INSIDE STANFORD MEDICINE

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Researchers have gained new insight into how neurons control muscle movement.

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South Bay cancer center opens to first patients

NORBERT VON DER GROEBEN

Kate Surman, Amir Dan Rubin, Evan Low, Lloyd Minor, Sridhar Seshadri, Beverly Mitchell and Kansen Chu attend the June 26 ribbon-cutting ceremony for the Stanford Cancer Center South Bay, which is located in San Jose near the intersection of highways 17 and 85.

By Sara Wykes

For 17 months, Leslie Trillo, of San Jose, has endured chemotherapy at a clinic in Campbell for the cancer that doctors found in her colon, lung and liver. When she learned that the clinic would close, with its physicians moving to the Stanford Cancer Center South Bay, she worried about whether she would feel comfortable at the new location.

"Some days you don't feel as great as you want to be," she said, "and when you're feeling like that, you need a soft place to land."

At the June 26 ribbon-cutting ceremony for the center, Trillo said she wasn't worried anymore. She'd had a look inside. "It's beyond what I expected," she said. "It's really been done with patients in mind. And it's wonderful to have it nearby."

Today, the Stanford Cancer Center South Bay opened its doors to its first patients, including Trillo.

Established to serve patients in the populous South Bay, the center is Stanford Health Care's first off-campus outpatient clinic for the diagnosis and treatment of cancer. It occupies an existing 70,000-square-foot building, located at 2589 Samaritan Drive in San Jose, that is visible from the intersection of highways 17 and 85.

Checking in once

A patient and family advisory council recommended ways to maximize patient comfort at the new cancer center. "This stunning new fa-

See CENTER, page 6

Side effect of flu vaccine yields insights into sleep disorder

By Jennie Dusheck

An international team of researchers has found some of the first solid evidence that narcolepsy may be a so-called "hit-and-run" autoimmune disease.

The researchers sought to determine why, of two different flu vaccines widely deployed during the 2009 swine flu pandemic, only one was associated with a spike in the incidence of narcolepsy, a rare sleep disorder.

A paper describing their findings was published July 1 in *Science Translational Medicine*. Lawrence Steinman, MD, a professor of pediatrics and of neurology and neurological sciences, is the senior author. The first author is Sohail Ahmed, MD, who was global head of clinical sciences at Novartis Vaccines at the time of the study.

Autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis, are well-known for taking decades to ravage the nervous system, joints or other organ systems. But since the late 1990s, researchers have hypothesized a different kind of autoimmune disease, one that may incur rapid, pinpoint damage and leave virtually no trace of its work. Narcolepsy is suspected of being one of these hit-and-run diseases.

Gene variants increase susceptibility

Narcolepsy is a chronic, incurable and lifelong brain disorder that interferes with normal sleep-wake cycles and causes an array of symptoms, including overwhelming daytime sleepiness and sleep attacks that can strike at any time — even in the middle of a conversation. What causes narcolepsy has been a source of fascination among scientists for decades.

Narcolepsy cases mostly occur at random, as opposed to being strictly inherited, although certain gene variants can make people more susceptible to it. For example, nearly everyone who has narcolepsy accompanied by cataplexy, a condition that causes sudden episodes of muscle weakness, carries a gene variant called HLA-

See NARCOLEPSY, page 7

Adolescents uncertain about risks of marijuana, e-cigarettes

By Erin Digitale

Teenagers are very familiar with the risks of smoking cigarettes, but are much less sure whether marijuana or e-cigarettes are harmful, according to a new study by researchers at the School of Medicine.

ANDREY_POPOV / SHUTTERSTOCK

A new study indicates that adolescents are confused about whether e-cigarettes are harmful.

While adolescents get clear messages from their families, teachers, peers and the media about the harms of smoking cigarettes, they receive conflicting or sparse information about the harms of marijuana and e-cigarettes, the study showed.

The findings were published online June 23 in the *Journal of Adolescent Health*.

"Kids were really good at describing the harmful things that happen with cigarette smoking, but when we asked about other products, there was a lot of confusion," said the study's lead author, Maria Roditis,

See E-CIGARETTES, page 6

Kennewick Man closely related to Native Americans, scientists say

By Krista Conger

DNA from the 8,500-year-old skeleton of an adult man found in 1996, in Washington, is more closely related to Native American populations than to any other population in the world, according to an international collaborative study conducted by scientists at the University of Copenhagen and the School of Medicine.

