between what we do and who we are. The field of medical humanities and the arts is a path to wellness, an inquiry into social justice and access and an opportunity to explore ourselves in relation to others. The human condition has tragedy and sorrow, transcendence, curiosity and grace. Rather than shy away from these complex areas of human experience, medical humanities embraces them. If you have not heard of medical humanities: hello and welcome! SM

— Contact Audrey Shafer at medmag@stanford.edu

A HOME FOR HUMANITIES AND THE ARTS

MEDICINE AND THE MUSE IS THE HOME FOR THE ARTS AND HUMANITIES AT THE Stanford School of Medicine. Audrey Shafer, MD, professor of anesthesiology, perioperative and pain medicine, founded the program in 2000 and continues to direct it.

The program aims to integrate the arts, humanities and qualitative social sciences into medical education, scholarly endeavors and the practice of medicine. Its many offerings and collaborations include:

• Pegasus Physician Writers, directed by Hans Steiner, MD, professor emeritus of psychiatry and behavioral sciences, for physicians and physicians-in-training to meet and workshop their creative writing. Participants recently wrote poetry read in concert with music performed by the St. Lawrence String Quartet, which is in residence at Stanford.

• The Program in Bioethics and Film, which creates films and education programs on important issues in health care. The program’s director, filmmaker-in-residence Maren Grainger Monsen, MD, most recently co-produced and directed *The Revolutionary Optimists*, about children in Kolkata, India, improving health in the slums and brickfields where they live.

• The Stanford Medicine Music Network, which invites musicians and music lovers to come together and share music. The program also collaborates with the Center for Computer Research in Music and Acoustics on its annual “Music and the Brain” conference.

• The Biomedical Ethics and Medical Humanities Scholarly Concentration, one of eight foundational areas in which medical students pursue in-depth study and mentorship.

• The Literature and Medicine Dinner and Discussion Series, designed and led by Medicine and the Muse assistant director Jacqueline Genovese and clinical assistant professor of medicine Benny Gavi, MD, which brings together Stanford physicians from different backgrounds and specialties to talk about literature and doctoring over a meal.

• Medicine and the Muse’s spring symposium, led by clinical associate professor of psychiatry and behavioral sciences Shaili Jain, MD, featuring medical students’ work in the arts and humanities. This year’s event will take place on April 27; the keynote speaker will be David Leventhal, executive director of Dance for PD, a dance program with therapeutic benefits for Parkinson’s patients (see page 24).
The role of art in medicine, at first glance, can appear amorphous, indistinct, even at odds with the basic tenets of science. And yet, the arts remain essential to that same human condition to which health care providers dedicate their lives — and they are key to the creativity of science.

At Stanford, about half of all medical students become involved with the arts and humanities through Medicine and the Muse, a program that integrates the arts and humanities into medical education, says Audrey Shafer, MD, director of the program and professor of anesthesiology, perioperative and pain medicine. About a dozen each year receive funding through the Stanford Medical Scholars Research Program to pursue MedScholars projects focused in the arts.

“The practice of medicine is a human endeavor,” Shafer says. “The arts enable us to think more critically about what medicine is and who we are, as well as helping us to understand the perspective of the patient, to have empathy for people who are ill.”

And, as you’ll read, the arts can play a role in helping to heal the healers themselves.

**BY TRACIE WHITE**

**PHOTOGRAPHY BY TIMOTHY ARCHIBALD**

NICK LOVE ILLUSTRATED

SEVERAL OF HIS FAVORITE MNEMONICS FROM ANATOMY LAB.
The graphic artist

The tall, fast-talking, blue-scrubs-wearing Nick Love leans closely into the whiteboard in Stanford’s clinical anatomy dissection lab, where he’s hung a poster-sized rendition of his multimedia illustration, titled *Sixteen Anatomic Mnemonics*.

Love has drawn upon his skills as a graphic artist and former medical illustrator — using graphic design software combined with hand-painted splashes of color — to create a work of art as his MedScholars Project. *Sixteen Anatomic Mnemonics* is an illustration that both entertains and serves as a memory aid. It exists in various forms: online at http://www.sixteenanatomicmnemonics.com/, as a book and, now, as a poster.

To each version he likes to add touches of something new. “I like to give a one-off artistic feel to the piece,” says Love, a medical student who has already earned a PhD in developmental biology, as he dabs short brushstrokes of white paint into the spaces between the 16 boxed illustrations on the poster board.

*Sixteen Anatomic Mnemonics* is decorated with brightly colored illustrations of 16 medical mnemonics, the whimsical expressions that share the same initial letters as the lists of body parts medical students must memorize. There are Andy Warhol-inspired Campbell’s-style soup cans that spell out the branches of the descending aorta: celiac trunk, superior mesenteric, renal artery, gonadal artery, inferior mesenteric, common iliac, and tiny toilet-sitting versions of Rodin’s *The Thinker* contemplate the rotator cuff muscles of the mnemonic SITS: supraspinatus, infraspinatus, teres minor, subscapularis.

The anatomy lab is where inspiration struck Love, as a first-year medical student. White-coated instructors would scrawl mnemonics across these same whiteboards, sing-songing the funny-bone-tickling memory devices for the edification of medical students.

Love chose 16 of his favorite mnemonics — most from his anatomy instructors, a few found online. He drew each one as a story within a story within a story that illustrates practical applications of anatomy. Visualizing these mnemonics could only help the memorization process, he figured.

Peer closely into the illustrated mnemonic for branches of the facial nerve: *to Zanzibar by motor car, please!* Then peer more closely at the words for the facial nerve branches, temporal, zygomatic, buccal, maxillary, carotid, posterior auricular, all illustrated with rainbow-colored Hot Wheels cars. And closer still, into the background where tiny Zanzibar maps float in space next to tiny floating faces, facial nerve branches sketched in.

“I like hiding things in all my projects,” Love says. “I’ve long been interested in the pop art movement, but I’m probably more of a science nerd at heart. In any case, I hope that my work will help people learn more about biomedicine.”

The dancer

Stanford medical student Amrapali Maitra joined the group of previously homeless and mentally ill women, many survivors of domestic violence, with trepidation. The exercise room in this shelter for homeless women in Kolkata, India, her new base for her anthropology research, was dark and dank. The group was mostly quiet, mostly sad, distracted or uninterested.

“I was nervous, but the music played and my body just sort of took over,” Maitra says. “I did what I like to do: folk movement, Bollywood dance, hip-hop. Everyone got so much joy from this. The women started clapping and laughing and dancing around. That opened me up to the worlds of these women.”

Morning after morning, these women who had escaped from violent homes, ending up first on the streets, then in the shelter, would find momentary comfort and healing through dance, Maitra says. The goal of her research, conducted in this shelter, was to explore experiences of domestic violence among poor and marginalized women in Kolkata. In writing about the experience, she explains how dance enabled her to connect with her research participants. “Through dance, I formed attachments with the women, across steep barriers of class and cultural difference. Movement equalized us; we found harmony in beats, steps and silence.”
Indian dance has been a part of Maitra’s life since she was a little girl studying the classical form known as Bharatanatyam. It continues to be so now, both as a medical student treating patients and as a PhD student studying domestic violence in India. Like other medical students passionate about the arts, Maitra has woven her talent together with her skills as a writer, researcher and health care provider into a pattern that she believes will best lead to the healing of others.

“Dance is a thread that has always been there,” says Maitra. “It’s a way of seeing and being in the world. I see how it shapes my approaches as a physician. It permits a different kind of expression than oral narrative.”

A native of Kolkata, Maitra studied history and literature as an undergraduate at Harvard University, always knowing she wanted to be a physician. Her MedScholars project entailed developing and implementing a domestic violence screening tool in Dhaka, Bangladesh. She has since spent 16 months conducting research in India, where dance has played a key role in helping her to connect with and help heal abused women. In India, dance is a big part of everyday life, both informal and formal, Maitra says, so it was just a natural extension for her to use her skills in traditional Indian dance to reach out to her research participants.

