Stem cell ‘therapy’ blinds three patients

By Becky Bach

Three people with macular degeneration were blinded after undergoing an unproven stem cell treatment that was touted as a clinical trial in 2015 at a clinic in Florida. Within a week following the treatment, the patients experienced a variety of complications, including vision loss, detached retinas and hemorrhage. They are now blind.

A paper documenting the cases was published March 16 in The New England Journal of Medicine. The article is a “call to awareness for patients, physicians and regulatory agencies of the risks of this kind of minimally regulated, patient-funded research,” said Jeffrey Goldberg, MD, PhD, professor and chair of ophthalmology at the School of Medicine and co-author of the paper.

The three patients — all women, ranging in age from 72 to 88 — suffered from macular degeneration, a common, progressive disease of the retina that leads to loss of vision. Before the surgery, the vision in their eyes ranged from 20/30 to 20/200. Now, the patients are likely to remain blind, said co-author Thomas Albini, MD, an associate professor of clinical ophthalmology at the University of Miami, where two of the patients were subsequently treated for complications from the stem cell treatments. “Although I can’t say it’s impossible, it’s extremely unlikely they would regain vision.”

Appealing to patients ‘desperate for care’

Two of the patients learned of the so-called clinical trial on ClinicalTrials.gov, a registry and results database run by the U.S. National Library of Medicine, where it was called “Study to assess the safety and effects of adipose-derived stem cells injected intravitreal in dry macular degeneration.”

Each patient paid $5,000 for the procedure. Any materials given to the patients did not mention a trial, although the consent form and other written information given to the patients did not mention a trial, Albini said.

“There’s a lot of hope for stem cells, and these types of clinics appeal to patients desperate for care who hope that stem cells are going to be the answer, but in this case these women participated in a clinical enterprise that was off-the-charts dangerous,” Albini said.

At the clinic, which is not named in the paper, the patients had fat cells removed from their abdomens and a standard blood draw. The fat tissue was processed with enzymes, with the goal of obtaining stem cells. Platelet-dense plasma was isolated from the blood. The cells were then mixed with the platelet-dense plasma and injected into their eyes. Patients reported that the entire process took less than an hour. Albini said. The patients had both eyes treated at once — another red flag, Albini and Goldberg said, because most doctors would opt for a conservative approach to observe how one eye responds to an experimental treatment before attempting the other eye.

Shoddy stem cell preparation may have led to some of the patients’ complications, which could have been caused by injection of a contaminant or the cell wash solution into the eye, Albini said. When injected into the eye, the stem cells also could have changed into myofibroblasts, a type of cell associated with scarring.

No evidence of vision restoration

But even if executed correctly, there is no evidence suggesting that the procedure could help restore vision, Goldberg and Albini said. In fact, there is sparse evidence that adipose-derived stem cells, the type of cells that the clinic claimed to use, are capable of differentiating, or maturing, into retinal pigment epithelium or photoreceptor cells, which play a critical role in macular degeneration and are the

Initial hospital costs for gunshot wounds just ‘tip of the iceberg’

By Devika G. Bansal

Gun violence resulted in initial hospitalization costs of more than $6.6 billion nationwide from 2006 through 2014 — an average of $734.6 million per year, according to a study by researchers at the School of Medicine.

The study was published online March 21 in the American Journal of Public Health. The lead author is medical student Sarabeth Spitzer. The senior author is Thomas Weiser, MD, associate professor of surgery.

“There is a high cost for these injuries, especially because they are preventable,” Spitzer said. The study included hospitalization costs of shooting injuries that were self-inflicted, unintentional or due to assault.

Little research on gun violence

At Stanford, 10 percent of trauma patients are admitted with gunshot or knife wounds — a small but important proportion of the patient population, Weiser said.

Despite the scale of the problem, there exists surprisingly

Psychiatrist advised producers of upcoming teen-suicide drama

By Erin Digitale

When Stanford psychiatrist Rona Hu, MD, was invited to help shape the script of a Netflix series about teenage suicide, she knew it would be an unusually good opportunity to communicate with teenagers about mental health issues.

“The new series, 13 Reasons Why, which premieres March 31, is based on a bestselling 2007 novel about a high-school student who dies by suicide after being bullied by her classmates,” Hu said.

“The show’s producers faced a challenge: They wanted to retain the book’s basic plot without romanticizing suicide, since such portrayals can contribute to suicide contagion. Hu agreed to advise them.

“It was a good opportunity to make sure that something about suicide was factually accurate,” said Hu, clinical associate professor of psychiatry and behavioral sciences. “The production team seemed very sincere about wanting to do good and not do harm.”

Hu has volunteered in suicide-prevention efforts for Palo Alto teenagers, so she was already accustomed to discussing the subject.

