INSIDE STANFORD MEDICINE

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The fall issue of *Stanford Medicine* looks at power and limits of diagnostics.
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Study: High-intensity statins lower mortality

By Yasemin Saplakoglu

A large national study has confirmed the value of high-intensity statin treatments for people with cardiovascular disease, according to researchers at the School of Medicine.

Over the duration of a year, the researchers found that patients taking high-intensity statins had an increased chance of survival over those on moderate-intensity statins. The study was published online Nov. 9 in *JAMA Cardiology*.

Statins, a class of drugs that lowers cholesterol levels in the blood, are commonly prescribed for preventing the acceleration of cardiovascular disease caused by the buildup of plaque in the arteries, which can lead to heart attacks and stroke.

Health-care providers have long debated the benefits of prescribing high-intensity statins to their patients with cardiovascular disease. Patients, in turn, have been hesitant to take them because of equivocal messages from their doctors and internet searches of patient and doctor perspectives.

Conflicting recommendations

"Previously, there was definitely a certain amount of fear on the patient's part because most people don't like taking medication," said Paul Heidenreich, MD, professor of cardiovascular medicine and the study's senior author. Some studies have shown an increased risk of side effects, such as diabetes or muscle damage, associated with higher-intensity statins.

In 2013, the American College of Cardiology and American Heart Association jointly recommended high-intensity statin therapy for patients with atherosclerotic cardiovascular disease who were no older than 75. The ACC/AHA guidelines differed, however, from guidelines established in 2014 by the Veterans Affairs Health Care System, which recommended only moderate-intensity statins, noting the lack of conclusive evidence that higher-intensity statins are more beneficial than those of moderate intensity.

In their study, Heidenreich and his team found evidence to support the ACC/AHA guidelines. They determined that high-intensity statins do in fact increase rates of survival, not only in younger and middle-aged patients with cardiovascular disease, but also in a patient population not well-studied: adults over 75.

"The greatest strength of this study is that we used a very large, well-defined clinical cohort," said Fatima Rodriguez, MD, a cardiology fellow at Stanford and the study's lead author. "The results show that high-intensity statins confer a survival advantage for patients with cardiovascular disease, including older adults."

ROB HYRONS / SHUTTERSTOCK.COM

A review of more than a half-million health records showed that patients taking high-intensity statins had an increased chance of survival over those on moderate-intensity statins. Statins are drugs that lower cholesterol levels in the blood.

Large sample size

The researchers studied the medical records of 509,766 patients across the country receiving care from the Veterans Affairs Health Care System. "This is a very large patient population rich in cardiovascular disease," said Rodriguez. "In addition to defining this large, national patient population, we also had access to their detailed clinical data, including comorbidities and cholesterol values."

The primary purpose was to look at overall patient death rates from 2013 to 2014, the researchers said. They included patients with coronary artery disease, cerebrovascular disease and peripheral artery disease. "These are basically the three main areas affected by plaque buildup — the heart, the brain and the large arteries of the rest of the body," Heidenreich said.

Patients were taking high-intensity, moderate-intensity or low-intensity statins in many **See STATIN, page 6**

PTSD changes the brains of boys and girls differently

By Erin Digitale

Traumatic stress affects the brains of adolescent boys and girls differently, according to a new brain-scanning study from the School of Medicine.

Among youth with post-traumatic stress disorder, the study found structural differences between the sexes in one part of the insula, a brain region that detects cues from the body and processes emotions and empathy. The insula helps to integrate one's feelings, actions and several other brain functions. **See PTSD, page 7**

ALTANAKA / SHUTTERSTOCK.COM

Existence of asymptomatic Ebola confirmed in study in Sierra Leone village

By Ruthann Richter

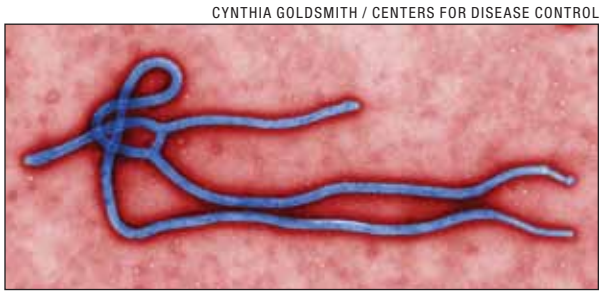
A year after the Ebola epidemic in West Africa, researchers from the School of Medicine and other institutions identified 14 individuals previously unknown to have had the disease in a Sierra Leone village that was an Ebola hot spot.

These individuals had antibodies to the virus, indicating they had been infected at one time. Yet 12 said they had had no symptoms during the time of active transmission in the village.

The research confirms previous suspicions that the Ebola virus does not uniformly cause severe disease, and that people may be infected without showing signs of illness, said Gene Richardson, MD, a former fellow in the Division of Infectious Diseases and Geographic Medicine at Stanford who is now a PhD candidate in anthropology at the university. The findings also suggest that the epidemic was more widespread than previously believed. Based on the results of the study, the researchers calculated the prevalence of minimally symptomatic infection to be 25 percent.

"The study corroborates previous evidence that Ebola is like most other viruses in that it causes a spectrum of manifestations, including minimally symptomatic infection," Richardson said. "It provides important evidence on that front. It also means

CYNTHIA GOLDSMITH / CENTERS FOR DISEASE CONTROL



A small number of villagers in Sierra Leone were infected with the Ebola virus but reported having no symptoms, a study found.

a significant portion of transmission events may have gone undetected during the outbreak. This shows there was a lot more human-to-human transmission than we thought."

The study was published online Nov. 15 in *PLOS Neglected Tropical Diseases.* The study also was presented Nov. 14 at the American Society of Tropical Medicine and Hygiene's annual meeting in Atlanta. Richardson is lead author of the study, and Paul Farmer, MD, PhD, a Harvard professor and director of Partners In Health, is the senior author.

Testing individuals

The research was done in the rural village of Sukudu in Sierra Leone, a **See EBOLA, page 7**

DNA sequencing determines lymphoma origin, prognosis

By Krista Conger

Sequencing tiny bits of DNA circulating in the blood of patients with lymphoma can accurately identify the cancer subtype and pinpoint mutations that might cause drug resistance, according to researchers at the School of Medicine.

This knowledge could help personalize cancer treatment by revealing which patients are likely to be treated successfully and those who may have a poorer prognosis.

Tracking sequence changes over time could also provide a kind of early warning system to identify the emergence of an aggressive form of the cancer by providing a real-time window into tumor evolution. The findings bolster the growing notion that noninvasive, blood-based biopsies of what's known as circulating tumor DNA are likely to transform cancer care.

"Now we can identify the subtype of the tumor, watch how it changes over time and begin to tailor our chemotherapy choices based on the presence or absence of specific mutations," said assistant professor of medicine Ash Alizadeh, MD, PhD. "We've moved beyond just measuring disease burden based on the amount of tumor DNA in the blood."

MARK TUSCHMAN

Maximilian Diehn and Ash Alizadeh have found a way to monitor cancer DNA in the blood of patients with lymphoma, which could help identify those who are likely to be treated successfully.

Alizadeh and assistant professor of radiation oncology Maximilian Diehn, MD, PhD, share senior authorship of the study, which was published Nov. 9 in *Science Translational Medicine*. Postdoctoral scholars Florian Scherer, MD, and David Kurtz, MD, and instructor Aaron Newman, PhD, are the lead authors.