“Certain things you can express through dance — feelings of rage, sadness, protest,” she says. “In the form of Indian dance I do, we are trained to express mood or emotions with the face and hands and body to show feelings of disgust or peace or anger or love. For me, moving with these women, I felt their pain, the abandonment and the abuse that these women have felt.”
The writer

During his surgery rotation in his third year of medical school, Matt Bucknor, MD, remembers standing by the side of a patient. He was dressed in the white coat of a physician, yet a nurse mistook him for a janitor. The experience was jarring, but not new, he says matter-of-factly.

“Implicit bias is alive and well. It touches every corner of our health care system,” says Bucknor, now an assistant professor of radiology at UC-San Francisco. While he was growing up in a diverse and tolerant Maryland suburb, and as an undergraduate at Harvard University, he says, racism had never felt like a barrier to his professional or academic development. As an African-American physician caring for patients, this changed.

And so he wrote about it.

For Bucknor, the art of writing, a passion that emerged just as he entered medical school, became a way to explore his experiences navigating the new world of medicine. Between rounds, whenever there were short breaks in the daily demands and long hours of medical school, he’d pause to jot down notes, fiddle with phrases.

“It renewed my energy,” says Bucknor. “Writing and communicating ideas helped sustain me in medical school and residency. It was a crucial outlet.”

His writings developed into a novel. He wrote the first third as his MedScholars project, then continued writing a 400-page first draft. The novel tells the story of Marcus, a young, black medical student in San Francisco confronting issues of race and identity while plunged into the physical and emotional demands of becoming a physician. Bucknor is still actively working on the book and also leads one of the Pegasus Physician Writers groups at Stanford.

Marcus’ words in the early pages of the novel could have been Bucknor’s own: “I count myself among a lucky few, a black man in America who has seen hard living, but never known it.

He writes about what he knows, such as the sorrows of dealing with the death of your first patient as a medical student:

I waded into that awful inevitable moment like a toddler pushed into the center of a pool. I felt ashamed and embarrassed. Kayla’s death wasn’t my fault. But there is no way that mattered because all I could feel was that it was entirely my fault.

And the joys of knowing a patient will survive:

That is my favorite part of the job. Knowing that someone is going to be okay, before anyone else. That moment — it feels like catching a firefly that no one else can see.
The musician

At the still point of the turning world.
Neither flesh nor fleshless; Neither from nor towards; at the still point, there the dance is, But neither arrest nor movement
— T.S. Eliot, Four Quartets

BEN ROBISON IS A MUSICIAN. It’s part of who he is. “For me, making music is like eating or breathing,” says Robison, a professional violinist with a doctorate in musical arts. Robison is in his fourth year of medical school and co-founded the Stanford Medicine Music Network, which brings musicians together to play music.

Together with Matthew Wetschler, MD, a painter and a third-year resident in emergency medicine, Robison is hoping to build a community of medical practitioners dedicated to what he calls “art-enabled reflective practice” — a foundation for reflection inspired by art.

Both men drew sustenance from their art during medical school. Painting and music provided this foundation for reflection, time away from the emotional strain from caring for the sick and injured. It rejuvenated them. And it helped to recharge their empathy, Robison says.

“Incredible health care workers in the ER and throughout the hospital take care of as many as 30 people a day,” Robison says. “People in extreme pain and distress. It is without a doubt a taxing job. You are busy being a doctor, a professional. It can be very analytic, with your time dominated by diagnosis, documentation, computers, treatments.”
There is little time for deep reflection.
“His art, my music — it was and is an incredible way for us to process what goes on in the hospital, the wonderful and the terrible,” Robison says. “We thought we could use the practice of art to inspire reflection and to offer shared empathetic experiences for health care providers — to heal those who heal others.”

With their MedScholars project and additional funding from Medicine and the Muse, Robison and Wetschler are planning to provide that sort of comfort to other health care providers, including physicians, nurses and technicians. They are organizing a tour of medical schools where they will present a two-hour concert and panel on art and wellness. They’ve also created a website, atthestillpoint.org, to support the tour — the name comes from a T.S. Eliot poem. The website is designed as a repository for pieces of artwork collected from health care providers. Their vision is to inspire reflective practice through both the appreciation and making of art. In the spring, they plan to take the show on the road, touring medical schools. Each event will include Robison improvising on the violin, a talk by Wetschler and a panel discussion, and will conclude with audience participation.

“Maybe it could be inspiring. Maybe it could help prevent burnout,” Robison says.

The project began with both of these artists posting their own artistic creations on the website — a Wetschler painting and a Robison musical composition. Their message:

“Here’s art. Be with art. Take that moment. As a musician our canvas is silence. Drop into that stillness and draw a line.

“Come from a point of stillness.”

The filmmaker

SLOWLY, THE LESBIAN, GAY, BISEXUAL AND TRANSGENDER VETERANS TELL THEIR STORIES — of being set up for a date rape by a superior, of rejection by the military they love, of the little boy who looked like a little girl who always wanted to join the military. They talk about mental illness, suicide, post-traumatic stress disorder, nightmares, insomnia. And then they speak of the healing that occurs from telling these stories.

“I was a victim of military sexual trauma; I had PTSD early on,” says one of the veterans speaking in the documentary The Camouflage Closet. “I was considered a broken soldier. I was a target of military sexual trauma. I was told I would be ruined if I told anyone. I was naive. I was 19.”

In his first year as a medical student, Michael Nedelman, already an experienced filmmaker, began work on his MedScholars project: The Camouflage Closet, a documentary about LGBT veterans’ experiences with PTSD, trauma and recovery. The idea for the film emerged in a San Francisco arts workshop just before he began medical school, less than a year after the repeal of the policy on LGBT military members known as “Don’t ask, don’t tell.”

The film explores healing through vignettes in which nine veterans talk to the camera about prejudice, humiliation, violence and resilience. As a way of accessing often hidden memories, Nedelman provided the veterans with cameras and trained them to create their own video narratives.

“They were able to tell their stories on their own terms,” he says. “I think the camera might have played a big role in accessing these memories.

“I’ve been a filmmaker since I was 16 or 17 years old,” says Nedelman, who has an undergraduate degree in film studies from Yale University. One of his early works was Vision Voice, which explores the lives of three women living with diabetes.
the body majestic

Photographer Max Aguilera-Hellweg, MD, focuses his lens on some of the most beautiful shots of all: details of the human body. He’s a master at portraying the intimate and sacred. His photos are visually stunning, often capturing moments when the human body is at its most vulnerable, open and splayed on an operating table.
Early in his career, he was hired as an apprentice to the iconic photographer Annie Leibovitz. From her, he learned not only the art of photography but also the discipline of persistence. That attribute came in handy when, at age 34, he decided to interrupt his career in photography and attend medical school at Tulane University. He received his MD in 2004.

Aguilera-Hellweg has photographed arresting pictures for this magazine as well as for National Geographic, Smithsonian, Rolling Stone, The New Yorker and many others. In his book, The Sacred Heart: An Atlas of the Body Seen Through Invasive Surgery, he surprises us with images that make us stop and ponder the intricate and awe-inspiring nature of the human body. For this issue of Stanford Medicine on art and medicine, it made perfect sense to talk to an artist and physician who personifies medicine and the muse.

Executive editor Paul Costello caught up with Aguilera-Hellweg between shoots at his home in Connecticut.

COSTELLO: How did your journey into photography begin?
AGUILERA-HELLWEG: Looking in my parents’ closet for my mom’s purses for money to go buy candy, I came across my father's photo albums from World War II in the Pacific. I’d never seen pictures like this. To see bombs exploding, it was a shock. It was like this whole world had opened up to me to see what was forbidden. I became obsessed about looking at the photographs. It just opened up the power of photography.