The finding challenges a 2014 study that concluded, based on anatomical data, that Kennewick Man was more related to indigenous Japanese or Polynesian peoples than to Native Americans. The study is likely to reignite a long-standing legal dispute regarding the skeleton's provenance and its eventual fate.

"Using ancient DNA, we were able to show that Kennewick Man is more closely related to Native Americans than any other population," said postdoctoral scholar Morten

See KENNEWICK, page 7

BRITTANY TATCHELL / SMITHSONIAN

A bust shows how Kennewick Man may have looked.

5 QUESTIONS

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

New guidelines for treating teen eating disorders

Eating disorders have been described in medical literature since the 1870s, but until now there have been no guidelines that codify the best way to treat children and adolescents affected by these conditions — only guidelines for adults.

James Lock, MD, PhD, professor of psychiatry and behavioral sciences at the School of Medicine and director of the Comprehensive Eating Disorders Program at Lucile Packard Children's Hospital Stanford, recently co-authored the first set of evidence-based guidelines for the treatment of eating disorders in children and teenagers. He talked with writer Erin Digitale about the rationale for the new guidelines, which were published in the May issue of the Journal of the American Academy of Child & Adolescent Psychiatry.

1 Why was a formalized set of guidelines needed?

LOCK: There have never been practice parameters that address eating disorders in children and adolescents, and expertise in treating these disorders has been sort of sequestered. Yet eating disorders are so prevalent and are such a severe problem: Lifetime prevalence in adolescent girls is around 1 percent, and the disorders have among the highest fatality rates of all mental illnesses.

Teens need treatment approaches that account for their level of physical and emotional development, the fact that their parents generally want and need to be involved in their recovery, and the fact that they have not usually had eating disorders for as long as adult patients with the same diagnoses.

James Lock

In addition, so many training programs in psychology and psychiatry don't really give opportunities for training in how to treat eating disorders. It's a terrible limitation of many training programs; they should all provide opportunities for learning about eating-disorder patients in a systematic way. I hope the new practice parameters will help facilitate that.

The fact that these guidelines were very thoroughly vetted should give caregivers confidence in them. There is consensus around these recommendations. Practice guidelines also become really important metrics for insurers when they're thinking about what to pay for and how to organize care.

2 There is a long history of removing young patients from their families as part of treatment for eating disorders, particularly anorexia nervosa. But that's not what the new parameters recommend. Why the shift?

LOCK: For many decades, the idea was that to treat eating disorders — especially anorexia nervosa, which has had a specific diagnosis since 1874 — it was necessary for medical and psychiatric reasons to take children out of their usual lives and put them in the hospital for long periods. But over the last 15-20 years, we've seen emerging alternatives, such as day and outpatient programs that are family-based. Research now shows that there's no difference in outcome between the two types of treatment. That doesn't mean inpatient treatment is not useful, but on average it's not better.

That's really important because the costs and harms of putting a 14-year-old in the hospital for months at a time are significant. And we also know that most people, when they get better, learn the most from therapy in the context of real life, where they can learn to manage the challenges they'll encounter in dealing with family, school and so on.

So our recommendation is that outpatient treatment is the first line of treatment. It's a strong statement that runs contrary to the history of treating kids and adults who have anorexia nervosa with prolonged hospitalization.

3 When families are involved in their child's eating-disorder treatment, what are they actually doing and how do they learn what to do?

LOCK: Families should be involved in the care of their children with any illness, including eating disorders. The odd thing was leaving parents out in the first place. At our Comprehensive Eating Disorders Program, parents help their children by learning how to prevent eating-disordered behaviors and promote normalized eating, and do so in a supporting and loving fashion. Because the behaviors and thinking associated with eating disorders are often not well-understood by parents, our team of professionals helps parents learn how to address them.

4 The new edition of the diagnostic and statistical manual of mental disorders, the DSM-5, included some changes to diagnostic criteria for eating disorders. How do these fit together with the new practice parameters?

LOCK: The changes to the DSM don't really change recommendations for care. But what's important about the DSM-5 is that it allows people who treat children and adolescents to diagnose them with eating disorders more accurately. You don't have to use adult metrics, and there is latitude to take parental perspective in mind, for example. So, for instance, an adolescent girl who meets most criteria for anorexia nervosa but has missed two menstrual periods instead of three, or a teen who has most characteristics of bulimia but is purging once a week instead of four times a week can be diagnosed. It allows caregivers to better map treatments onto the guidelines we've developed. Clinicians have written a lot about the need for the diagnostic modifications that are included in the DSM-5, and we're very happy about most of those changes.