“In the novel, Thirteen Reasons Why, the book’s main character, Hannah, records cassette tapes that she arrange to have sent to people who bullied her. Two weeks after her death, they receive the tapes, on which Hannah explains how each of them contributed to her desire to die.

‘Concerned by a number of things’

“I was concerned by a number of things,” Hu said, describing her reactions to the novel. “There are only teenagers in the book; parents are barely mentioned. If teens are contemplating suicide to get back at bullies, they may not realize how much collateral damage they can do to people.
Researchers create three-dimensional bladder reconstruction

By Jackie Flynn

The way doctors examine the bladder for tumors or stones is like exploring the contours of a cave with a flashlight. Using cameras attached to long, flexible instruments called endoscopes, they find that it’s sometimes difficult to orient the images. It’s like trying to keep track of a cave while you are looking at the walls with a flashlight. The images are often blurry and details are difficult to see.

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MARCH 27, 2017 INSIDE STANFORD MEDICINE

Researchers create three-dimensional bladder reconstruction

The contours of a cave with a flashlight. Using cameras attached to long, flexible instruments called endoscopes, they find that it’s sometimes difficult to orient the images. Each kind of bias may result from many mechanisms. For example, in small studies, it’s easier to get “statistical significance” if the effect size is large. With large effects are also more likely to be published. Even independent of statistical significance, larger effects are more likely to be published than smaller effects.

Ioannidis said that in the data they examined, the influence of different kinds of bias changed over time and seemed to depend on the individual scientist. “We show that some of the patterns and risk factors seem to get worse over time.” He said, “This is particularly driven by the social sciences, so if you broke scientific fields into big bins of biology, medicine, physical sciences and social sciences, it seems that the social sciences are seeing the more prominent warning of these biases over time.”

One of the most unexpected findings of the study, Fanelli said, was that the kinds and amounts of bias were very irregularly distributed across the literature. “Although bias may be worrying only in specific research areas, it is non-existent in many others,” he said. “So bias does not undermine the scientific enterprise as a whole.”

Another finding of the study is that the relative magnitude of biases closely reflects the level of attention they receive in the literature. That is, the kinds of biases that researchers are more concerned about are in fact the ones they should be concerned by. “Our understanding of bias is improving, and our priorities are set on the right targets,” said Fanelli. But that’s not the case everywhere, he said. “We perhaps understand bias better, but we are far from having rid science of it.”

Indeed, our results suggest that the challenge might be greater than many think because interventions might need to be tailored to the needs and problems of individual fields. One-size-fits-all solutions are unlikely to work.

Solutions and interventions

Ioannidis likewise cautioned that the data are purely observational, not experimental, and the question of how to reduce bias is far from decided. For example, he said, just because small studies tend to give exaggerated results doesn’t mean we should stop doing them. “One might say immediately, well, we need to do large studies,” he said. “That would be an interesting approach but I don’t think we can’t necessarily translate an association directly into an effective intervention.”

The way doctors examine the bladders of mice and humans is far from being the only example of bias in scientific research. “I think that one can take each one of these biases and say, ‘Well, let’s try to reduce it or eliminate it,’” he added. “Some of them are easier to reduce or eliminate than have ever been thought to get ‘statistical significance’ if the effect size is large. With large effects are also more likely to be published. Even independent of statistical significance, larger effects are more likely to be published than smaller effects.

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Five types of pediatric brain cancer were safely and effectively treated in mice by an antibody that causes immune cells to engulf and eat tumors without hurting healthy cells. Many childhood brain tumors are inoperable. Some also lack effective chemotherapy drugs, making radiation and chemotherapy toxic to the developing brain that they cause devastating long-term side effects. The technology has immense potential, given that its three-dimensional renderings are based on endoscopy images taken of the internal anatomy. The team was also able to navigate around a virtual model, Liao said.

Although the team developed the technology to reconstruct human organs, it could be applied to other hollow organs where doctors routinely perform endoscopy, including the bladder. "We've shown that bladder cells make "eat me" signals that are displayed on their cell surfaces, while healthy cells do not. However, cancer cells hide these "eat me" signals by producing large quantities of CD47, a "don't eat me" protein that is found on the surface of both healthy and malignant cells. When CD47 is blocked by antibodies, immune cells can detect the cancer cells' "eat me" signals. Macrophages then selectively target, engulf and destroy the cancer cells without harming healthy cells, because normal cells lack the "eat me" signals," Liao said.

Study highlights

The Stanford team conducted a long series of experiments using different combinations of tumor cells and healthy cells in culture, as well as in various mouse models in which human brain cancer cells had been implanted in mice. Highlights of their experiments include:

• The team confirmed that all the various cancers tested express the CD47 "don't eat me" signal.

• In a dish, Group 3 medulloblastoma cells treated with anti-CD47 antibodies were engulfed and eaten by macrophages, while healthy brain cells were not harmed.