The researchers conducted a study of 92 prospectively enrolled patients with diffuse large B-cell lymphoma. DLBCL is the most common type of non-Hodgkin lymphoma and is highly biologically variable. As a result, patients vary widely in their response to treatment. About one-third of seemingly successfully treated patients eventually relapse, or their tumors become resistant to treatment. Additionally, a form of indolent B cell lymphoma, which progresses slowly with only mild symptoms, can transform without warning into an aggressive form of the disease.

'Transformation is very difficult to detect'

"This transformation is very difficult to detect, and usually requires an invasive biopsy to diagnose," said Diehn. "Our approach will allow us to monitor patients over time with a simple blood test, and may help us identify transformation much earlier."

The researchers used an enhanced version of a technique they developed called CAPP-Seq to isolate and sequence circulating tumor DNA, or ctDNA, from blood samples from the patients. Unlike previous studies, which tracked lymphoma progression by monitoring the sequence of just one cancer-associated protein, CAPP-Seq can identify a much larger range of mutations in the tumor genome.

They then compared the ctDNA sequences obtained from the patients' stored blood samples with those of the tumor cells from invasive biopsies, and paired the information with what was known about the course of the patient's disease and eventual outcome. They found that low levels of ctDNA after diagnosis but before treatment correlated strongly with progression-free survival in the patients. Those with higher levels of ctDNA faired more poorly overall. Furthermore, they were able to detect the presence of ctDNA in the blood of relapsing patients on average six months before any clinical symptoms appeared and as long as 2.5 years before clinical signs of relapse.

Determining cancer's cell of origin

Perhaps even more importantly, however, the researchers found they could use CAPP-Seq to determine the type of B cell from which the cancer originated and predict prognosis. About two-thirds of people with the germinal center subtype live for five years or more after diagnosis, while those with activated B-cell-like tumors have a poorer prognosis with current treatment regimes. These subtypes are known to predict differential responses to emerging targeted therapies, but they are cumbersome to measure accurately and require biopsies.

Finally, the researchers were able to predict from the ctDNA sequences those patients whose disease was transforming into a much more aggressive form prior to the emergence of clinical symptoms, and even to identify and track specific mutations known to inhibit the response to the targeted therapy with a drug known as ibrutinib.

"In this study we've shown five distinct ways — by quantifying tumor burden, identifying disease subtype, cataloging mutations, predicting transformation and providing early warnings of recurrence — that circulating tumor DNA can yield potentially clinically useful information," said Diehn. "Now we're eager to conduct prospective studies in recently diagnosed patients to learn how we can best improve patient care."

Alizadeh and Diehn are both investigators at the Ludwig Center for Cancer Stem Cell Research and Medicine at Stanford.

The team's work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Other Stanford co-authors of the study are research associates Henning Stehr, PhD, and Chih Long Liu, PhD; former research assistant Alexander Craig; postdoctoral scholars Mohammad Esfahani, PhD, and Daniel Klass, PhD; former postdoctoral scholar Alexander Lovejoy, PhD; graduate student Jacob Chabon; research assistant Li Zhou; clinical trials assistant Cynthia Glover; assistant professor of surgery Brendan Visser, MD; associate professor of surgery George Poultsides, MD; professor of medicine Ranjana Advani, MD; clinical assistant professor of medicine Lauren Maeda, MD; clinical assistant professor of medicine Neel Gupta, MD; professor of medicine Ronald Levy, MD; assistant professor of pathology Robert Ohgami, MD, PhD; and clinical assistant professor of pathology Christian Kunder, MD, PhD.

Newman, Klass and Alizadeh are co-inventors on patent applications related to CAPP-Seq, and Newman, Diehn and Alizadeh are consultants for Roche Molecular Systems. Lovejoy and Klass are currently employed by Roche Molecular Systems.

The research was supported by the Damon Runyon Cancer Research Foundation, the American Society of Hematology, the V Foundation for Cancer Research, the German Research Foundation, the Stanford TRAM Pilot Grant, the American Society of Clinical Oncology and the National Institutes of Health.

Stanford's departments of Medicine and of Radiation Oncology also supported the work. ISM

More GABA in one brain region linked to better working memory

By Bruce Goldman

The amount of a particular chemical in a particular part of your brain predicts your ability to simultaneously hang onto several bits of information in your working memory, a School of Medicine scientist and his UC-Davis collaborators have learned.

The discovery helps to clarify at least one aspect of the brain's mysterious ways, and could someday help guide therapies for those whose working memory could stand improvement.

And whose couldn't?

Working memory is the brain function that lets you carry on a phone conversation while adding three numbers in your head and remembering that you need to steer the car onto the freeway exit in about two minutes — all this time not forgetting who you're talking to. Like a computer's RAM, working memory serves as a buffer where information, derived from the senses or retrieved from long-term memory, can be temporarily placed so the conscious brain can process it. It's tied to assessments of cognitive capacity such as IQ, and to real-world outcomes such as academic performance.

Jong Yoon

Load, maintenance, distraction resistance

As most people eventually find out, working memory declines with age.

"Deficits in working memory also characterize various neuropsychiatric conditions and are particularly evident in schizophrenia," said Jong Yoon, MD, an assistant professor of psychiatry and behavioral sciences at Stanford and a psychiatrist at the Palo Alto Veterans Affairs Health Care System who sees numerous patients with this disorder.

Yoon is the lead author of the study, which was published Nov. 16 in the *Journal of Neuroscience*. The study teases apart three key components of working memory and shows that one component, but not the other two, is tied to the amount of a chemical called GABA in a brain area known as the dorsolateral prefrontal cortex, or DLPFC. Richard Maddock, MD, a professor of psychiatry at UCD, is senior author of the study.

This component, referred to as load, is a measure of the number of separate bits of information a person's working memory can store at the same time. A second component, maintenance, denotes how long information can be stored in working memory before it's lost. A third, distraction resistance, gauges how well an individual's working memory holds onto information in the face of interfering stimuli.

See GABA, page 7

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STANFORD MEDICINE

Blocking CD47 could boost immunotherapy for canine cancer

By Christopher Vaughan

Blocking a cell surface protein called CD47 may help treat at least one kind of cancer in dogs, according to a study by researchers at the School of Medicine and other institutions.

The work expands on research by Irving Weissman, MD, professor of pathology and of developmental biology, and his colleagues, who found that blocking CD47 might be useful in treating nearly every kind of human cancer.

The study was published online Nov. 14 in *Cancer Immunology Research*.

Kipp Weiskopf, MD, PhD, a former student at the School of Medicine, is lead author of the study. Weissman, director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, and Jaime Modiano, VMS, PhD, of the University of Minnesota, share senior authorship.

'Don't eat me'

The CD47 protein acts as a "don't eat me" signal to immune cells called macrophages, which normally engulf and devour cancer cells and other diseased and dying cells. It turns out that nearly every kind of cancer uses CD47 to evade these macrophages. Covering up the CD47 "don't eat me" protein allows the immune cells to find and swallow cancer cells. An anti-CD47 antibody is currently in a small, phase-1 clinical trial in cancer patients at Stanford and elsewhere.

Weiskopf and his fellow researchers took canine lymphoma, one of the most common cancers in dogs, and put it into laboratory mice. Weiskopf then injected the mice with CV1, a molecule he helped develop to bind tightly to the CD47 receptor and block the "don't eat me" signal. In some cases, they also used a specially devised antibody against a protein called CD20 to act as an "eat me" signal to attract immune cells to the cancer.

NORBERT VON DER GROEBEN

The work expands on research by Irving Weissman and his colleagues, who found that blocking CD47 might be useful in treating nearly every kind of human cancer.