5 What take-away messages do you want physicians or other caregivers to get from the new parameters?

LOCK: First, that outpatient treatment is the best line of attack for treating childhood and adolescent eating disorders. Intensive interventions such as hospitalization should be reserved for patients who don't respond to first-line therapies. Second, medication is definitely not a strategy that we know to be useful for children or adolescents who have anorexia nervosa or bulimia nervosa. Clinicians should think carefully about their reasons for prescribing psychiatric medications to these patients. Finally, we want people to be reminded that these disorders are very prevalent and serious, and that it's important to learn about how to take care of these kids. **ISM**

Out-of-pocket health costs tied to antimicrobial resistance

By Beth Duff-Brown

The high out-of-pocket costs for antimicrobial drugs in many developing countries is leading to an increase in drug-resistant pathogens, according to a study by Stanford University researchers.

Many government-run public health systems in developing countries have instituted copayments for visits to clinics and prescription drugs. However, the study's authors found evidence to suggest that such policies are associated with increased antimicrobial resistance, likely because high out-of-pocket costs have prompted low-income patients to turn to the black market or informal clinics for antibiotic and antiparasitic drugs.

The quality of unlicensed drugs is often poor. In addition, caregivers at such clinics may prescribe antimicrobials excessively and inappropriately, as well as provide inaccurate course and dose instructions, the researchers said. If patients don't take the proper dose of a drug, or take one that's been improperly manufactured, microbes can more easily evolve resistance to it.

Some four-dozen countries — from the Central African Republic to Sri Lanka to Russia — are particularly vulnerable to antimicrobial resistance, given their high burden of infectious disease and the high cost of treating resistant microbes. What's unfolding in these countries could undo decades of progress in declining morbidity and mortality from infectious diseases around the world, the researchers said.

"Understanding the drivers of antibiotic resistance in low- to middle-income countries is important for wealthier nations because antibiotic-resistant pathogens, similar to other communicable diseases, do not respect national boundaries," said Marcella Alsan, MD, PhD, MPH, the lead author of the study, which was published July 9 in *Lancet Infectious Disease*.

Alsan is an assistant professor of medicine at Stanford, an investigator at the Veterans Affairs Palo Alto Health Care System and a core faculty member at the Center for Health Policy/Center for Primary Care and Outcomes Research.

"Out-of-pocket health expenditures are a major source of health-care financing in the developing world," said Jay Bhattacharya, MD, PhD, senior author of the study and a professor of medicine, a senior fellow at the Freeman Spogli Institute for International Studies and another core faculty member at CHP/PCOR.

Fostering drug resistance

Purchases of drugs, including antimicrobial agents, constitute an estimated 70 percent of out-of-pocket health expenditures in India and 43 percent in Pakistan. In the sample of low- and middle-income countries used in the study, 49 percent of health expenditures were, on average, private. And the majority of those private health expenditures — some 76 percent — were out-of-pocket.

The study included 47 countries: 23 in Africa, eight in the Americas, three in Europe, eight in the Middle East, three in Southeast Asia, and two in the Western Pacific.

The data set for the main analysis is from the first global report by the World Health Organization on antibiotic resistance. The report, which came out last year, indicates that antimicrobial resistance is a "serious, worldwide threat to public health."

And the Stanford researchers believe this is, in part, due to high out-of-pocket costs.

"To our knowledge, we are the first to emphasize the idea that copayments imposed in the public sector of a health-care system lead to overuse of a medication or product in the private sector," the authors wrote. "Conventional teaching in health economics — which focuses on their effect on the demand for care within a single insurance system — is that copayments tend to discourage use."

The most prominent and convincing evidence for this, the authors wrote, was the 15-year RAND health insurance experiment conducted in six U.S. cities on 2,000 households. That study found that the increase in copayments led to a significant decline in the use of antibiotics, "providing evidence that the demand for health care is not completely inelastic."

However, when the regulated public sector and unregulated private sector are selling the same or similar products, a price increase in one does not necessarily reduce the overall demand, the authors found. In fact, it may increase demand because higher dosages of drugs will be required to fight more resistant microbes, which are the result of poorly made and prescribed drugs in the private sector.

"Even if total consumption of antibiotics were unchanged, the shift of more patients to less-regulated providers could lead to more antibiotic resistance," the authors wrote.