• In mice with a partially functioning immune system that had been transplanted with any of the five types of pediatric brain tumors, treating the mice with anti-CD47 antibodies significantly reduced the presence of cancer cells.

• In mice, the antibody crossed the blood-brain barrier in significant amounts after being injected into the peritoneal cavity, a finding important for testing because some other forms of immunotherapy are unable to cross this barrier. In mice transplanted with Group 3 medulloblastoma, anti-CD47 antibodies were three to four times more effective in an initial tumor xenograft than given in the peritoneal space, but better at treating metastases if given directly into the cerebrospinal fluid.

• Mixing healthy neural progenitor cells with anti-CD47 antibodies did not cause any damage to the neural progenitor cells, either in their viability or ability to proliferate, suggesting that the antibodies would not interfere with brain development.

• In mice with a fully functioning immune system that had been transplanted with a high-grade glioma cell line, anti-CD47 antibodies significantly prolonged the survival of the animals, from an average of 21 days for those in the untreated group to 32 and 38 days for those receiving low and high doses of antibodies, respectively.

• In mice treated with anti-CD47 antibodies, their brains, examined after treatment, showed that macrophages concentrated at the sites of the tumors. Further tests showed that macrophages got inside the tumors. The anti-CD47 antibody completely eliminated all tumor cells in the mice, indicating that the antibodies may not be able to completely penetrate large tumors, the researchers noted.

To maximize their effects, the antibodies will likely need to be combined with other forms of cancer treatment, a concept the researchers plan to investigate further. "We think antibody combinations, including those that stimulate both innate and adaptive immunity, will be able to treat a much broader set of patients than one antibody alone," Liao said. The researchers are planning to use the antibody to treat human subjects with brain tumors and other cancers for which there is currently no effective treatment.

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After years of preparation, students ‘match’ to residencies

By Tracie White

At 8:55 a.m., as Nuriel Moghavem got up from his table to accept the sealed, red envelope with his future hidden inside, his two younger brothers punched him in the shoulder — for luck.

The neurologist-in-training, who is also passionate about health care policy and took a year off from medical school to work as a legislative assistant in Sacramento, was, for the moment, at loose ends.

“Oh yeah, now I’m nervous,” said Moghavem, taking deep breaths and staring at his shoes while his brothers grinned at him from behind.

He was one of 70 soon-to-be graduating Stanford medical students who took part in Match Day on March 17 at the Li Ka Shing Center for Learning and Knowledge. Thousands of other medical students across the United States were, at the same moment, also waiting to find out where they would be spending the next three or more years of their lives as residents. The scene was nerve-wracking.

“You kind of put all your eggs in one basket, and today you’re going to see if they hatch,” said Kelsey Hirotsu, who dressed up in heels and curls to find out where she would be spending the next three or more years of her life as residents.

“Congratulations to all of you,” Lloyd Minor, MD, dean of the School of Medicine, opened the ceremony, applauding the accomplishments of the students, and congratulating them: “You’re embarking upon a tremendously exciting period in your career and your life of medicine,” he said. “Congratulations to all of you.”

Next, Charles Prober, MD, senior associate dean for medical education, took the podium to start the countdown.

“The envelopes cannot be opened, anywhere in the country, until 9 a.m. Pacific time,” Prober told the crowd of students, families, friends and advisors seated at tables in Berg Hall. With several minutes left to wait, Prober described for the crowd some of the history of Match Day.

The matching process is a tradition that dates back to 1952, with residency assignments ultimately determined by a nonprofit organization, the National Resident Matching Program. The organization uses a computer algorithm to align the choices of the applicants with those of the residency programs. It’s a roughly year-long process for medical students who, in their final year of medical school, fill out applications in the summer, wait until the fall to find out where they would be matched and wait inside the soon-to-be opened envelopes. The 70 students would be waiting for luck.

“Ten, nine, eight …” At exactly 9 a.m., the students began punching him in the shoulder — for luck.

“Sixty-six percent are going to two states: California and Harvard,” Prober said — Harvard traditionally is a popular matching spot for Stanford students. “I’m so incredibly happy,” said Coughlan, adding that while opening her letter, “I literally almost collapsed.”

Across the room, Moghavem took his time. He watched as emotion erupted around the room, then with his parents and brothers gathered close around, he carefully opened his envelope with shaking hands, read the letter, nodded his head and hugged his mom. He matched at Stanford, his first choice.

“We have big shoes to fill,” said his brother, Eli Moghavem, nodding to the youngest brother, a senior in high school, who was busy uploading the news to his friends on Snapchat. Moghavem said that making a difference in people’s lives is what motivates him. American-born but of Iranian descent, he worried about other Iranian-born medical students matching this day whose plans may have been disrupted by the Trump administration’s proposed travel ban.