They found that when anti-CD20 antibody alone was used to treat the dog cancer in mice, none of the mice survived. When CV1 was used by itself to treat the cancer, only 20 percent of the mice survived. But when the anti-CD20 antibody and CV1 molecule were used together, 100 percent of the mice survived with no further evidence of disease. They seemed to be cured.

Leading cause of illness in dogs

Cancer is among the leading causes of illness in dogs, and clinical trials with actual cancer-stricken dogs are the next step. "We hope that these studies help companion animals and further inform us about treating disease in humans," Weiskopf said.

Weissman noted that it is an important first step that the molecular tools used to target human CD47 also work against dog cancers, at least when tested in a mouse host. "This should provide impetus to produce even more effective anti-CD47 proteins that are designed for optimal targeting of dog — and separately, cat — CD47 molecules and cancers," he said. Weissman is also director of the Stanford Ludwig Center for Cancer Stem Cell Research and Medicine.

Other Stanford co-authors of the study are graduate student Amira Barkal; former postdoctoral scholar Susan Prohaska; former medical school student Aaron Ring, MD, PhD; and former lab technicians Peter Schnorr and Kelly McKenna.

Researchers from the University of Minnesota, Elanco Animal Health U.S. Inc. and the Genomics Institute of the Novartis Research Foundation also co-authored the study.

The work was supported by the National Institutes of Health, the Morris Animal Foundation, the Joseph and Laurie Lacob Gynecologic/Ovarian Cancer Fund, Ludwig Cancer Research, the Siebel Stem Cell Institute, the Thomas and Stacey Siebel Foundation, Stanford SPARK, the Skippy Frank Fund for Life Sciences and Translational Research, and an anonymous donors fund.

Stanford's departments of Pathology and of Developmental Biology also supported the work. **ISM**

Three faculty members elected fellows of AAAS

Two professors at the School of Medicine and one at the School of Earth, Energy & Environmental Sciences have been elected fellows of the American Association for the Advancement of Science.

They are among 391 new AAAS fellows chosen this year by their peers for scientifically or socially distinguished efforts to advance science or its applications.

Andrew Hoffman

Andrew Hoffman, MD, professor of endocrinology, was selected for contributions to the field of epigenetics, particularly for discerning underlying mechanisms of genomic imprinting and long-range chromatin interactions. Hoffman's lab examines the role of insulinlike growth factors in normal physiology and in oncogenesis.

Lawrence Steinman

Lawrence Steinman, MD, professor of neurology and neurological sciences, was selected for discoveries about the molecular basis for lymphocyte homing to the brain in relapsing multiple sclerosis, which led to an effective approved therapy for multiple sclerosis. Steinman, who holds the George A. Zimmermann Professorship, focuses his research on understanding the pathogenesis of autoimmune diseases, particularly multiple sclerosis.

Steven Gorelick

Steven Gorelick, PhD, professor of Earth system science, was selected for contributions to improving the understanding of mechanisms of subsurface contaminant transport and for pioneering leadership in developing optimization models for hydroeconomic analysis. Gorelick, who holds the Cyrus F. Tolman Professorship, studies groundwater management, water resources vulnerability in developing regions, optimal remediation design, hydrogeophysics and ecohydrology. **ISM**

New compliance, study management resources available for researchers

Spectrum, the Stanford Center for Clinical and Translational Research and Education, recently established two new groups to assist Stanford researchers in managing studies and complying with the labyrinth of government regulations associated with clinical research.

OnCore training

The first, Spectrum's OnCore support team, is currently scheduling training sessions for groups interested in using the OnCore clinical research management system. The schoolwide adoption of OnCore will make it easier for investigators to manage clinical research and monitor participant recruitment. OnCore also provides tools for multisite study management. For more info, contact the manager of this group, Yona Shulaker, at shulaker@stanford.edu, or visit http://medicine.stanford.edu/news/current-news/standard-news/department-wide-roll-out-planned-for-oncore.html.

Clinical research guidance

The second resource, the Clinical Research Quality Office, is staffed with experts who can help research teams understand clinical research regulations and adopt best practices. They can also help groups prepare for audits by industry sponsors or the Food and Drug Administration.

CARTOONRESOURCE / SHUTTERSTOCK.COM

"Looks like you're on top of the new regulations."

This office will be developing School of Medicine clinical research policies, standard operating procedures and systems for tracking regulatory compliance. It is currently focused on tracking Stanford studies listed on ClinicalTrials.gov and training researchers on upcoming results-posting regulation changes. It is under the leadership of faculty director Mark Pegram, MD, professor of oncology, and administrative director Jennifer Brown, RN. For more information, visit https://spectrum.stanford.edu/page_listings/detail/clinical-research-quality--2. **SM**

$25 million awarded to joint center for the study of regulatory science

The Food and Drug Administration has awarded the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation a five-year, $25 million grant.

The collaborative venture is one of five FDA Centers of Excellence in Regulatory Science and Innovation intended to advance the science of regulation. New technologies in biomedical research require new approaches to evaluating safety and effectiveness.

The UCSF-Stanford center launched in 2014 with an initial $3.3 million grant from the FDA to develop projects that can help with regulating health care. For example, one project, headed by Russ Altman, MD, PhD, professor of bioengineering, of genetics of medicine and of biomedical data science at Stanford, uses natural language processing and machine learning to analyze the contents of enormous databases of adverse effects from drugs reported by patients and clinicians.

Altman and Kathy Giacomini, PhD, professor of bioengineering and therapeutic sciences in the UCSF School of Pharmacy, lead the center. Altman is also director of Stanford's biomedical informatics training program.

The new $25 million grant supports research, collaboration and education. Researchers will use the grant to address how to regulate the development and approval of new medical products; provide public lectures, panel discussions and workshops on FDA regulations; and provide training in regulatory science. **ISM**

Stanford's inaugural health-focused hackathon brings innovators together

By Ula Chrobak

Stanford students, faculty and health professionals, as well as designers and entrepreneurs from across the United States, teamed up for a weekend of health care innovation Nov. 5-6 at the inaugural health++ hackathon.

Participants pitched their projects, formed teams and went from idea to prototype in 36 hours. The goal: create a design, app or business plan that improves health care affordability and access.

Health care systems can be slow to embrace new technologies, said Oliver Aalami, MD, clinical associate professor of surgery, who was a faculty adviser for the event. Aalami said many doctors already rely on smartphones for sharing diagnoses and prescribing advice, making that a good platform for innovations.

Aalami added that while a number of health care technology projects have formed at Stanford, the interdisciplinary connection to bring them to fruition has been lacking. "The left arm doesn't know what the right arm is doing," he said.

RACHEL LESLIE

Participants in Stanford's health++ hackathon present their prototypes and business models to judges during the project expo.

Interdisciplinary teamwork

Of the 257 hackathon participants, about half were Stanford undergrads and a quarter were Stanford physicians, business students and graduate students. The rest were designers, engineers and entrepreneurs from other institutions and private companies.

"It's incredible to see the energy and interest not just from the engineering school — traditionally I think hackathons appeal the most to engineering students — but the design school and business school have been super-excited as well," said Sherman Leung, a Stanford computer science major who helped organize the event. "It's the first time in my Stanford career that I've seen something so interdisciplinary."

The event's co-founders were undergraduates Jason Wang and Shivaal Roy, who are now co-presidents of the Stanford student group Stanford Healthcare Innovations in Future Technologies. The group teamed up with other undergraduates, as well as with medical students and physician advisers, to make health++ happen.