COSTELLO: When did you get your first camera?
AGUILERA-HELLWEG: My father worked in a warehouse when I was in 10th grade. A 35mm Canon camera, it was called a Canon S, had fallen from a shelf at the warehouse. It was broken and they gave it to my dad. We just had to get it repaired.

COSTELLO: Here you have this great career in photography, and then at 34, you decide to go to medical school?
AGUILERA-HELLWEG: I was shooting a surgeon for an article in Savvy magazine. It was my first time in the operating room, and I walk in there, and normally you would see a patient lying on a bed prone, but she had him hanging vertically, which allowed his vertebrae to be stretched out. I was busy shooting her hand and at one moment she steps aside and says, “Here. Take this picture.” There was an exposed spinal cord. It was the most intimate, most beautiful, most precious place I’d ever seen in my whole life. It was like going to the moon. That moment changed my life. Besides taking the photograph, I decided this is who I wanted to be the rest of my life, this is where I wanted to explore. I wanted to look inside the body and see what this incredible mystery was. Becoming a doctor allowed me to cross that line from having the secondary experience as a photographer to having the primary experience of my subjects.

COSTELLO: You left medicine after the second year of a three-year residency. Why?
AGUILERA-HELLWEG: I loved it but I knew that if I stayed on for the extra years of training that I needed, I would never leave. At that time, I could leave freely. I could go back and pursue the things that I truly love, taking photographs and making films. It was a tremendous experience going through medical training and caring for patients.

COSTELLO: How do you use your medical training for your art?
AGUILERA-HELLWEG: First, it has given me a level of depth and understanding of the human body and human nature. As a photojournalist, basically I am always persistent. I don’t take no for an answer. In a health care setting, I do take no for an answer. I am acutely aware of the stress the patient’s under or the doctor is under and what might go wrong. I have a proper sense of reality in the operating room. It is reverential.

COSTELLO: Do you have a favorite medical photo?
AGUILERA-HELLWEG: My most favorite picture is a photograph I took at an autopsy. His gut is open and you see all his viscera but they are using a common soup ladle to get out the fluids that had dispersed into his open abdominal area. There are two doctors in the photo; one has a Pyrex quart-size measuring cup in his hand, in which they were collecting the fluids. A soup ladle and a Pyrex cup. It just was so truthful. It just is what it is. Nothing more. Nothing less.

COSTELLO: Is there a bridge you hope to create between art and medicine?
AGUILERA-HELLWEG: I would hope it is to accept our frailty, to accept our mortality and to appreciate life. When I was taking care of patients, most people thought they were going to live forever. Well, we don’t. Hopefully, my photography de-mystifies the human body and makes people appreciate their lives. Most people look at hospitals from afar. You drive by, “Oh, there’s a hospital.” There are incredible things going on in a hospital all day long, all night long — stories of people fighting for survival. When you drive by, you oblivious.
I am an ophthalmologist who loves art. While I have studied the physiology of the retina, I have also studied the role of vision in art. And I have seen how exposure to art and to the humanities is useful to medical students: Art appreciation won’t cure kidney disease, but it enlarges experience, culture and communication—and in that sense helps make better doctors.

I’ve taught undergraduates, medical students and physicians at Stanford for many years about vision and art, exploring how eyes are built, how they process visual information and how they are affected by disease.

Of all aspects of vision, color always seems especially fascinating. And yet, color is a strangely superimposed sense because our ability to see different hues evolved long after retinal circuitry was developed for contrast, form, depth and motion (which depend only on brightness). Thus, color vision has surprising implications for art, beyond the mere presence of a spectrum—and art can elucidate the physiology.

What follows is a collection of insights into how we see color and how artists use it, consciously or unconsciously, to shape their work.

Photoreceptor cells in our retinas (the rods and cones) receive light and change it to a neural signal. But they cannot transmit images directly to the brain because we have 120 million photoreceptor cells and only 1 million optic nerve fibers. The retina must code and simplify the visual information, and in a very real sense we begin to think about what we see inside the eye. Retina is embryologically brain, and retinal cells process the photoreceptor signals to recognize contrast and to fix upon light-dark boundaries. This codified information, such as the edges of objects or faces, lets the brain reconstruct a visual world.

Where does color fit into this system? Humans can see a wide range of colors because we have three different types of cone photoreceptor cells. The rod cells are sensitive only to dim light and serve our night vision without seeing color. The cones work over a broad range of brighter light, and each of our cone types is predominantly sensitive to blue, red or green light. However, even though different colors produce a different pattern of stimulation among the three cones, color recognition is not quite so simple. Because the innate circuitry in the retina is wired for comparisons and contrast, colors must also be analyzed this way. The retina actually compares the amount of blueness with yellowness, and redness with greenness, and it is the balance of these comparisons (rather than absolute wave-
length) that ultimately allows the brain to recognize a sensation of color. And there is another problem. Although colors are analyzed by blue-yellow and red-green comparisons, the basic circuitry that identifies edges, form, motion and depth responds only to changes in brightness. These discriminations are colorblind, and the sensation of color is superimposed later in the brain upon a “black and white” image of the world.

One positive effect of the comparative nature of color perception is that it helps us maintain constancy in the way we see colored objects under different conditions. It would be distressing, for example, if faces changed color when we went from indoor lighting to outdoor lighting. This is illustrated in FIGURE 1, which shows a Rubik’s Cube in white, yellow or blue light. We recognize the different colors on the cube despite the altered illumination because their relationships to each other within each cube are unchanged (even though two “red” squares have quite different colors when seen in isolation above the photographs). Artists have to face this same perceptual conundrum, especially an artist like Claude Monet, who liked to paint the same scene in different seasons and lighting — creating, for example, 25 paintings of haystacks, more than 30 of Rouen Cathedral and roughly 250 of water lilies in his garden. He had to make decisions on whether to paint what he perceived or what he knew to be true. FIGURE 2 shows some of the variations in colors of his water lily leaves.
The fact that brightness trumps color in judging form is well-illustrated in FIGURE 3, which shows a drawing by German expressionist Ernst Ludwig Kirchner, with yellow buildings and green trees — except that none of the colors are placed accurately within the lines. Somehow this is not very disturbing, and the drawing is lovely, because we recognize the subjects from the sharp black outlines that stimulate form and depth perception. Our brain fills in the colors for us.

An even more striking illustration depends on the property of “equiluminance,” or equal brightness. Since we need light-dark contrast for recognition of objects and depth, different colors that have the same physical brightness do not define objects very well. FIGURE 4 shows a simple statement that would be clear in black print, but it is nearly invisible when written in green letters with the same luminance as the red background. The text disappears in a grayscale (brightness-sensitive) image.

Artists are taught in school not only about colors having hue and saturation, but also having “value” — the art-speak term for brightness. Awareness of value is necessary to avoid unwanted illusions, such as an image that’s barely discernible from its background. Kirchner again gives us a good example, as you can see in FIGURE 5. His up-rooted tree in the forest is hard to recognize because the blue trunk and green leaves have similar brightness, as do the rocks near the bottom. You can see this confusion in the grayscale version. We don’t know whether Kirchner planned this deliberately, but he surely recognized the effect. His portrait of a woman with an unrealistic blue face is very different, and the face is easily recognized because her dark eyes, mouth and hair contrast normally with her lighter, albeit blue, skin.

One of the more magical effects artists can create with color is a sense of flicker or movement. Adjacent areas of equiluminant color appear unstable because they have equal brightness and do not activate recognition of form and location. Monet used this effect strikingly in his painting Sunrise (Marine), FIGURE 6, which is a companion to the famous Impression, Sunrise that gave the Impressionist movement its name.
pink reflections on the water are nearly equiluminant to their surroundings, and thus they glow and shimmer in a way that high-contrast white spots would not.