“I’m fortunate. I was born in this country so I didn’t have to worry about that, although my family all comes from Iran,” he said, adding that he’s the first doctor in his large, extended family.

“I expect a lifetime of family memories, sending me weird pictures of their rashes,” he said. His shoulders sagged a bit with relief and joy, and he smiled.

After years of preparation, students ‘match’ to residencies

Graduating medical students Grace Laidlow, Tom Roberts and Grace Hunter compare results on Match Day after they and their peers were handed envelopes revealing where they would be spending their residencies.

Coughlan matched in orthopedic surgery at the University of California-San Francisco.

“I’m so incredibly happy,” said Coughlan, adding that while opening her letter, “I literally almost collapsed.”

“Congratulations to all of you.”

Mar 27, 2017 INSIDE STANFORD MEDICINE
Researchers look to Lego for automation of biology experiments

**By Andrew Myers**

Elementary and secondary school students who later want to become scientists and engineers often get hands-on inspiration by using off-the-shelf kits to build and program robots. But so far it’s been difficult to create robotic projects to truly interest the “nerd” science—biology, chemistry and medicine — so called because experiments in these fields often involve fluids.

Now, Stanford bioengineers and their collaborators have shown how an off-the-shelf kit can be modified to create robotic systems capable of transferring precise amounts of fluids between flasks, test tubes and experimental dishes.

By combining the Lego Mindstorms robotics kit with a cheap and easy-to-find plastic syringe, the researchers created a set of liquid-handling robots that approximate the performance of the far more costly automation systems found at universities and biotech labs.

“We really want kids to learn by doing,” said Ingmar Riedel-Kruse, PhD, assistant professor of bioengineering. “We don’t have a few relatively inexpensive parts, a little training and some imagination, students can create their own liquid-handling robots and then run experiments on them — so the students learn about engineering, coding and the wet sciences at the same time,” he said.

Robots meet biology

A paper describing the work was published March 21 in PLoS Biology. Riedel-Kruse is the senior author. The lead author is postdoctoral scholar Lukas Gerber.

The robots are designed to pipette fluids from and into cuvettes and multiple well plates — types of plastic containers commonly used in laboratories. Depending on the specific design, the robots can handle liquid volumes far smaller than a microliter, a droplet about the size of a single coarse grain of salt. Riedel-Kruse believes that these Lego designs might even be useful for specific professional or academic liquid-handling tasks that normally require robots costing many thousands of dollars.

His overarching idea is to enable students to learn the basics of robotics and the wet sciences in an integrated way. Students could learn to collaborate while also developing STEM skills, such as mechanical engineering and computer programming. They could also gain a deeper appreciation of the value of robots in life sciences experiments.

Riedel-Kruse said he drew inspiration from constructionism, a learning theory that advocates project-based learning in which students make tangible objects and connect different ideas and areas of knowledge and thereby construct mental models to understand the world around them. One of the leading theorists in the field was Seymour Papert, whose seminal 1980 book Mindstorms was the inspiration for the Lego Mindstorms kits.

“I saw how students and teachers were already using Lego robotics in and outside school, usually to build and program moving car-type robots, and I was excited by that,” he said. “But I saw a vacuum for bioengineering-like machines to bring this kind of constructionist, hands-on learning with robots to the life sciences.”

Do it yourself

In their PLoS Biology paper, the team members outlined how to design and build plans and several fundamental experiments targeted to elementary, middle and high school students. They also offer experiments that students can conduct using common household consumables like food coloring, yeast or sugar. In one experiment, colored liquids with distinct salt concentrations are layered atop one another to teach about liquid density. Other tests measure whether liquids are acids, like vinegar, or bases, like baking soda, or which sugar concentration is best for yeast. Yet another experiment uses color-sensing light meters to align color-coded cuvettes.

The coding aspect of the robot is elementary, Riedel-Kruse said. A simple programming language allows students to place symbols telling the robot what to do: Start, Turn motor on. Do a loop. And so forth. The robots can be programmed and operated in different ways. In some experiments, students push buttons.

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As Moore’s law hits limits, new generation of brainlike computers emerges

**By Nathan Collins**

For five decades, Moore’s law held up pretty well: Researchers and engineers have shrunk the individual transistors that could fit on a chip doubled, all while costs steadily declined. Today, however, transistors and other electronic components are so small they’re beginning to bump up against fundamental physical size limits.

Moore’s law has reached its end, and it’s going to take something different to meet the need for computing power — orders of magnitude more than what people have built, even today — even though it used vastly less energy and remarkably unreliable components: biological neurons.

How does the brain do it?

While others have built brain-inspired computers, Boahen said, and he and his collaborators have developed a five-point prospectus — manifesto might be the better word — for how to build neuromorphic computers that directly mimic in silicon what the brain does in flesh and blood.