"We have such a perfect ecosystem with the hospital, the graduate schools, the undergraduate school," Aalami said. "It's just a perfect ecosystem to have amazing things happen."

Winning projects

A novel pill-bottle sticker that makes prescription labels more accessible to people with visual impairments, called Pharmassist, won the grand prize at the event. When placed on a smartphone, the sticker's unique pattern would enable the phone to read aloud the prescribing information, track the number of pills left and help order a refill.

"By getting together at the hackathon with a team of five people, it was so awesome that we could build a working prototype in 36 hours," said Pharmassist lead team member Zahoor Zafrulla.

Zafrulla said he would have needed a week to 10 days to complete the project on his own. As a full-time engineer, he said, this was not possible. Zafrulla's team included experts in biomedical engineering, biology and computer science.

"They're coming to the event with very deep experience and an understanding of what the problem is, and basically saying, 'OK, let's spend two days and see how we can prototype something to address this problem,'" said Leung.

The other grand prize winners were Foot++, a muscle stimulator for people with a gait abnormality known as foot drop, and Benjamin, an app that informs users of lower-cost options for prescription drugs and insurance plans. A total of 12 teams won prizes.

The prizes were awarded based on problem-solving potential and feasibility to implement. The goal was not to create a finished product, which is hard to do in a mere 36 hours. Instead, the biggest impact of bringing together clinicians, business experts and engineers for the weekend was to create a starting point for future innovation.

"We hope that hackathon can serve as a launching pad, sparking future collaborations and getting people from all departments thinking about health care innovation," Wang said.

Health++ organizers are already looking forward to next year. Aalami said that Stanford Health Care plans to contribute deidentified medical records next year, which could be used by hackers in big data projects.

The event organizers are excited about the potential for the event to initiate an interdisciplinary community of collaborators on health care issues.

"A ton of problems in health care require interdisciplinary thinking," Roy said. "We hope health++ can help facilitate that paradigm shift."

Other advisers for the event were Robert Chang, MD, assistant professor of ophthalmology; Ami Bhatt, MD, PhD, assistant professor of hematology and of genetics; and Marta Zanchi, PhD, a Biodesign faculty member. **ISM**

THOMAS LAU

Panelists from industry and academia discuss opportunities for innovation in health care affordability at the hackathon, which took place Nov. 5-6.

Fall issue of *Stanford Medicine* looks at power, limits of diagnostics

By Rosanne Spector

In the future, your toilet might save your life.

Of course, your toilet would have to be very special to accomplish this, but that's what Sanjiv Gambhir, MD, PhD, professor and chair of radiology, and his colleagues are working on in his lab at the School of Medicine.

Gambhir envisions a future in which we nearly continuously monitor our health. So he's developing diagnostic tools, such as a "smart" toilet to detect diabetes and a smart bra to detect breast cancer. As he explains in the new issue of *Stanford Medicine* magazine, the resulting data might tell each of us, or our health-care team, if something is amiss right away.

"The future is all about being able to intercept diseases early and, ideally, prevent them. If we can actually do something about a disease such as an aggressive cancer, then it is worth monitoring for it," Gambhir said in the lead article of the magazine's special report on diagnostics.

He and other researchers in the field of diagnostics are taking advantage of advances in biomedical research, engineering and computer technology to make diagnostics more informative and less invasive. One Stanford team, for example, is helping to create a real-life version of the tricorder, a sci-fi device used by the character Dr. McCoy on *Star Trek* to diagnose patients. Another team is developing an imaging method for cancer patients that eliminates radiation exposure and might even help fight the disease.

"The future is all about being able to intercept diseases early and, ideally, prevent them."

Falling short of potential

At present, however, diagnostic methods fall short of their potential. According to a 2015 National Academy of Medicine report, "The delivery of health care has proceeded for decades with a blind spot: Diagnostic errors — inaccurate or delayed diagnoses — persist throughout all settings of care and continue to harm an unacceptable number of patients."

Part of the problem, said Gambhir, is that research aimed at improving diagnoses receives much less funding than research on new treatments.

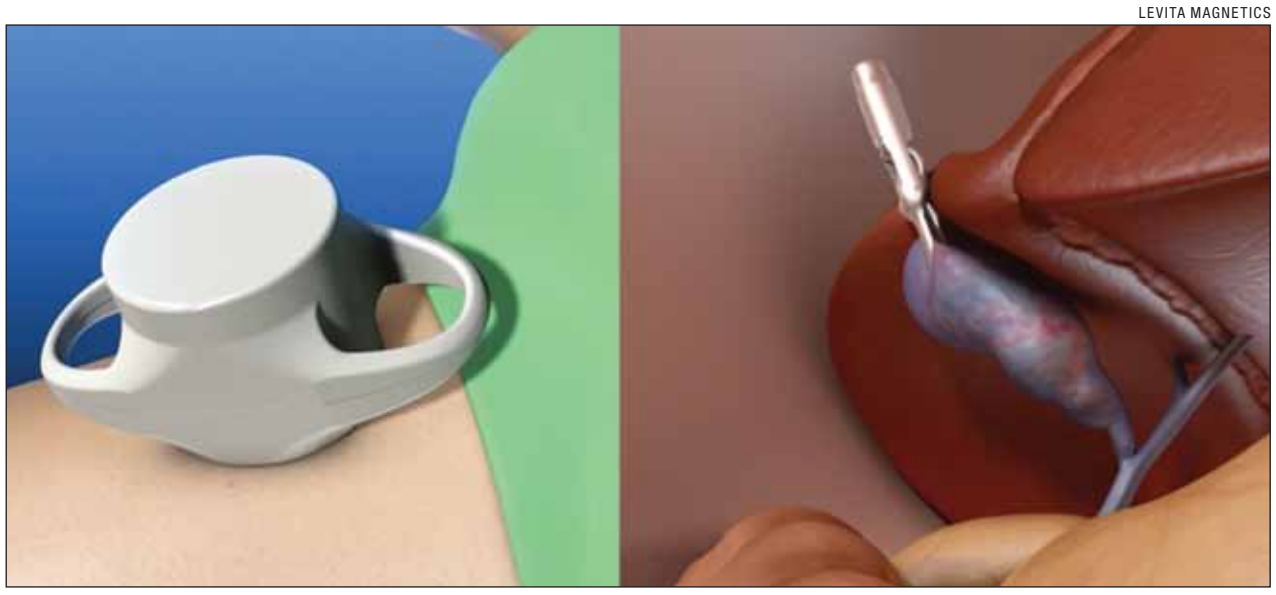
The fall magazine, produced with the support of Stanford's Department of Radiology, includes a Q&A with Travis Tygart, the CEO of the U.S. Anti-Doping Agency. The online version of the magazine includes an edited recording of the conversation with Tygart about cleaning up sports.

Also in the special report:

- The story of Gambhir's quest to save his son after he was diagnosed with a brain tumor — and his son's legacy to diagnostics.
- An article about how School of Medicine Dean Lloyd Minor, MD, discovered the cause of

Magnetic tool makes gallbladder-removal surgery less invasive

LEVITA MAGNETICS



LEVITA MAGNETICS

Top: In an illustration of how the magnet-driven tool works, the external magnet is depicted on the abdomen (left), and the grasper, which is attracted to the magnet, is attached to the gallbladder (right). Below: A photo of the tool, which has received clearance by the Food and Drug Administration.

By Sara Wykes

Researchers at School of Medicine and three hospitals in Chile have demonstrated the safety of a new magnet-driven device that enables surgeons to make fewer incisions while performing laparoscopic gallbladder surgery.