Ophthalmology has heightened my appreciation of art, and a love of art has broadened my outlook as a physician in our complex and diverse society. Medical school is long and arduous, and we might do well to keep our students in touch with the arts and history.

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a new rhythm
DANCE BENEFITS PARKINSON’S PATIENTS

Sherry Brown walks gingerly into the dance class, her right elbow anchored at her side, her hand cupped in a ball. Her balance is uneven, so she takes care in finding a seat among the circle of chairs in the light-filled room at the Stanford Neuroscience Health Center. As the slow, rhythmic keyboard music begins, her arms, stiffened by Parkinson's disease, open in a wide, upward arc as if embracing the sky.

“You get a sense of your body and are pushing your body to do things you don’t think you can accomplish,” says Brown, who was diagnosed in 2008 with

BY RUTHANN RICHTER
PHOTOGRAPHY BY TIMOTHY ARCHIBALD
the neurodegenerative disease. “There is something about
the music and movement together that seems to help at a dif-
ferent level. … I come out of the class feeling energized and
relaxed, all at the same time, and ready to move.”

Brown is among some 20 students who have found a wel-
coming community at the Dance for Parkinson’s Disease
class, also known as Dance for PD. The class is not only
physically therapeutic but often gives students a psychologi-
cal boost. People struggling with movement and speech be-
cause of the disease say the sessions are liberating, providing
a new way to express themselves.

The program, begun 15 years ago in Brooklyn, New York,
and now offered in 16 countries, was introduced at Stanford
last year with the opening of the new neuroscience center. It
is not a traditional dance class in any sense, but rather a group
also are learning to be in their bodies in a conscious way.”

Brown, 74, gray-haired and slender, is a marriage and
family therapist who maintains an active social life despite
her physical challenges. She says the disease crept up on her,
gradually narrowing her world. Her movements became
slower, more labored, and she no longer easily stood straight.
She began to feel some weakness in her right hand, which
would tire after writing a few words. She would easily lose
her balance and began to have debilitating falls, including
one in which she broke her hip and another in which she
struck her head on a rock while sweeping the walk outside
her home. When she was diagnosed with Parkinson’s, she
says, she fell into despair.

“I definitely went through a grieving period. I felt like my
life was over,” she says over a cup of tea at her dining room
table. She now has a part-time personal assistant who helps
around the house, though she is able to prepare the tea herself.

Parkinson’s, which affects as many as 10 million people
worldwide, can cause rigid limbs, tremors, lack of muscle
control and slowed movement. Patients may have impaired
walking and balance and are more prone to falls. Some also
suffer from depression and may experience a cognitive de-
cline, with slowed thinking or memory problems.

Brown says daily tasks became a challenge, as she could no
longer stab a piece of lettuce with a fork, handle a pair of scis-
sors or easily get up out of a chair. She stopped accepting new
referrals to her therapy practice. She no longer drove on the
freeway and began to miss out on important social occasions because of disease-related fatigue.

“I spent about a year really being aware of all the losses,” she says.

Gradually, however, her life began to open up again as she came to a place of acceptance and began to improve physically with the help of new medication, physical therapy, fitness training, daily walks — and dance.

**On the move**

During a recent Friday session, Ganley, a petite woman with short-cropped hair, opens with some gentle stretching exercises in the chair, as the keyboardist plays his own rhythmic composition, which has an ethereal quality. Participants, seated in a circle, cross their feet back and forth, then move one foot to the right while gesturing to the left. The sequence is repeated on the opposite side, requiring focused concentration.

“That tickled my brain,” Ganley says with a smile. Then she begins a sequence of movements to the lyrics “Autumn leaves are falling, falling” as the dance students join in, rolling their hands in space like leaves being tossed in the wind, then gently falling down.

The class has many interactive moments, including one in which the instructor prods the students to “say something with the body” to a neighbor in the circle, who responds in kind. The exercise is repeated with a different partner, and the results then are displayed for the entire class. “Beautiful,” Ganley says as heads nod.

On this day, the 75-minute session includes other improvisational exercises, as well as a traditional Israeli circle dance with a rather challenging series of steps. It closes with dancers individually calling out their names, then using a gesture to express what they are grateful for. Some blow kisses; others use a sweeping move of the arm to encompass everyone in the room. “Each of us is a living poem to be savored and acknowledged,” Ganley says.

Brown, neatly dressed in black pants and a tailored shirt, says the class has a mindful, meditative quality. “It’s totally creative and totally accepting of whatever your abilities are,” she says.

With her new medication regimen and her physical activities, she is able to do many things that weren’t possible before. For instance, in one class, she found she could again...
stand on her toes and keep her balance. And during a flamenco dance routine, she found herself snapping her once-rigid fingers. “It just came to me,” she says. The dance class “challenges you in ways you would not have thought possible.”

The class also has helped improve the fluidity of her movements. “I think the rhythm helps keep things more even. I feel my gait is more even. In general, my body feels more in tune — more rhythmic. It’s subtle.

“I think it has helped me a lot to appreciate what I can do — big and little things both,” she adds. “I feel that with all things I am doing — the exercise, the dance, the medications — I am definitely delaying the severe symptoms of the disease. I am pleased that I am able to have the life that I have at this point.”

The program was started in 2001 by Olie Westheimer, executive director of the Brooklyn Parkinson Group, who walked into the Brooklyn studio of the Mark Morris Dance Group one day with the idea of creating a dance class for members of her group, says David Leventhal, a former Mark Morris company member who is now Dance for PD’s program director. Westheimer felt patients were spending a lot of time dwelling on the disease and shuttling to doctors’ and therapists’ offices, and she wanted them to do something positive and beneficial together. Leventhal became one of the first instructors.

“I thought it was the most enjoyable teaching experience I had ever had because people were so focused on learning and trying to absorb as much as we had to offer,” Leventhal says. “They were so engaged as students right away because for them it was not just an activity they added to their week but an essential portal for them to experience what possibilities were still available to them. It became a way of accessing their true selves — who they were as people, rather than as patients.”

Helen Bronte-Stewart, MD, a Stanford professor of neurology and neurological sciences and a former professional dancer, says she has always tried to incorporate exercise, yoga and dance

‘the PD dancers
HAVE TOLD US THIS TYPE OF DANCE
RESTORES THEIR SELF-IMAGE
AND BRINGS THEM JOY.’
as part of the standard therapy for her Parkinson’s patients.

“If you improve your core strength, then the negative effects like difficulty of getting out of chairs, getting out of a car, will be better,” says Bronte-Stewart, who refers to the process of exercise and balance training as “training the machine.”

“You have to keep training that motor system — training the brain — as a way of continuing movement in a disease that otherwise limits movement, counteracting the stiffness and slowness that the brain wants to impart on the musculoskeletal system,” she says.

“As physicians, we stress the importance of physical activity, social interaction and mental stimulation to our patients with Parkinson’s disease,” she adds. “Dance for PD gives them all three. But it is much more than a possible therapy or treatment; the PD dancers have told us this type of dance restores their self-image and brings them joy.”

When the neuroscience building was in the planning stages, Bronte-Stewart says she was determined to include a dance studio and helped design the space with a flexible floor and glass walls on two sides. She and Ganley obtained a grant from the National Parkinson Foundation for the class, which is free and is open to all in the community.

“The worlds of dance and medicine have been far apart for a long time. That is why this is so exciting,” Bronte-Stewart says. “If you have a chronic debilitating disease, you begin to get an image of yourself as someone who can’t move. But you can go to this class and do something beautiful and graceful and be part of a community that accepts you. That is what we should capture, as much as whether your motor function is better.”

**Backed by research**

Leventhal says the program initially met with some skepticism in the medical community.