The first two points of the prospectus concern neurons themselves, which unlike computers operate in a mix of digital and analog mode. In their digital mode, neurons send discrete, all-or-nothing signals in the form of electrical spikes, akin to the ones and zeros of digital computers. But they process incoming signals by adding them all up and firing only once a threshold is reached — more akin to a dial than a switch.

That observation led Boahen to try using transistors in a mixed digital-analog mode. Doing so, it turns out, makes chips both more energy efficient and more robust when the components do fail, as about 4 percent bust when the components do fail, as about 4 percent

30 years in the making

It’s a moment Boahen has been working toward his entire adult life, and then some. He first got interested in engineering and neuroscience while growing up in Ghana. But the more he learned, the more traditional computers looked like a giant, inelegent mess of memory chips and processors connected by weirdly complicated wiring.

Both the need for something new and the first ideas for what that would look like crystallized in the mid-1990s. Even then, Boahen said, some researchers could see the end of Moore’s law on the horizon. As transistors continued to shrink, they would bump up against fundamental size limits. Eventually, they’d get so small that only a single lane of electron traffic could get through under the best circumstances.

What had once been electron superfreeways would soon be more like roadways, and that meant engineers could fit more components on a chip, those chips would become more and more unreliable.

At around the same time, Boahen and others came to understand that the brain had enormous computing power — orders of magnitude more than what people have built, even today — even though it used vastly less energy and remarkably unreliable components: biological neurons.

The future of the future

But it’s not just a vision. Over the last 30 years, Boahen’s lab has actually implemented most of its ideas in physical devices, including Neurogrid, one of the first truly neuromorphic computers. In another two or three years, Boahen said, he expects they will have designed and built computers implementing all of the prospectus’s five points.

Don’t expect those computers to show up in your laptop anytime soon, however. Indeed, that’s not really the point: most personal computers operate nowhere near the limits on conventional chips. Neuromorphic computers would be most useful in embedded systems that have extremely tight energy requirements, such as very low-power neural implants on or in computers in autonomous drones.

“It’s complementary,” Boahen said. “It’s not going to replace current computers.”

The other challenge: getting others, especially chip manufacturers, on board. Boahen is not the only one thinking about what to do about the end of Moore’s law or looking to the brain for ideas. IBM’s TrueNorth, for example, takes cues from neural networks to produce a radically more efficient computer architecture. On the other hand, it remains fully digital, and, Boahen said, 20 times less efficient than step-by-step building plans that have already been built with TrueNorth’s 28-nanometer transistors.

Boahen is also a member of Stanford SystemX and the Stanford Computer Forum. His work was supported by a Director’s Pioneer Award and a Transformative Research Award from the National Institutes of Health and a grant from the U.S. Office of Naval Research.

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Blinded
continued from page 1
cells some researchers are targeting to de-
velop therapies. The study, a ‘‘very well-founded evidence for the positive potential of stem therapy for many human diseases, but there’s no excuse for not designing a trial properly and basing it on preclinical research,’’ Goldberg said.
The ‘‘trial’’ lacked nearly all of the components of a properly designed clini-
cal trial, including a hypothesis based on laboratory experiments, assignment of a control group, and proper col-
lection of data, masking of clinical and patient groups, and plans for follow-up, Goldberg and Albini said. ‘‘There was a whole list of egregious things,’’ Albini said.

Gun
continued from page 1

little research on gun violence from a public health perspec-
tive. This is, in part, due to a measure Congress passed in 1996 that restricts federal funding for firearms research, Spitzer said.

Past studies have looked into the total costs of firearm injuries — medical as well as social — but most have focused either on par-
ticular states or within narrow time ranges. Analyzing data from 2012, a Member File investigation estimated that the annual cost of gun violence in America exceeds $22.3 billion, as much as $3.4 billion of which includes emergency services, police investigations and long-term medical- and mental-health care costs. The actual costs of hospital visits is difficult to tease out from these fig-
ures, and it is unclear who actually ends up paying for these.

‘‘Firearm injuries are tied to one of the most con-
troversial political issues in the country, so it is impor-
tant for all sides to have access to fact-based research,’’ Spitzer said. ‘‘Cost information can be especially help-
ful when making health policy decisions.’’

The Stanford team set out to estimate the national medi-
cal costs of firearm injuries over a nine-year period by using publicly available data in the Nationwide Inpatient Sample, the largest database in the United States, which houses information from about 8 mil-
lion hospital discharges each year. The researchers picked patients who were admit-
ted for firearm-related injuries and analyzed the severity of their wounds, the cost of their care, where they were hospitalized and how they paid for the hospitalizations.

Government bears large share of cost
Spitzer and her colleagues interrogated the data to address two primary questions: What were the total medical costs when gunshot victims were first hospital-
ized, and where did the financial burden of medical care fall?

The team found that the government bears about 40 percent of the total costs. ‘‘It’s a very high financial bur-
do,’’ Spitzer said.