Each year, more than 1 million people in the United States have their gallbladders removed, putting that procedure, called a cholecystectomy, on the nation's top-10 list of surgeries. The gallbladder is closely sheltered in the curve of the liver, so removing it can be tricky. Even in the most skilled hands, manipulating the laparoscopic instruments used in the surgery poses a risk of causing internal damage that can lead to scarring.

The new magnet-driven device makes the surgery less invasive by obviating the need for an incision through which an instrument is inserted to retract the gallbladder. Instead, an external magnet does that job.

In a paper published online Oct. 24 in *Annals of Surgery*, the researchers shared the results of a 50-patient clinical trial in which they demonstrated the safety of the device. Homero Rivas, MD, assistant professor of surgery at Stanford and director of innovative surgery at Stanford Health Care, is lead author of the paper. The senior author is Mario Uribe, MD, of the Hospital Salvador in Santiago, Chile.

Nationwide, the device, which has received clearance from the Food and Drug Administration, is in use at Stanford Medicine and two other medical centers.

"Laparoscopy has truly revolutionized surgery over the past 30 years or so, and with very good results, but it still relies on a given number of incisions and instruments," Rivas said. "Surgeons and patients continuously search for painless, scarless operations. This device takes a step toward that goal by reducing the need for fixed, transabdominal instruments."

How it works

The device has two parts: an external magnet and a slender rod with a detachable clip that includes a magnet. The rod, with the clip at its far end, looks much like the reaching devices that people can use to grab objects from high shelves. A surgeon inserts the rod through the belly button and manipulates its clip to grasp the gallbladder. The clip is then released from the rod but remains connected to the gallbladder. The external magnet is placed on the abdomen to control the movement of the clip attached to the gallbladder. A rod with a camera attached to it sends video to a monitor in the operating room, giving the surgeon an inside view of the area near the gallbladder. Other instruments are inserted through incisions to detach the organ, after which the rod that was earlier unhitched from the clip is reconnected to it and used to remove the organ from the patient.

The study documented an average hospital stay for patients of 22 hours, and an average pain score of 0.6 on a scale of 0 to 10 seven days after surgery. The average time for patients to return to work was five days.

The device was the idea of Alberto Rodriguez-Navarro, MD, who specialized in minimally invasive surgery in his native Chile and is now CEO of Levita Magnetics, the San Mateo-based company he founded to develop the magnetic surgical system.

Rivas said he has used the device primarily for cholecystectomies, but he believes it is versatile enough to be applied to bowel resections, appendectomies, hysterectomies, gastrectomies and other abdominal surgeries. "I hope that greater availability of the device will allow other innovators to propose other uses that even its pioneers have not thought of," Rivas said.

Surgeons at three Santiago hospitals — the Hospital Salvador, the Hospital Luis Tisne and the Hospital Padre Hurtado — also are co-authors of the study.

The research was supported by a grant from the Chilean Economic Development Agency and sponsored by Levita Magnetics.

Stanford's Department of Surgery also supported the work. ISM

certain patients' extraordinary hearing problems — for instance, hearing the sound of their own eyeballs moving — and went on to find a cure.

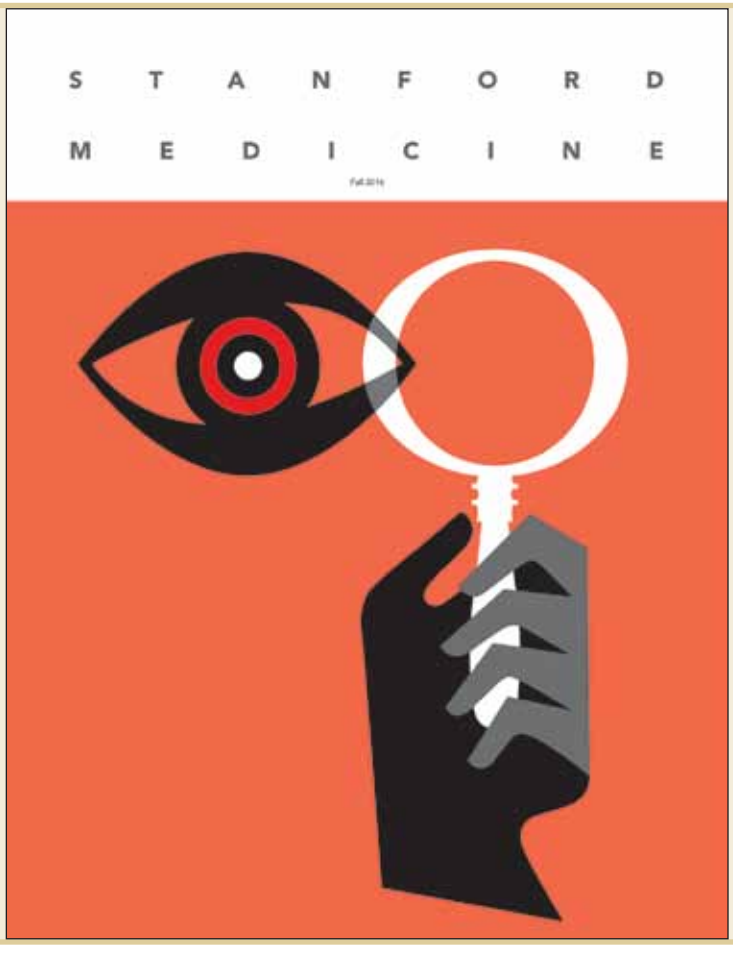
• A sampler of diagnostic tools emerging from Stanford, including a magneto-sensor that detects cancer proteins with sensitivity hundreds of times greater than current methods, an ultrasound camera-in-a-pill that can see through the walls of intestines, and a software program for analyzing tumor tissue samples that determines a prognosis more accurately than people can.

• An article on the stethoscope, asking whether the 200-year-old device is still relevant. A video about the stethoscope, featuring Stanford clinicians, including professor of medicine and bestselling author Abraham Verghese, MD, is available in the magazine online.

• A story about a family seeking an explanation for a mysterious seizure disorder striking two of their children, and how using computers to mine genetic data can secure answers more quickly.

The issue also includes an essay by physician-journalist Nancy Snyderman, MD, a consulting professor with Stanford's Center for Innovation in Global Health, on the collision of science and politics, and an excerpt from *Drug Dealer, MD,* a new book by Stanford assistant professor of psychiatry Anna Lembke, MD, on how doctors are fueling the opioid epidemic.

The magazine is available online. Print copies are being sent to subscribers. Others can request a copy by calling 723-6911 or by sending an email to medmag@stanford.edu. ISM



5 QUESTIONS

an occasional feature in which an expert answers five questions on a science or policy topic

Douglas Owens on new statin recommendation

The U.S. Preventive Services Task Force now recommends adults ages 40 to 75 with no history of heart disease — but who nevertheless have at least one risk factor and an elevated risk of cardiovascular disease — take a low- to moderate-dose statin.

The independent panel of experts in prevention and evidence-based medicine issued the recommendation in the Nov. 13 issue of JAMA.

An estimated 505,000 adults died of coronary heart and cerebrovascular disease in 2011. The prevalence of heart disease increases with age, ranging from about 7 percent in adults ages 45-64 to 20 percent in those 65 and older. It is somewhat higher in men than in women.

Douglas Owens, MD, was a member of the task force when the guideline was developed. He is a professor of medicine at the School of Medicine and director of the Center for Health Policy and Center for Primary Care and Outcomes Research. The centers are part of Stanford Health Policy. He is also a physician with the Veterans Affairs Palo Alto Health Care System.