Global health challenge

"Antimicrobial resistance is a growing, global public health challenge that could undo decades of progress in declining morbidity and mortality from

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STANFORD MEDICINE

Cystic fibrosis deadlier for Hispanics than non-Hispanics

By Erin Digitale

Cystic fibrosis is more deadly for Hispanic than non-Hispanic patients, a disparity that is not explained by differences in their access to health care, according to a new study from the School of Medicine.

MyMy Buu

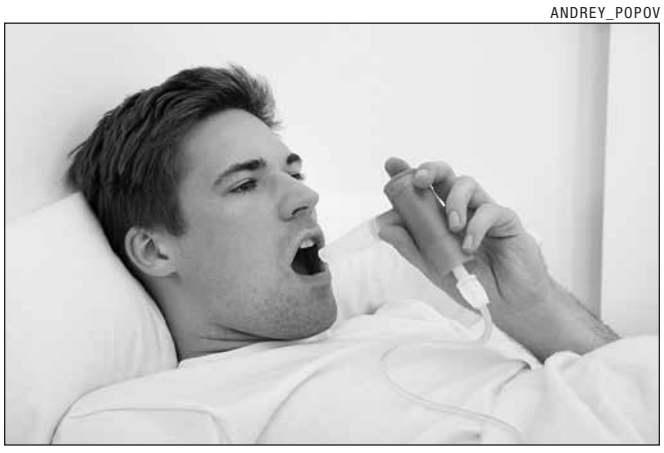
The study, published online June 18 in *Chest*, tracked more than 1,700 California residents with cystic fibrosis. Between 1991 and 2010, Hispanic CF patients were almost three times as likely to die as non-Hispanic CF patients, the study found. The gap in survival existed in spite of the fact that both groups visited CF specialty clinics equally often. Furthermore, the study uncovered genetic differences between the two groups that may have put Hispanic patients at a disadvantage when it came to being able to benefit from new CF therapies.

"We need to ask if the care model for patients with CF is working for this minority group," said MyMy Buu, MD, the study's lead author and an instructor in pediatric pulmonary medicine. "We want to make sure that what we are doing is not inadvertently causing disparities." Buu is also a pediatric pulmonologist who cares for children with cystic fibrosis at Lucile Packard Children's Hospital Stanford.

"Given that CF is now identified shortly after birth through newborn screening in California, our study calls for an urgent need to identify the factors involved in this disparity," said Carlos Milla, MD, associate professor of pediatrics and co-senior author of the study. "This will be crucial to develop treatment regimens that guarantee that all children with CF can benefit from early diagnosis and the novel treatments being introduced." Milla also directs the Stanford Cystic Fibrosis Center.

Cystic fibrosis is a genetic disease that causes serious lung and digestive problems. Although it used to kill most patients in childhood, new treatments have dramatically improved survival rates. Today, more than half of CF patients in the United States live past age 40. The drug Ivacaftor, which greatly improves lung function for the 4 percent of CF patients who share one specific mutation in the disease-causing gene, became the first CF medication to treat the cause of the disease rather than its symptoms when it was approved in 2012.

ANDREY_POPOV



In California, Hispanic patients with cystic fibrosis were three times as likely to die from the disease as their non-Hispanic counterparts.

Eliminating possible explanations

Buu's team used data from the Cystic Fibrosis Foundation's patient registry, examining all California residents who were diagnosed as children during the study period of 1991-2010. Of the 1,719 patients studied, 28 percent were Hispanic. California has the largest proportion of Hispanic CF patients in the United States; nationally, about 7 percent of CF patients are Hispanic.

During the study period, 9.1 percent of the Hispanic patients and 3.3 percent of the non-Hispanic patients died.

Carlos Milla

From the data, the researchers were able to eliminate a number of possible explanations for the difference in mortality rate. For instance, Hispanic patients were not being diagnosed late, were not sicker at the time of diagnosis and did not lack access to CF specialty centers; rather, they were diagnosed at the same age as non-Hispanic patients, started out equally ill and used specialty care equally often. Hispanic and non-Hispanic patients also had the same rates of CF complications, such as bacterial infections of the lung and CF-related diabetes.

However, the researchers did find important clinical and social differences between the groups. At age 6, the earliest that lung function is routinely and reliably measured for patients with CF, Hispanic children with CF had worse lung function than non-Hispanic kids with the disease. The gap in lung function persisted as the children aged, although it did not widen. And although the same proportion of patients in both groups eventually developed CF complications, the complications struck Hispanic patients earlier in life. Hispanic patients lived in poorer neighborhoods and were more likely to be covered by public health insurance than their non-Hispanic counterparts.