The researchers found that victims paid for hospital costs through Medicare, Medicaid, private insurance or out of their pockets. Patients were overwhelmingly male, and there was a correlation between their insur-
ance status and how they sustained their injuries. For example, shootings of young and poor individuals in-
sured by Medicaid comprised two-thirds of firearm inj-
uries, and they were most often victims of assault. In contrast, older Medicare-insured patients were more likely to suffer from self-inflicted gunshot wounds.

The study captures costs for a very limited experi-
enced because the costs of firearm injuries continue in many different ways, Spitzer said. ‘‘There’s a cost if you’re readmitted, there’s long-term rehab, and a lot of these patients end up needing long-term health care,’’ she said, adding that she and her colleagues will next systematically analyze costs of hospital readmissions.

‘‘It’s amazing that we don’t know as much about the medical costs of firearm injuries,’’ said David Hemen-
way, director of the Harvard Injury Control Center, who was not involved in the study. [‘‘This study’] high-
lights that this is just the tip of the iceberg.’’

Other Stanford co-authors of the study are Kriwan Stanescu-Mayer, MD, associate professor of surgery; Da-
vid Spain, MD, professor of surgery; and research scien-
tific Tshilidzi Tembe.

The research was supported by the Stanford Medical Scholars Fellowship Program.

Fathers, in addition to mothers, now sought for Stanford eating-disorder study

By Erin Digita

Mothers who have previously had an eating disorder often struggle to teach their children healthy eating habits, research has shown. Now, a School of Medicine study of how to help them is being expanded to include fathers, mak-
ing it the first study in the world to off-
er this type of targeted intervention for dads.

“We have really sparse information on fathers with eating disorders,” said Shiri Sadeh, PhD, a visiting scholar at Stanford who is helping to lead the new study. “Although eating disorders are very stigmatized in women, there is even more stigma in men. And men may not understand the potential impact of their eating disorder on their children, since feeding is, in many families, still perceived as an issue that mothers worry most about.”

In 2014, Sharvit and her collaborators began testing a method aimed at helping mothers with a history of eating disor-
ders to develop healthier feeding strategies in their treatment group, and young children. The researchers began their study in women who were living with their partners and small children. The eligibility criteria for the study have been extended, and the researchers are now recruiting families with a child be-
tween the ages of 1 and 5 whose mother or father has had anorexia nervosa, buli-
mia nervosa or binge-eating disorder in the past. The study had previously in-
cluded only two-parent families; single-
parent families are now also being asked to join. For the 16-week study period, the researchers will work with the par-
tent to build healthy family interactions ac-
sisting with Title 21, Part 1271.10, of the Code of Federal Regulations. The FDA released more specific guidelines in Oc-
tober 2015, after these procedures were performed, establishing the requirement for FDA oversight and approval for these types of procedures.

“We expect health care providers to take every precaution to ensure patient safety, but this definitely shows that the lack of oversight can lead to bad patients and bad outcomes. It’s alarming,” Albini said.

The au-
thors acknowl-
edged that it is difficult for pa-
tients to know whether a clini-
cal trial, or a stem cell therapy, is leg-
itimate. Goldberg recommended that patients consider a stem cell treatment consult a website, which is main-
tained by the International Society for Stem Cell Research. It is also advisable to check if a trial is affiliated with an aca-
demic medical center, Goldberg said.

In an email, Thomas Weiser, MD, assistant professor of ophthalmology at the University of Rochester Medical Center, Researcher from the University of Miami, Univer-
sity of Rochester, Stanford and a clinician who treats eating

“Jim is also a good person and it’s not a backfire, Sharvit said. “There is a lot of evidence that the more you control or manage your children’s eating, the more they are likely to suffer from self-inflicted gunshot wounds.

The researchers hypothesize that the study will help parents avoid pressuring children to eat too little or too much, that children will take more responsibility for their own decisions.

The additional principle investigator is James Lock, MD, PhD, professor of psy-
chiatry and behavioral sciences at Stan-
ford. Field sites include the adolescent eating disorders at Lucile Packard Children’s Hospital Stanford.

Fathers of children interested in partici-
ating in the research can contact Sadeh-
Sharvit at 407-494-903 or shiri@stanford.

It is also advisable to check if a trial is affiliated with an academic medical center, Goldberg said.

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Fathers of children interested in partici-

Earlier this month, the federal government released a report that is a risk factor for suicide. Among it, the report included data showing increases in rural areas of Northern California, which is noteworthy. According to the data the CDC examined, Bay Area counties have rates that are very similar to the state rate of around 5 to 6 suicide deaths per 100,000 young people. While rural counties have much higher rates. The top three were Mendocino (16.2 per 100,000), Lake (15.2 per 100,000) and Humboldt (12.5 per 100,000) counties.