Beth Duff-Brown, the communications manager at Stanford Health Policy, recently asked Owens some questions about the new statin guidelines.

1 What prompted this new recommendation by the task force?

OWENS: Cardiovascular disease is the leading cause of death in the United States, accounting for 1 in 3 deaths among adults due to heart attack and stroke. And statins can provide an important benefit to people at elevated risk of cardiovascular disease. But in order to know whether statins are going to be beneficial, it's important to know something about the patient's cardiovascular risk.

We reviewed the literature comprehensively — including 19 randomized clinical trials involving more than 73,340 patients, as well as additional observational studies — to understand both the benefits and the harms of statins. We concluded that the benefits outweigh the harms in appropriate patients at increased risk of cardiovascular disease. The primary benefit of statins is a reduction in your chance of having a heart attack or stroke.

2 What are statins and why do they offer such benefit?

OWENS: A statin is a drug that reduces the production of cholesterol by the liver. High cholesterol is a significant risk factor for cardiovascular disease and stroke, and statins help prevent the formation of the so-called bad cholesterol. Statin drugs also help lower triglycerides, or blood fats, and raise the so-called good cholesterol, HDL.

ROGER ASHFORD / SHUTTERSTOCK.COM

While there are some reported side effects from the use of statins, such as muscle and joint aches, most people tolerate statins fairly well. There is mixed evidence about whether statins may result in a modest increase in the chance of diabetes, but the task force assessed the benefits to clearly outweigh harms in patients at increased risk of cardiovascular disease.

Douglas Owens

3 Who should be taking low- to moderate-dose statins?

OWENS: The task force recommends that clinicians offer statins to adults who are 40 to 75 years old and have at least one existing cardiovascular disease risk, such as diabetes, hypertension, high cholesterol or smoking. They also must have a calculated risk of 10 percent or more that they will experience a heart attack or stroke in the next decade.

The task force recommends clinicians use the American College of Cardiology/American Heart Association risk calculator to estimate cardiovascular risk because it provides gender- and race-specific estimates of heart disease and stroke.

For people with a risk of 7.5 to 10 percent of heart attack or stroke over the next decade, the task force recommends individual decision-making, as the benefits of statins are less in this age group because these people have a lower baseline risk of having a cardiovascular event.

The task force also looked at initiation of statins in people 75 or older and found there wasn't enough evidence to determine whether people in this age group who have not previously been on a statin would benefit from starting a statin. So the task force suggests people in this age group consult their physicians about whether a statin may be beneficial.

4 Do these new statin guidelines override the task force recommendation in 2008 that adults be screened for lipid disorders due to high cholesterol?

OWENS: Yes, this recommendation replaces the 2008 recommendation on screening for lipid disorders in adults.

The accumulating evidence on the role of statins in preventing heart disease has now led the task force to reframe its main clinical question from "Who should be screened for dyslipidemia?" to "Which population should be prescribed statin therapy?"

We recommend that physicians go beyond screening for elevated lipid levels and assess overall cardiovascular risk to identify adults ages 40 to 75 years who will benefit most from statin use.

5 What does the task force hope to accomplish with the new recommendation?

We hope this guideline will help both clinicians and patients decide what their cardiovascular risk is and what steps they can take to reduce those risks, which include a healthy lifestyle, a healthy diet and exercise, and for appropriate patients at elevated risk for cardiovascular disease, potentially a statin.

We also hope to highlight areas that would benefit from additional research. Further research on the long-term harms of statin therapy, and on the balance of benefits and harms of statin use in adults 76 years and older, would be helpful in informing clinicians and patients. **ISM**

Statin

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different but commonly prescribed forms, such as rosuvastatin and atorvastatin. The researchers also followed one group that wasn't taking any statins. Patients had different severities of cardiovascular disease, making some more likely to be prescribed higher-intensity statins than others. So the researchers assigned each patient a score for the propensity to receive high-intensity statins and adjusted the results of the study accordingly.

The results showed a 9 percent increased chance of survival for patients taking high-intensity statins compared to those receiving moderate-intensity treatments. "We found basically the same risk reductions reviewed by the Veterans Affairs guidelines, but they didn't think the benefit was significant because the sample size was small," Heidenreich said. "We have so many more patients, we can be confident that it wasn't due to chance."

> "The greatest strength of this study is that we used a very large, well-defined clinical cohort."

Examining specific patient groups

The study considered data from patients over 75 — a group little studied in clinical trials. It found that patients between the ages of 75 and 85 taking high-intensity statins had a survival-rate benefit comparable to that of younger patients: a 9 percent higher chance of survival compared to those on moderate-intensity statins.

"Our results suggest that clinical trial data from heart studies for those younger than 75 could also be applied to this older population," Heidenreich said.

Paul Heidenreich

Finally, they studied the effect of different doses within the high-intensity statin group. Patients treated with the maximum dose of statins were 10 percent more likely to survive than patients on submaximal doses. "This suggests to practitioners that instead of starting a patient on a low dose, just to go ahead and put them on the maximum dose they can tolerate," Rodriguez said.

A limitation of the study was that the researchers were unable to determine whether patients died of cardiovascular disease or another cause.

Settling the debate

The next step, researchers said, is to find out why some patients who should be on high-intensity statins are not. They hope doctors will take their study's results into consideration when prescribing statins. "There are a lot of guidelines and recommendations out there, so I think we also have to make the system better," Rodriguez said. "Maybe hospitals can employ a clinical reminder to doctors, a message that pops up on the doctor's screen that asks why a cardiovascular patient isn't on a high-intensity statin."

The researchers also hope to follow up on longer-term data from these patient populations. "Not only do we hope to continue studying this population, but we also hope to study patients without prior cardiovascular disease but who are at high risk for it," said Rodriguez.

Finally, they hope these results will help to settle the debate on which guidelines doctors should use when prescribing statins to patients. Heidenreich said, "We think this should give clinicians, physicians and nurse practitioners more comfort in following the American College of Cardiology and American Heart Association guidelines and putting people with prior cardiovascular disease on a high-intensity statin."

The work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Other Stanford affiliated co-authors are David Maron, MD, clinical professor of medicine and Joshua Knowles, MD, PhD, assistant professor of medicine.

Stanford's Department of Medicine supported this study. **ISM**

PTSD

continued from page 1

The findings were published online Nov. 11 in *Depression and Anxiety*. The study is the first to show differences between male and female PTSD patients in a part of the insula involved in emotion and empathy.

"The insula appears to play a key role in the development of PTSD," said the study's senior author, Victor Carrion, MD, professor of psychiatry and behavioral sciences at Stanford. "The difference we saw between the brains of boys and girls who have experienced psychological trauma is important because it may help explain differences in trauma symptoms between sexes."

Smaller insula in traumatized girls

Among young people who are exposed to traumatic stress, some develop PTSD while others do not. People with PTSD may experience flashbacks of traumatic events; may avoid places, people and things that remind them of the trauma; and may suffer a variety of other problems, including social withdrawal and difficulty sleeping or concentrating. Prior research has shown that girls who experienced trauma are more likely to develop PTSD than boys who experience trauma, but scientists have been unable to determine why.

The research team conducted MRI scans of the brains of 59 study participants ages 9-17. Thirty of them — 14 girls and 16 boys — had trauma symptoms, and 29 others — the control group of 15 girls and 14 boys — did not. The traumatized and nontraumatized participants had similar ages and IQs. Of the traumatized participants, five had experienced one episode of trauma, while the remaining 25 had experienced two or more episodes or had been exposed to chronic trauma.