“There was one neurologist who told us, ‘I think the program is great. But I can never recommend it because dancing is a frivolous activity and that would tarnish my reputation as a serious doctor,’ ” he says. “There is a lot of misconception about the amount of learning and skill and brain work and physical work that somebody has to do to execute a dance. It’s the opposite of frivolous. It directly addresses what people are struggling with. Over 15 years, people have come to recognize that.”

In fact, published studies have shown that Parkinson’s patients who do some form of dance experience measurable physical and psychological improvements. More than a dozen studies have shown that twice-weekly dance classes improve balance, motor skills, freedom of movement and endurance. One study, published in 2011 in *Frontiers in Aging Neuroscience*, found that even after a single class, patients were able to move their limbs more easily, tap their fingers and change their facial expressions. (Loss of facial muscle control can lead to muted expression.) The study participants also described many improvements in the quality of their lives, with one saying, “I want to fly. It gives me a swinging feeling. I feel relaxed after the dance lesson. Before, I’m always very stiff.”

Research suggests dance has benefits beyond basic exercise for these patients because it is a rich experience involving multiple senses, creative expression and social interaction. Moreover, unlike exercise classes, participants are motivated to attend, rarely

**WEB EXTRA**

See Stanford’s Dance for PD class in action at http://stan.md/2kH6Gmj

CONTINUES ON PAGE 40
picture imperfect
children depict chronic pain  

By Erin Digitale

By the time she sees them, psychologist Anya Griffin’s young patients have been in pain for months to years. In 2015, concerned that standardized questionnaires and 1-to-10 pain scales didn’t give a personalized view of their struggles, Griffin, PhD, decided to try something different.

Then newly hired as clinical director of the Pediatric Rehabilitation Program at Stanford Children’s Health’s Center for Rehabilitation Services, Griffin borrowed an approach that originated in public health research: asking patients to take photos to convey their perspectives, a method called photovoice.

Many of Griffin’s patients have complex regional pain syndrome, in which pain from an injury spirals out of control. The nervous system magnifies sensory input so that the lightest touch can cause fiery pain. Young people with the condition stop attending school, hanging out with friends, playing sports, taking music lessons, feeling like normal kids. The pain becomes its own disease.

“I am not in their bodies and I can’t possibly know what that experience is like,” Griffin says. “I wanted to capture that so that I understand what they’re experiencing and how it impacts their lives.”

The photovoice project is supported by a Medicine and the Muse seed grant, which helped fund the purchase of cameras for patients to use. At the conclusion of the rehabilitation program — which lasts four to 12 weeks and includes medical evaluation and treatment, intensive physical and occupational therapy, and individual, group and family sessions with pain psychologists — Griffin has each patient pick a “before” and “after” photo and explain them. Here are two examples; a third is available on our website at http://stan.md/2kjZU8j.
“That was one of my very first days in the program,” says Laura, 14, of the photo of herself making blue footprints. A dancer before she fractured her left foot at age 10, Laura (a pseudonym) had been in pain for three years by the time she started the pain rehabilitation program in May 2015. The pain had spread all the way to her left hip, leaving her unable to walk without a cane. Dancing, singing and other art forms she’d once loved had fallen out of her life.

Painting with her feet was kind of fun. “But I couldn’t concentrate on the fun,” Laura says. “I was just constantly making sure I wouldn’t fall, focusing on the pain in my foot.”

Partway through the program, Laura videotaped herself and several other patients dancing. “When I was having a really bad pain flare-up, I’d go back and watch that video,” she says. “I’d think, oh yeah, I can do this! The pain isn’t everything. It isn’t me.”

By the time Laura’s parents took her to her grandma’s farm to celebrate her rehabilitation, she had progressed from walking without a cane to walking without a limp to running. With her CRPS in remission, she could also sit in the grass and feed her grandma’s goats, which would have been impossible a few months earlier.

“In the second photo I was finally at peace with myself,” she says. “I wasn’t battling my foot.”

When she entered the rehabilitation program in May 2015, 15-year-old Lily (a pseudonym) had excruciating pain in her left leg and her right arm, the symptoms of 10 months of CRPS. She was in a wheelchair and taking so many medications that she has little memory of the period. “My life was shattered; there was no putting it back together,” she says.

But with treatment, her life did come back together in a new way that she depicted in the second photo. “You can see it’s even more beautiful with all the different pieces. If you hold it up to the light it shines through and has this beautiful mosaic effect.”

Lily’s mom remembers how her initial bewilderment at watching Lily break the blue glass in the photos gave way to new understanding. “She said, ‘See all these jagged edges? That’s the pain. It hurts, and nobody can touch me.’ It put a new picture in my head of how bad it was for her.”

— Contact Erin Digitale at digitale@stanford.edu
WITH 10 MORE WEEKS until her baby was due, Sunnyvale mother Sici Tsoi’s ultrasound looked good, her doctors said. But her baby’s heart rate was slow. Her doctors sent her to a San Francisco hospital for a second evaluation, but the new medical team told Tsoi the same thing. The structure of the baby’s heart looked fine, but something was wrong with the heartbeat.

Scheduled for an emergency C-section, Tsoi checked into Lucile Packard Children’s Hospital Stanford, where doctors pulled baby Astrea from her mother’s womb and swiftly took the infant away.

Tsoi had two healthy daughters at home, and so she and her husband, Edison Li, assumed the doctors would make sure Astrea was fine.

Even hours after Astrea was born, Tsoi and Li waited patiently to hear how their new daughter was doing. They hadn’t even seen her, remembers Tsoi, and she and her husband just hoped for the best. “All I knew was that I gave birth, and I was very happy.”

By Jennie Dusheck
Illustration by Jason Holley
A strea was anything but well. Every few hours, she went into cardiac arrest, and it was all her doctors at Packard could do to keep her alive. The struggle to save her included a genetic analysis that eventually morphed into a study of genetic mosaicism, a condition in which some of a person’s cells carry different gene variants than the rest. Mosaicism could explain many undiagnosed conditions. In September, a team of researchers published their study of Astrea’s heart in the scientific journal Proceedings of the National Academy of Sciences.

Getting on the Case
While Astrea’s parents waited calmly for word, Astrea was fighting for her life. Her doctors quickly diagnosed her with a heart arrhythmia called long QT syndrome. In long QT syndrome, a segment of the heart’s rhythm — the time between the start of the Q wave and the end of the T wave — is a little longer than normal. It’s often caused by a genetic defect and can be mild or severe.

For Astrea, the defect was severe. And, despite excellent care and treatment with different drugs known to help long QT syndrome, the medical team couldn’t keep her heart beating. They hoped that knowing the nature of the gene defect causing the problem would help them choose the right drug. But that would take time to discover and they didn’t have time.

When Tsoi’s doctors came to see her the morning after Astrea was born, she thought they were coming to check on her. She was surprised to learn that they were there to tell her that Astrea would soon be undergoing surgery to implant a pacemaker, which would regulate her heart rate better, as well as an implantable defibrillator, which would kick start her heart each time it stopped. Tsoi and Li were only now beginning to realize how possible it was that Astrea could die.

The pacemaker and defibrillator would give Astrea’s doctors time, but they knew it might not be a long-term solution. And knowing what kind of genetic defect was causing her heart to malfunction could help, too. Fortunately, just hours after Astrea was born, her case was discussed at a regular weekly meeting of Stanford Medicine’s Center for Inherited Cardiovascular Disease. Present were experts in cardiovascular genetics who could help, including Euan Ashley, FRCP, DPhil, and James Priest, MD.

“We realized how sick this child was,” Priest says, “and we had a new tool — rapid whole-genome sequencing — that could make a faster and more comprehensive diagnosis than the available clinical genetic testing. So that night I went and talked to the parents and the rest of the team, collected a blood sample and we started the test.”

On Astrea’s third day of life, Priest, an instructor in pediatric cardiology, looked at the DNA from her blood cells for any of several gene variants known to cause long QT syndrome. He found a suspicious mutation, but he immediately ran up against two problems.