One difficulty is that many rural counties generally lack the financial support to provide the same access to evidence-based interventions across large rural areas as is possible in urban areas with more telehealth and telepsychiatry capacity, which we at Stanford have done in a small way by providing this kind of support to a pediatric practice in Monterey. There may be value in expanding these types of support to more rural counties to expand access to mental health care.

What else did the report reveal?

ADELSHEIM: When you look broadly at the entire county and note the rate of suicides in males aged 20 to 24, it raises important questions about how young people who are no longer high school age can access mental health services. I think we need to recognize their crises and refocus access to mental health care across the board. We also need to start asking why these young men are less likely to access mental health care settings.

The contrast between youth suicide rates in rural and urban areas of Northern California is also noteworthy. According to the data the CDC examined, Bay Area counties have rates that are very similar to the state rate of around 5 to 6 suicide deaths per 100,000 young people. While rural counties have much higher rates. The top three were Mendocino (16.2 per 100,000), Lake (15.2 per 100,000) and Humboldt (12.5 per 100,000) counties.

Additional from page 1

Steven Adelsheim, MD, clinical professor of psychiatry and behavioral sciences at the School of Medicine and a child and adolescent psychiatrist.

ADELSHEIM: We have formed many productive partnerships. We’re doing a lot of work with schools in Santa Clara and San Mateo counties, where we’ve been providing direct care, prevention efforts, early intervention, and training and support for school staff around suicide prevention. We’re working with groups like Project Safety Net in Palo Alto and the HEARD Alliance to increase the range of support available for young people, as well as providing community education. We’re also working to launch a program for youth with early signs of psychosis to help decrease suicide risk among those in the early stages of serious psychiatric conditions.

In addition, we’ve partnered with Mills Peninsula Hospital to have Stanford child and adolescent psychiatrists staff several pediatric inpatient mental health beds. Having hospital beds available for youth in crisis is important, but only one piece of the puzzle. We also want to be able to help young people much earlier.

To that end, we’ve been developing a local version of the headspace model, based on a successful Australian program of the same name, for providing out-patient counseling and other early-intervention services to youth. Santa Clara County has allocated funding for two staff positions, a youth development specialist and a school employment specialist, and we’re partnering with the county to potentially access additional innovation grant funding to support the development of two county headspace sites.

The headspace model is designed to help young aged 12 to 25, so it’s a potential access point for young people aged 20 to 24 who might not otherwise get mental health care. Our marketing for headspace will include messages saying that this is a place to go for help recovering from breakdowns and other difficult life events, rather than overburdening us as a mental health clinic. We hope this approach will help us draw in a larger swath of young people.

Overall, we are supporting a broad range of community-based services. We want to have capacity that stretches from prevention to early intervention to acute care services, and we’re really proud to partner with so many community groups to work toward this worthy goal.
Conference on future of medical education set for April 22-23

By Tracie White

Stanford Medicine X|ED, an academic conference on the future of medical education, will be held April 22-23 at the Erskine Sheng Center for Learning and Knowledge at the School of Medicine.

In its inaugural year as a stand-alone conference, the event will be held to increase diversity within the health care workforce and among medical educators, and the application of “precision education” — meeting the needs of future learners through new technology and tools, and personalized education.

The Medicine X|ED conference began two years ago as a part of the academic health-innovation conference Medicine X, but it has been spun off as a separate event this year.

“Medicine X aims to transform health care by elevating under-heard voices from its front-line stakeholders including patients, caregivers, providers — people with expertise to transform academic medicine from the bottom up,” said Lawrence Chu, MD, professor of anesthesiology, perioperative and pain medicine at Stanford and founder and director of Medicine X. “We realized that in order to make real impactful change in health care, we needed to dedicate resources to reach the future leaders of tomorrow early enough to make a difference. Medicine X|ED is our answer to that unmet need.”

Examining ways to improve medical education

The conference will bring together a broad range of stakeholders in health care education — from patients, providers, researchers, industry leaders, designers, technologists and medical educators. The goal is to examine new methods of improving medical education, organize the stakeholders together, and challenge educators to examine medical education in the ways we look at medical treatment, where we use data and analytics to better understand the patient, in order to tailor the best therapy and treatments for an individual person — precision health,” Chu said. “This new concept, precision education, applies a similar approach for training an educational experience, looking at a learner’s entire learning footprint — how many times a learner interacts with an online learning management system, opens an email or webpage, quiz question, app, flashcard.”

Keynote speakers at the conference will be:

• Clay Johnson, MD, the inaugural dean of the new Dell Medical School at the University of Texas-Austin.
• Dan Schwartz, PhD, dean of the Stanford Graduate School of Education and the author of a new book, “The ABCs of How We Learn.”
• Neha Sangwan, MD, developer of a program for health care workers’ own care, a program she calls “self-care.”
• Erik Brodt, MD, a physician who works to improve Native American health and medical training, who will speak about using digital media storytelling to inspire American Indian youth.