The researchers saw no differences in brain structure between boys and girls in the control group. However, among the traumatized boys and girls, they saw differences in a portion of the insula called the anterior circular sulcus. This brain region had larger volume and surface area in traumatized boys than in boys in the control group. In addition, the region's volume and surface area were smaller in girls with trauma than among girls in the control group.

Findings could help clinicians

"It is important that people who work with traumatized youth consider the sex differences," said Megan Klabunde, PhD, the study's lead author and an instructor of psychiatry and behavioral sciences. "Our findings suggest it is possible that boys and girls could exhibit different trauma symptoms and that they might benefit from different approaches to treatment."

Victor Carrion

The insula normally changes during childhood and adolescence, with smaller insula volume typically seen as children and teenagers grow older. Thus, the findings imply that traumatic stress could contribute to accelerated cortical aging of the insula in girls who develop PTSD, Klabunde said.

"There are some studies suggesting that high levels of stress could contribute to early puberty in girls," she said.

The researchers also noted that their work may help scientists understand how experiencing trauma could play into differences between the sexes in regulating emotions. "By better understanding sex differences in a region of the brain involved in emotion processing, clinicians and scientists may be able to develop sex-specific trauma and emotion dysregulation treatments," the authors write in the study.

To better understand the findings, the researchers say what's needed next are longitudinal studies following traumatized young people of both sexes over time. They also say studies that further explore how PTSD might manifest itself differently in boys and girls, as well as tests of whether sex-specific treatments are beneficial, are needed.

The work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Additional co-authors of the paper were Mira Raman, a scientific programmer at Stanford; and a researcher from Iowa State University.

Carrion is a member of the Stanford Neurosciences Institute.

The research was supported by the National Institutes of Health, the National Alliance for Research on Schizophrenia and Depression, and the American Foundation for Suicide Prevention.

Stanford's Department of Psychiatry and Behavioral Sciences also supported the work. ISM

Ebola

continued from page 1

country where Richardson and his colleagues cared for hundreds of patients in Ebola treatment units managed by Partners In Health.

The village, with about 900 residents, had been one of three major hot spots in the Kono District, in the eastern part of the country, during the heat of the Ebola crisis between November 2014 and February 2015. There were 34 reported cases of Ebola in the village, including 28 deaths.

More than 28,000 cases of Ebola infection were reported in Africa during the epidemic, the largest and longest in history. More than 11,000 people are estimated to have died because of the disease.

In the aftermath, Richardson and his colleagues decided to go back to the village to try to determine whether the Ebola infection could be minimally symptomatic, as previous studies have suggested. He worked with a local physician and two community health workers in gathering data for the study, a process that was approved by the local village chief.

They used a test known as the ELISA assay, a technique that can detect the presence of an antibody. They first made sure the test was accurate by comparing results from 30 Ebola survivors in Sukudu with those of 132 people in other villages where the virus had not been reported.

Richardson said the test proved to be a reasonable measure of viral antibodies. The researchers then recruited 187 men, women and children from Sukudu who had likely been exposed to Ebola, either because they were living in the same household or had shared a public toilet with a person confirmed to have had the disease.

Of these, 14 were found to be carrying antibodies to Ebola, indicating they had been infected at some point, though they had not been included in the original count. Twelve of them said they had had no symptoms of the disease, which typically causes fever, unexplained bleeding, headache, muscle pain, rash, vomiting, diarrhea, breathing problems and difficulty swallowing. Two recalled having had a fever at the time of the outbreak, the scientists reported.

Gene Richardson

In combining the initial reports of 34 infections with the 14 newly identified cases, the researchers calculated the prevalence of minimally symptomatic infection in the village to have been 25 percent.

Richardson said it is unknown if an asymptomatic individual is capable of transmitting the virus. Because these individuals did not have an active case of the disease, "They were not passing it along in the usual way, through vomiting or diarrhea," he said. "It's unclear if they can pass it along it sexually."

Working in other Sierra Leone villages

The virus has been shown to hide out for months in semen, even after symptoms have subsided, with some published cases of survivors transmitting the virus through sexual contact.

Richardson said the study indicates that public health efforts to prevent infection and contain the virus during the epidemic were not entirely effective.

"It reminds us that we need to do a much, much better job in future epidemics," Richardson said.

He and his colleagues are now working in other villages in Sierra Leone where public health surveillance was poor during the epidemic, testing and interviewing individuals to get a better handle on the true number of people affected during the crisis.

"We expect to find a lot more undocumented survivors, so we can begin to answer the question of what was the true burden of disease," he said.

Other Stanford co-authors of the paper are Michele Barry, MD, director of the Stanford Center for Innovation in Global Health, and James Holland Jones, PhD, associate professor of Earth systems science and a senior fellow at the Woods Institute for the Environment.

Researchers from Partners in Health, Brigham and Women's Hospital, UC-San Francisco, the Kono District Ebola Response Centre and the Kono District Health Management Team in Sierra Leone also co-authored the study.

The study was funded by the Stanford Center for Innovation in Global Health. ISM

GABA

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The DLPFC, a broad swath of neural tissue on the forebrain surface, has been shown in animal studies and in observations of brain-damaged patients to be integral to high-level executive functions in the brain, such as planning, prioritizing and avoiding distractions. It has likewise been strongly implicated in working memory. The DLPFC orchestrates activity in numerous distant centers throughout the brain, including the visual cortex, which is located near the brain's surface but in the hindbrain.

Tie to working-memory capacity

"No previous study has ever pinpointed GABA's link with working memory in humans," said Yoon. "Working memory is a complex process, requiring coordinated activity in centers throughout the brain. Yet, remarkably, the amount of this one chemical in a single part of the brain accounts for close to one-third of the variance in individuals' load capacity."

In the study, 23 healthy participants ages 19-32 were subjected to batteries of tests of working memory. Yoon reasoned that different components of working memory would involve different neurotransmitter inputs. So he devised working-memory tests that separated the measurement of load, maintenance and distraction resistance.

Participants repeated several related tasks. In the simplest, they were shown a drawing of a face and then, after a two-second delay, shown a second face and asked whether it was the same as or different from the first one. Variations of this task — initially presenting two faces instead of just one; lengthening the intervening delay; or displaying a different, irrelevant face between the initial and final displays — tested load, maintenance and distraction resistance, respectively. The investigators compared individuals' error rates on the simple version of the task with outcomes on tasks taxing one or another working-memory component more heavily. The smaller the deterioration in performance on a test of a particular working-memory component, the greater the individual's capacity regarding that component was judged to be.

Stop and go signals

Using an advanced imaging method, the scientists measured GABA levels in the DLPFC and, for comparison, in the visual cortex. GABA, secreted by nerve cells, is an inhibitory neurotransmitter: Its uptake by other nerve cells inhibits their firing.

Yoon and his associates also measured levels of an excitatory neurotransmitter, glutamate. By far the two most abundant neurotransmitters in the brain, GABA and glutamate are considered to be that organ's stop and go signals.

Individuals with higher levels of GABA in their DLPFC performed better on tests of their load capacity — the ability to juggle more bits of information — the researchers found. In contrast, no significant association emerged linking GABA levels in the DLPFC to maintenance or to distraction resistance, or tying participants' load capacity to GABA levels in the visual cortex. Nor did imaging reveal any connection between performance on tests of load capacity and levels of glutamate in the DLPFC.