First, he wasn’t positive that the mutation was capable of causing a heart problem as serious as hers. Second, the abnormal DNA was present in very small amounts. It didn’t make sense. Strands of DNA come in pairs, one from the mother and one from the father, so he’d expect half or even all of the DNA to have the mutation. Instead it was just 8 percent.

Because of that odd ratio, Priest wondered if Astrea might be a mosaic of two kinds of cells, normal and deadly. It was possible, he knew, for a mutation to have occurred when her cells were first dividing as an early embryo, just hours after conception, leaving a small lineage of related cells marked for a separate fate.

He suspected the deadly genetic mutation causing the problem might be hidden away deep inside Astrea’s heart.

But it would take a diverse group of nearly 30 researchers at many institutions, and a combination of some of the fastest and most cutting-edge genome sequencing ever conducted, to uncover the mystery of her illness.

Connecting the Dots
Once newborn Astrea had her two implants, she spent six weeks at Packard gradually recovering from open heart surgery and undergoing more tests. But no one knew how long the implanted pacemaker and defibrillator would keep her alive and the genetics team scrambled to find out what was making her heart stop.

Connecting all the dots was a huge challenge. “It was two to three weeks of high-intensity work and about as dramatic as it gets,” says Ashley, a professor of medicine and of genetics who directs the Stanford Center for Inherited Cardiovascular Disease and co-directs Stanford Health Care’s Clinical Genomics Service.

First they had to confirm that the variant was real. They did this by turning to colleagues at a sequencing firm called Personalis, which Ashley had co-founded with other Stanford faculty. “The Personalis team dropped everything and
came in weekends to carry out in-depth sequencing of Astrea and her parents,” says Ashley. The company’s scientists established that the gene variant was real and present in Astrea’s cells but not in her parents’ cells. That showed that it was a new mutation.

To find out if the particular mutation they had identified could cause long QT syndrome, Priest and Ashley gave the sequence to a team of collaborators at Gilead, a company that designs drugs to treat the disease. Gilead reported that the gene variant would cause long QT syndrome. Moreover, they said, this particular mutation was especially deadly.

Next the Stanford team wanted to be sure that Astrea really was a mosaic individual; they needed to show that individual cells actually had different genomes, some carrying the deadly mutation, some healthy. Each cell’s genome would have to be individually mapped. “That field was founded by Stephen Quake,” says Ashley, “so having him here at Stanford, I called him and asked if he could help.” Quake, PhD, a professor of bioengineering and of applied physics, and his team were able to look at individual cells from Astrea’s blood and show that most of her cells had normal genes, but 8 percent carried the mutation for long QT syndrome. Astrea’s blood cells were definitely mosaic. But it wasn’t yet clear if her heart tissue was also a mosaic.

As the weeks passed, Astrea began to struggle. Despite the implanted pacemaker and defibrillator, she developed an enlarged heart. At 7 months old, she looked healthy to her parents. But the defibrillator was going off frequently and sending silent signals to the hospital staff. Alerted by the signals, Astrea’s doctors told Tsoi to bring her baby in; Astrea was in grave danger, they said.

Once at the hospital, her heart stopped again. She needed a heart transplant, and her name was quickly added to a waiting list for a donor heart. Tsoi says, “I thought it would be at least a year of waiting.”

But only five weeks later, someone from Stanford called. “Are you driving? Are you in a safe place?” the voice asked. It was news of a donor.

On the day of the transplant, Tsoi and Li took their two older daughters and picnicked on the Stanford campus, waiting patiently once more to hear news of Astrea. In the evening, when the surgery was over, they went to see her. “The first thing I saw was the monitor,” says Tsoi. “That was the first time I’d ever seen the green line — the heartbeat line — so stable and regular.”

As a transplant patient, Astrea’s problems weren’t over, but her healthy new heart enabled her parents and doctors to breathe easier.

The pressure on the genetics team to understand her condition was lessened. And the tissue from Astrea’s original malfunctioning heart allowed researchers to determine that, indeed, 8 percent of the heart cells carried the deadly mutation they believed had been causing her long QT syndrome.

By now, Astrea’s mosaicism had become a problem of intense academic interest, initially triggered by the desire to help the baby. The team wondered if a heart with just 8 percent mutant cells could really have caused Astrea’s severe long QT syndrome. That was so few cells. Wouldn’t the 92 percent healthy cells have prevented such severe effects?

The Stanford team contacted colleagues in the computational cardiology lab of Johns Hopkins professor of biomedical engineering Natalia Trayanova, PhD, experts in the computer modeling of cardiac electrical activity. Their eventual computer model of a heart with a mosaic of healthy and mutant cells in the organ’s electrical tissue acted exactly the way Astrea’s real heart did. “It was an important moment: A mosaic heart really could cause heart block and cardiac arrest,” says Ashley.

MIGHT OTHER HEART PATIENTS BE MOSAICS?

The team had solved the genetic mystery. Not only did they diagnose Astrea’s problem but they had also revealed a new way to identify what might be causing genetic diseases that have no obvious source.

“We’d thrown everything we had at diagnosing the baby,” says Ashley, “but still we wanted to know, how common is this?”

To find out how often mosaicism might explain undiagnosed arrhythmia, the team partnered with a genetic testing company with a database of arrhythmia cases. “We asked them, ‘How many cases of mosaicism have you seen when you looked at genes that cause arrhythmia?’ The answer was about 0.1 percent,” Priest says.

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Last spring, *The New Yorker* published a piece on epigenetics and cancer that triggered a storm of complaints from molecular biologists, who called the article “misleading” and even “horribly damaging.”

The article’s author, Siddhartha Mukherjee, MD, DPhil, an assistant professor of medicine at Columbia University, issued a rebuttal. But even after the dust settled, many seemed to agree that Mukherjee had ignored traditional genetics and that his description of epigenetics — how cells regulate the activity of genes — was too streamlined to satisfy the biologists.

Yet it likely wasn’t just Mukherjee’s approach that triggered the anger. Cancer researchers are beginning to embrace a new paradigm: that how cancer cells behave and evolve is a response to their environment, not just to genetic mutations. That paradigm is meeting significant resistance from researchers who have spent a lifetime with the idea that cancer cells result from mutations.

“There’s definitely an old-school crowd who think if we just sequence deep enough, we’ll solve all the problems,” says Alexander Anderson, PhD, chair of integrated mathematical oncology at the Moffitt Cancer Center, in Tampa, Florida. Epigenetics, he says, is transforming our concept of cancer biology.

**BY JENNIE DUSHECK**

*Photograph by Timothy Archibald*

Parag Mallick showed that cancer cells could become 40 times more drug-resistant without genetic changes.
BEYOND MUTATION
FOR DECADES, RESEARCHERS HAVE ACCEPTED THE IDEA THAT CANCER RESULTS from genetic mutations in individual cells. And indeed if you look at tumor cells, they differ genetically from healthy cells nearby — sometimes dramatically so. The theory has been that a carcinogen, such as asbestos or cigarette smoke, induces mutations in a cell’s DNA that eventually cause it to become cancerous. That bad cell and its descendants multiply faster than healthy cells and take over.

But, strangely, most of the things that cause cancer, including tobacco smoke and asbestos, don’t cause genetic mutations. Rather than modifying the genes themselves, smoke and asbestos alter the activity of genes through a collection of processes called epigenetics.

Epigenetics consists, among other things, of tiny modifications — either to the DNA itself or to proteins called histones that wrap around the DNA and change the activity of the genes. (Like Mukherjee, we are leaving a lot out.)

For example, if you spend every weekend gardening, changes in the activity of genes in the skin cells of your hands will produce callouses. Our callouses might seem very ordinary to us; they come and go depending on what we’ve been up to recently. But what if the genes whose activity changes to produce them could mutate so that our callouses became permanent? What if some babies were born with calloused hands?