Key events over the two-day event include:

• Diversity 2.0 — a main stage breakout panel session focused on advancing the conversation on diversity and inclusion within medical education.
• Patient-Centered Outcomes Research and Comparative Effectiveness Research — a main stage breakout session.
• A main stage panel on the role of games in medical education, moderated by Parvati Dev, PhD, former director of Stanford University Medical Media and Information Technology.

Among the many workshops and learning labs, scheduled topics include design thinking for future doctors, integrating the expanding health care system, developing leadership and self-empowerment and games as solution for medical training.

For more information or to register for the conference, visit: https://medicinex.stanford.edu/ed.

Team led by Sanjay Basu wins third place in data analysis contest

A team led by Sanjay Basu, MD, PhD, assistant professor of medicine, has been awarded third place in a contest designed to promote the sharing of clinical trial data.

Contestants used a data set to identify a new scientific or clinical finding. The data set was developed during the Systolic Blood Pressure Intervention Trial, known as SPRINT, which compared intensive management to standard management of blood pressure.

The Massachusetts Medical Society sponsored the contest, called the SPRINT Data Analysis Challenge, which encourages researchers to promote the sharing of reuse of clinical trial data.

Basu’s team used the data to develop and validate a clinical decision score that identifies patients who will benefit from intensive blood pressure treatment. The work could potentially reduce the chance of life-threatening side effects, such as kidney failure.

A first-, second- and third-place winner were selected from 143 entries based on which entry provided the most clinically useful information. Judging was done by a panel of experts and crowdfunding by the public.

The three winners will present their findings at a meeting in April.

Basu’s team included Joseph Rigdon, PhD, a Stanford engineering research associate, and researchers from the University of Michigan.

Renamathy Dhanaasekaran, MD, instructor of medicine, has received one of three 2017 Junior Faculty Development Awards from the American College of Gastroenterology. The award, which provides $100,000 a year for three years, supports junior investigators working toward independent careers in clinical research in gastroenterology or hepatology. Dhanaasekaran’s project is “Plasma glycoproteomic biomarkers for invasive human hepato cellular carcinoma,” and her mentor is Dean Felder, MD, PhD, professor of medicine and of pathology.

Alfredo Dubra, PhD, was appointed associate professor of ophthalmology, effective Oct. 1, 2016. His focus is on using optical imaging technologies to reveal ocular, vascular, neurodegenerative and systemic diseases.

David Kingsley, PhD, professor of developmental biology, has received the 2017 Genetics Society of America Medal. The award honors outstanding contributions to the field of genetics in the past 15 years. Kingsley was recognized for his experimental work, beginning with different species of three-spine stickleback fish, which provided insights into how vertebrates evolve in natural environments. He has now expanded his inquiry into understanding human traits, including aspects of skin, skeletal and brain evolution.

Karim Sallam, MD, clinical instructor of medicine, has received the American College of Cardiology’s William W. Parmer Young Author Achievement Award. The award recognizes two papers published in the Journal of the American College of Cardiology by authors early in their careers. Sallam’s paper, published Nov. 8, 2016, was “Patient-specific and genome-edited induced pluripotent stem cell-derived cardiomyocytes elucidate single-cell phenotype of Brugada syndrome.” His mentor is Joseph Wu, MD, PhD, professor of medicine and of radiology and director of the Stanford Cardiovascular Institute.

O F  N O T E

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retnamathy dhanaasekaran
alfredo dubra
karim sallam

david kingsley

Sanjay Basu


Lego continues from page 5

stem-ready

Riedel-Kruse said these activities meet several important goals for promoting multidisciplinary STEM learning as outlined by the Next Generation Science Standards and other national initiatives. He stressed the cross-disciplinary instruction value that integrates robotics, biology, chemistry, programming and hands-on learning in a single project.

The team has co-developed these activities with students and a science teacher, and then tested them with elementary and middle school students over the course of several weeks of instruction. Instructions for developing the robots are now ready for wider dissemination to an open-access community that can expand upon the plans, capabilities and experiments for this new breed of fluid-handling robots, and they might even be suitable to support certain research applications.

“We would love it if more students, do-it-yourself learners, STEM teachers and researchers would embrace this type of work, get excited and then develop additional open-source instructions and lesson plans for others to use,” Riedel-Kruse said.

For more information, see the PLoS Biology paper and Riedel-Kruse’s lab website.

Other co-authors of the paper are a science teacher at Isaac Newton Graham Middle School in Mountain View and one current and two former high school students.

Funding was provided by grants from the National Science Foundation.

Stanford’s Department of Bioengineering, which is jointly operated by the School of Medicine and the School of Engineering, also supported the work.