Schizophrenic patients, Yoon said, are known to be deficient in an enzyme essential to GABA production. So, drugs that boost GABA levels or function in the brain might prove helpful in restoring their impaired working memory. He plans to test this hypothesis.

The work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

The study was funded by the National Institute for Mental Health.

Stanford's Department of Psychiatry and Behavioral Sciences also supported the work. ISM

Cyberknife used to treat rare condition in pediatric patient

By Joe Molica

In October 2014, Kendall Kemm's parents received devastating news: Their then-10-year-old daughter had suffered a hemorrhagic stroke.

Kendall's stroke was a result of an arteriovenous malformation, or AVM, a rare defect that results in a tangle of abnormal blood vessels that disrupts the normal flow of blood. AVMs are most often found in the brain or spinal cord and affect less than 1 percent of the population.

Kendall survived, and is being treated at Stanford Health Care through stereotactic radiosurgery, which uses radiation to shrink and ultimately destroy the AVM in her brain.

Kendall travels from Pennsylvania to Stanford for treatment because Stanford Health Care offers a unique approach using CyberKnife technology, which delivers radiation with unprecedented precision. The CyberKnife was invented at Stanford, and is used to treat a variety of conditions. Steven Chang, MD, professor of neurosurgery, and Scott Soltys, MD, assistant professor of radiation oncology, oversee Kendall's treatment.

"When Kendall had her stroke, it was devastating," said Kendall's mother, journalist Leslie Gudel Kemm. "We spent the better part of the first month crying, and then doing research. So few doctors want to treat kids with this condition, but when we connected with Dr. Chang, he said, 'We can treat this.'"

Kendall's Crusade

Grateful for the care she received at Stanford Health Care and Lucile Packard Children's Hospital Stanford, Kendall brainstormed ways to help others with the same condition. Together with her family, she formed Kendall's Crusade. The nonprofit aims to provide financial assistance to families affected by AVM, raise overall awareness of the condition and support neurosurgery research.

Kendall returned to Stanford in October to continue her treatment. With funds raised through Kendall's Crusade, she presented a check to Chang to help fund his research on treatment and support a patient travel fund for AVM patients.

"When I first met Kendall and her family, they were so determined to learn all they could about AVMs," Chang said. "Although some AVMs are inoperable, the CyberKnife opens up additional treatment options that other technology doesn't allow."

Kendall's AVM is now approximately 90 percent gone, with her next MRI scheduled for next year. Additional treatments will be considered as her progress is monitored. Kendall has remained positive and devoted to her mission to help fellow AVM patients.

"I'm grateful for what we've been able to do for the other kids that are going through the same thing as me," she said. "But I want us to get to a point where the research will help to develop a cure, so no other kids have to go through this. ISM

NORBERT VON DER GROEBEN

NORBERT VON DER GROEBEN

Top: Accompanied by research associate Lorelei Shoemaker (left), Kendall Kemm visits a neuroscience lab, where she gets a close look at a human brain. Below: Kendall helps Shoemaker with an experiment.

OF NOTE

reports on significant honors and awards for faculty, staff and students

CHRISTOPHER ALMOND, MD, was promoted to associate professor of pediatrics, effective Aug. 1.

BEN BARRES, MD, PhD, professor of neurobiology, of developmental biology and of neurology and neurological sciences, has received the Society for Neuroscience's Ralph W. Gerard Prize in Neuroscience, the society's highest award. He will share the $25,000 prize with fellow recipient Thomas Jessell, PhD, of Columbia University. The prize honors outstanding scientists who have made significant contributions to neuroscience. Barres' research focuses on the role of glial cells in development and synapse function and in diseases such as Alzheimer's.

CHRISTOPHER CONTAG, PhD, professor of pediatrics and of microbiology and immunology, will receive the 2017 Britton Chance Biomedical Optics Award from SPIE, the international society for optics and photonics. The award recognizes outstanding lifetime contributions to biomedical optics. Contag develops and uses optics-based imaging tools to study biology in living animal models of human disease, and for early detection of cancer in patients.

CHRISTINA CURTIS, PhD, assistant professor of medicine and of genetics, was named a 2016 Kavli Frontiers of Science Fellow by the National Academy of Sciences. The program selects outstanding young scientists to attend symposia, thereby promoting communication and collaboration. In her research, Curtis uses experimental and analytical approaches to improve the diagnosis and treatment of cancer.

JAMES DUNN, MD, PhD, was appointed professor of surgery, as well as surgeon-in-chief at Lucile Packard Children's Hospital Stanford and chief of pediatric surgery at the School of Medicine, effective Oct. 1. He specializes in using surgical and bioengineering techniques to help children with short bowel syndrome, which can occur in preterm infants and infants with congenital anomalies.

BRICE GAUDILLIERE, MD, PhD, was appointed assistant professor of anesthesiology, perioperative and pain medicine, effective Sept. 1. His research combines high-dimensional mass cytometry analysis with machine-learning-based biocomputation to study the human immune system's response to perturbations, such as pregnancy. His clinical interests include surgical trauma, ischemic stroke, pregnancy and preterm labor.

JAMES JACOBS, MD, PhD, was appointed associate professor of psychiatry and behavioral sciences, effective Sept. 1. He is the executive director of Vaden Health Center and associate vice provost for student affairs.

DAVID MAAHS, MD, PhD, was appointed professor of pediatrics, effective Sept. 1. He is chief of the division of pediatric endocrinology. His research and clinical focus is on improving care for children with Type 1 diabetes.

ROBERT MALENKA, MD, PhD, professor of psychiatry and behavioral sciences and the Nancy Friend Pritzker Professor in Psychiatry and Behavioral Sciences, has been awarded the Julius Axelrod Prize by the Society for Neuroscience. The $25,000 prize recognizes exceptional achievements in neuropharmacology and an exemplary commitment to mentoring young researchers. Malenka's interests include translating research on synaptic transmission into clinically useful therapies.

ARASH MOMENI, MD, was appointed assistant professor of surgery, effective Sept. 1. He is the co-director of the hand transplant program. He specializes in microsurgical reconstruction of the breast, head and neck, trunk and extremities.

PRITHVI MRUTHYUNJAYA, MD, was appointed associate professor of ophthalmology, effective Sept. 1. He is the director of ocular oncology. He specializes in the treatment of pediatric and adult ocular cancers and conditions affecting the retina. His research interests include ocular cancer imaging, genetics and tumor biopsy.

LIDIA SCHAPIRA, MD, was appointed associate professor of medicine, effective Sept. 1. Her research focuses on cancer survivorship and on improving communication between caregivers and patients.

ALEX SOX-HARRIS, PhD, was appointed associate professor (research) of surgery, effective Sept. 1. He is the director of clinical research for the Department of Surgery, and his research focuses on the evaluation of health-care quality and efficacy.

ERIC SUN, MD, PhD, was appointed assistant professor of anesthesia, perioperative and pain medicine, effective Sept. 1. His research interests include health economics and policy, with a focus on economics and policy in the perioperative setting. ISM

Ben Barres

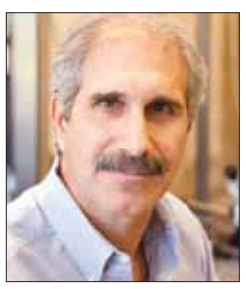
Christopher Contag

Christina Curtis

James Dunn

James Jacobs

David Maahs



Robert Malenka

Arash Momeni

Prithvi Mruthyunjaya

Lidia Schapira

Alex Sox-Harris

Eric Sun