Amazingly, modern evolutionary biologists are moving to the view that that’s exactly how wild plants and animals often evolve. It all starts with the phenotype, which is every single trait of an organism or cell — everything but the genes. The phenotype includes the enzymes encoded by genes, myriad metabolic pathways, the shape of a nose or the hands, a vast repertoire of behavior and even memories of an equation or a loved one.

We already know that the same genes can produce alternate phenotypes, depending on just how the genes are expressed. That phenotypic plasticity delivers different castes of ants, all from the same genotype; hands that look different from our feet, even though they have the same genotype; and identical twins of different heights and personalities. All these changes arise from the way the immediate environments of cells, organs or whole individuals interact with genes. The differences in gene activity are mediated by an array of hormones, transcription factors and other mechanisms.

‘GENES ARE FOLLOWERS, NOT LEADERS’
EVOLUTIONARY BIOLOGIST MARY JANE WEST-EBERHARD, PHD, ONE OF THE LEADERS OF THE movement to reframe evolution, has laid out the experimental evidence showing that the plasticity of an organism’s characteristics, or phenotype, foreshadows its evolution. In essence, you can start with an epigenetic variant — think calloused hands — and later that particular trait can become permanently fixed in the genes. In fact, ostrich chicks do just that, hatching with callouses that help protect their young chests from the hot, rocky ground.

Famously, West-Eberhard, staff scientist emerita at the Smithsonian Tropical Research Institute, said, “Genes are followers, not leaders, in evolution.”

Now that same idea of genes as followers is invading the theory of cancer. It seems that cancer cells, too, can first begin to change through temporary epigenetic changes, instead of by means of mutations in the DNA.

A SYSTEMS APPROACH
“THERE’S A FEELING IN THE FIELD THAT WE HAVE TO START THINKING MORE HOLISTICALLY,” Anderson says. And the key to that, he says, is math.

One of a few researchers with a strong understanding of both cancer biology and the mathematics needed to build a new model of cancer based on a systems approach, says Moffitt Cancer Center’s Anderson, is Stanford assistant professor of radiology Parag Mallick, PhD.

Mallick, who works at the Canary Center at Stanford for Cancer Early Detection, describes a paper he and his colleagues published in May 2016 in Genome Medicine: “We found that when you treated cells with a chemotherapeutic
that drives Mallick’s research. Viewing cancer as a dynamically evolving adaptive system, his team aims to discover what triggers their sudden transformation, or state changes, from quiet and comparatively harmless tumor cells into peripatetic, metastatic cells that migrate all over the body, invading and altering other tissues.

When cancer cells transition to metastatic behavior, it can happen quite suddenly, says Mallick. Nonmetastatic tumor cells might sit quietly inside a tumor with a clear boundary. But when metastasis starts, they break through the wall of the tumor and launch themselves out into the rest of the body. “Cancer cells will spontaneously start to move in one direction,” he says. But what makes cancer cells suddenly get the travel itch? And more generally, adds Mallick, “What are the origins of such state changes? How do you describe them? How do we model them? What’s governing their behavior?”

Of course, the behavior of cancer cells, like that of healthy cells, is hugely complex. For example, cells might behave in a cancerous way for reasons that are deep in their genes, or the change could be driven by signals from the environment. And metastatic cells might circulate in the blood for long periods before beginning to colonize other parts of the body.
Yet we do know that no single governor gives a top-down order to all the cells; instead, just like a flock of birds taking wing, the cells all begin moving at once, responding to one another.

BUILDING THE MODEL

In an attempt to detect, predict and prevent such transitions, Mallick and his colleagues’ massive computer model of cancer will include every level of organization, starting from molecular processes and the behavior of individual cells to the growth of whole tumors and their metastasis, as well as immune responses throughout the body. “We’re working on coalescing all of that information into what, in our mind, is the first-ever truly multiscale data set,” he says.

Mallick’s forte is finding ways to connect all these different levels of organization. One connection is the sudden transition from the independent behavior of cancer cells to group behavior. Another might be a nutrient gradient across a tumor that connects the effects of nutrients on individual cells with those on the whole tumor.

“If you are modeling water,” he says, “there’s a particular sort of math that you use to describe the behavior of single atoms, and a very different sort of math for describing the flow of rivers.” For a multiscale model of water, you would need a way for those two to connect.

The ultimate goal of the model is to explain cancer, but it also has immediate medical uses. For instance, Mallick is using the model as a tool to help identify markers of important transitions in the life of populations of cells — to cancer, to drug resistance or to metastasis. Such markers are essential to developing tests for diagnosing cancer and for investigating how patients respond to treatment over the course of their disease.

Our understanding of cancer biology has taken off in recent years, but it’s not yet clear where it’s leading researchers. Just as it’s difficult to see which way the individual birds in a flock will turn from moment to moment, it’s difficult to predict which discoveries will transform our understanding of cancer. But changes in the understanding of both basic evolutionary biology and systems biology are helping researchers see things in new ways.

— Contact Jennie Dusheck at dusheck@stanford.edu

FEATURE Expressions

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This interview was condensed and edited by Paul Costello.

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Dance

People tell us, ‘I always look forward to coming to class because it’s so uplifting,’ Bronte-Stewart says.

She says dance is a form of mental as well as physical training. “When you think of it as a neurologist, they are planning, using their executive function and they are sequencing. These are all frontal-lobe functions that can be impaired in Parkinson’s.”

Bronte-Stewart says animal studies suggest there may be a biological basis for improved neurologic function among dance participants. For instance, research shows that if animals are able to do a physical activity they enjoy, they experience less inflammation, which may help counter the disease, and are able to regenerate adult stem cells, which can help build muscle and other tissues.

“It’s not too much of a stretch to suggest that dance possibly may improve the brain’s regeneration of its own stem cells,” she says.

Dance classes may also counter some of the cognitive and mood issues that affect patients, who may withdraw and suffer social isolation and poor self-esteem. The classes provide a social setting where everyone is accepted, regardless of their limitations, and studies show participants feel their mood lighten and their anxiety decline. In a 2015 study published in Journal of Neural Transmission by Westheimer and colleagues from four universities, participants reported feeling less helpless, grateful for the companionship and a general sense of improved health.

Albert Cohen, one of the Stanford dance students, says he appreciates the sense of camaraderie and caring among the students. “The attitude there is positive and receptive, which is worth a lot,” says Cohen, 87. “I’m not sitting in a room doing nothing. So it’s very beneficial.”

A musicologist and former chair of Stanford’s Department of Music, Cohen suffered a major fall in the summer that fractured his hip and pelvis. When he and his wife, Betty, returned after a two-month hiatus, class members embraced them with hugs and good wishes. Betty Cohen says the gathering is the highlight of her week.

“You’re getting out. You’re with other people. You are exposed to music, which helps the brain. There is rhythm and movement. I think all of this is helpful,” she says. “It really is more than the dance and the music. It’s greater than the sum of its parts. Something emanates from the heart and soul. It helps me...
emotionally accept everything that I’m finding hard to accept.”

Caregivers are encouraged to attend the classes to support their partners and to share a positive experience. “I think the class allows care partners to see their loved ones and companions in a different light and enjoy an hour together when they are not dealing with the struggle of daily life but see each other as dance partners and as co-learners. That’s very important,” Leventhal says. Stanford medical students and undergraduates also participate in the class through specially designed coursework.

Juan Bulnes, who was diagnosed with Parkinson’s in 2008, regularly attends class with his wife, Margaret. He often does the movements in his chair, as he is shaky on his feet and afraid he will fall, he says.

“There is joy in the dancing class,” says Bulnes, a 74-year-old computer scientist. “We do some of the same movements as in other classes, like tai chi or physical therapy, and here we do them with an added, special flair that comes from conscious dance movements, such as gracefully waving your hands to imitate falling leaves, rain, wind or reaching for the stars. Integrating physical exercise, rhythm, music and imagination makes dancing a very liberating experience.”

LEVENTHAL, who gave up performing five years ago to devote all of his time to the project, has been making the program more widely available and providing opportunities for practice between classes. The flagship Dance for PD program in New York has developed three DVDs, which have been distributed to 4,000 people worldwide, and last year began live streaming classes from Brooklyn and Toronto.

Mark Morris Dance Group, together with the New York creative agency SS+K, has also created Moving Through Glass, custom software for use on the Google Glass platform to help Parkinson’s patients navigate the world outside the dance studio. The application enables users wearing the device — a head-mounted display in the form of a pair of eyeglasses — to play modules in which Mark Morris dancers give prompts, taking them through home exercises to help with specific problems, like regaining balance or unfreezing the limbs. The app is being evaluated at three locations around the country, including Stanford, where Bronte-Stewart has recruited dance class participants to try it out.

Dance for PD, meanwhile, is becoming a widely accepted form of Parkinson’s therapy. Stanford recently added a second class that meets on Monday afternoons.

Sherry Brown attends both the Monday and Friday sessions, as she is determined to do what she can to forestall any further physical decline. “I do have fears about the future and there’s nothing I can do about that. I like to stay in the present as much as I can,” she says.

The dance class helps set aside her fears, at least for the moment. “It has helped me adjust to the future. It becomes a little less scary about the unknown, seeing other people go through it,” she says. “It focuses you on the present, and the rest of your worries fade into the distance. You are focused on the here and now.”

— Contact Ruthann Richter at richter1@stanford.edu

FEATURE

MAKE IT MORE ACCESSIBLE

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The team’s work may offer a new way to finally determine the cause of arrhythmias that previously had been a mystery, says Priest. About 30 percent of heart arrhythmia patients don’t have a genetic diagnosis. “Maybe,” he says, “there are additional mutations that are in the heart only. Genetic tests are nearly always done on blood or other easily acquired tissues. So it’s easy to imagine a mosaic gene variant that occurs only in the heart and doesn’t show up in the blood.” The same reasoning, he says, could apply to other parts of the body.

“And that really is a brand-new phenomenon,” Priest adds. Until recently, he says, no one has thought of looking for mosaic gene variants as the cause of these kinds of diseases.

“I think there’s enough evidence now to suggest that a large number of people have some level of mosaicism,” says Ashley. That said, the genetic mosaics are probably harmless in most people. This one just happened to cause severe effects, even if only in a few cells.

Whether Astrea might have other health effects from the mutation is unlikely but not impossible. Astrea’s mother says that when her daughter was first born, “we asked, ‘Is she safe now? Is she stable now?’ One of the doctors told me, ‘We don’t know. But even for your two older girls, there’s no guarantee they’ll be healthy tomorrow. So treat Astrea like a normal kid and make every day count.’”

Tsou says this advice inspired her to become a different kind of mother. “I used to be very strict, but since that day whenever I want to do something with the kids, I just do it as soon as possible.” She advises other parents, “Don’t think too much about the future. Don’t wait. Just do it.”

In September, Astrea celebrated her third birthday. She does cartwheels with her older sisters and loves to listen to the music from Frozen, which always comforted her through her many weeks in the hospital. Riding home in the car with her mother recently, Astrea said, “I don’t want to go home. I want to play outside.”

“And so we did,” says her mother.

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WHAT YOUR WEARABLE KNOWS

Changes in usual patterns can tip you off to illness

Michael Snyder, PhD, was on a flight to Norway in the summer of 2015. Outfitted with eight biosensors, he noticed that his heart rate had risen and his oxygen levels had dropped. The Stanford professor and chair of genetics knew this pattern was typical for a plane flight, but something was off. Usually his heart rate only rose at the beginning of the flight and the oxygen dipped much less, returning to normal after landing. However, this time, both oxygen and heart rate remained altered.

Soon enough, Snyder developed a fever. Two weeks prior, he had been helping his brother build a fence in rural Massachusetts. He was worried he might have been bitten by a tick and contracted Lyme disease, so he convinced a Norwegian doctor to write him a prescription for the antibiotic doxycycline.

Blood tests subsequently revealed that he had indeed been infected with Lyme disease.

What happened to Snyder is an example of the type of early warning of disease that wearable sensors can supply, according to a recent digital health study in his lab. Using continuous data from biosensors plus periodic lab tests, the research team collected nearly 2 billion measurements from 60 people, including weight, heart rate, oxygen in the blood, skin temperature, sleep, activity, calories expended, acceleration, and exposure to gamma rays and X-rays. They first established baseline ranges for each participant; by monitoring deviations from those baselines, they were later able to detect the onset of infection, inflammation and even insulin resistance.

The results of the study, published in January in PLOS Biology, raise the possibility of identifying inflammatory disease in individuals who may not even know they are getting sick. For example, in one instance, higher-than-normal readings of heart rate and skin temperature correlated with increased levels of C-reactive protein in blood tests. C-reactive protein is an immune-system marker for inflammation and often indicates infection, autoimmune diseases, developing cardiovascular disease or even cancer.

Snyder’s own data revealed four separate bouts of illness and inflammation, including the Lyme disease infection. “Wearables helped make that initial diagnosis,” he says of the Lyme disease.

Wearables could also help identify people with insulin resistance, a precursor to Type 2 diabetes. The research team designed and tested an algorithm combining participants’ daily steps, daytime heart rate, and the difference between daytime and nighttime heart rate. The algorithm could identify individuals in the study who seemed to be developing insulin resistance.

Today’s wearables — smart watches and fitness monitors — primarily measure activity, but Snyder says they could easily be adjusted to more directly track measures of health. Every person’s wearables could carry normal baselines for dozens of measures, and automatic data analysis could combine patterns of outlier data to flag the onset of ill health and provide opportunities for intervention, prevention or cure.

“We have more sensors on our cars than we have on human beings,” Snyder says. In the future, he predicts, that situation will be reversed. — JENNIE DUSHECK
Around 6 p.m. on Dec. 6, 2-year-old Eva Sandoval was wheeled across the hall from her twin sister, Erika. It was the first time in the girls’ lives that they had been in different rooms. The conjoined twins had just been separated at Lucile Packard Children’s Hospital Stanford, and Eva was being moved to another operating room in preparation for both girls’ reconstructive surgeries.

“We know that this is the right path for them: to be independent, to have the chance to succeed and explore on their own everything the world has to offer,” said the twins’ mother, Aida Sandoval, soon after the 17-hour separation.

“The results are as good as we could have asked for,” says lead surgeon Gary Hartman, MD, professor of surgery. The surgery, Hartman’s seventh conjoined-twin separation, was the culmination of plans launched when Aida was referred to Packard Children’s during her complex pregnancy. More than 100 hospital staff in nearly every department have taken care of Eva and Erika, who were born there in August 2014.

As they prepared, doctors warned the family that there was a 30 percent chance one or both girls would not survive separation. • “Before separation, you could think of their anatomy as two people above the ribcage, merging almost into one below the bellybutton,” says Peter Lorenz, MD, professor of surgery, who led the reconstructive phase. The girls had separate hearts, lungs and stomachs; a shared diaphragm muscle; one liver; one bladder; two kidneys; and three legs.

In surgery, the liver and bladder were both divided in two. Each sister now has one leg and one kidney. Tissue from their third leg, which would not have functioned for standing or walking, helped close Erika’s surgical opening.

Recovering at the hospital, Eva and Erika are happy and chatty, and are doing well in physical therapy, where they have been re-learning skills such as sitting up. Aida and husband Arturo are eager to welcome the girls back to the family’s home in Antelope, California, after they leave the hospital. “It’s amazing how strong these girls are, and it’s amazing what their team performed,” Aida says. — ERIN DIGITALE