The research also showed that, between the two groups, different mutations prevailed in the disease-causing gene, which is called the CF transmembrane conductance regulator gene. Hispanic patients tended to have rare and poorly characterized mutations in their CFTR gene, whereas non-Hispanic patients had more common mutations that have been more extensively researched.

Looking ahead

"We are moving in the direction of gene-mutation-directed therapy," Buu said. "The CF research community is trying to understand these mutations, and those that are most frequent in the whole CF population are being studied first." This puts Hispanic patients with rarer mutations at a disadvantage in terms of being able to benefit from new therapies, she said. "It will take longer to get to them, but there are efforts to understand all the mutations of the CFTR gene."

The next step, Buu said, is to try to identify the factors that appear to contribute to the higher mortality rate among Hispanic CF patients so that effective interventions could be implemented early. For instance, Buu's team wants to investigate why lung function is lower in young Hispanic CF patients, as well as how the onset of CF complications could be delayed in Hispanic children.

"We hope to create awareness of this disparity, and we hope that it is modifiable," she said.

Other Stanford-affiliated co-authors of the study are Lee Sanders, MD, associate professor of pediatrics; Jonathan Mayo, data analyst in pediatrics; and Paul Wise, MD, professor of pediatrics. Milla and Sanders are members of Stanford's Child Health Research Institute.

The research was funded by the Cystic Fibrosis Foundation, the Ernest and Amelia Gallo Endowed Postdoctoral Fellowship, the Lucile Packard Foundation for Children's Health, the National Institutes of Health and the Child Health Research Institute.

Stanford's Department of Pediatrics also supported the work. **ISM**

Antimicrobial

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infectious diseases," the authors wrote. "Common bacterial pathogens have increasingly developed resistance to most of the currently available antibiotics. This phenomenon, coupled with a dry antibiotic pipeline, has led the World Health Organization to warn of a 'post-antibiotic era, in which common infections and minor injuries can kill.'"

Resistant organisms are more difficult to treat and associated with higher morbidity and mortality than their susceptible counterparts. The Centers for Disease Control and Prevention estimates that resistance to antibiotics causes 2 million illnesses and 23,000 deaths a year in the United States. Estimates of the impact of antimicrobial resistance on the U.S. economy include $20 billion in direct health-care costs, with additional indirect costs as high as $25 billion a year.

The concern over rising antimicrobial resistance is not limited to the developed world, the authors wrote, noting the accelerating rates of resistance among intestinal, respiratory and sexually transmitted pathogens in developing countries.

Alsan and her co-authors believe that controlling the spread of resistant bacterial pathogens is an urgent, global public health priority.

Though no previous research has examined the relationship between out-of-pocket payments and antibiotic resistance in low- and middle-income countries, the authors wrote that their findings are consistent with the work of researchers who have found that supplier-induced demand is an important determinant for excess use of health care.

Traditionally, cost-sharing in the form of copayments has been viewed as a way to curtail the overuse of medical care. However, in many low- and middle-income countries, copayments may have an unintended consequence, the authors wrote.

Most developing economies have a robust, informal, private health-care sector that operates alongside the more traditional one. If the public and private health sectors serve as substitutes for one another to some degree, the prediction from consumer theory is that higher copayments for medication will shift more consumers to the private sector in search of cheaper drugs. The authors developed a mathematical economic model to demonstrate this point.

They used the recently published data set collected by the WHO to assess the role of such out-of-pocket payments, while adjusting for other key predictors, on the prevalence of antimicrobial resistance across a sample of low- and middle-income countries.

The authors found that out-of-pocket health expenditures were statistically more important than any other country-level environmental factors — including poverty, livestock production, access to sanitation and other institutional features of the health sector — in predicting patterns of antimicrobial resistance across low- and middle-income countries. Moreover, this pattern was driven by countries that require copayments on medications in the public sector.

"Our work highlights an underappreciated policy lever to address this problem of antimicrobial resistance: rolling back cost-sharing arrangements for medications in the public sector," they wrote.

Other Stanford co-authors are Lena Schoemaker, a research data analyst at CHP/PCOR, and Karen Eggleston, PhD, a CHP/PCOR fellow and fellow at the Shorenstein Asia-Pacific Research Center in the Freeman Spogli Institute.

The study was funded by the National Institutes of Health.

Stanford's Department of Medicine also supported the work. **ISM**

Beth Duff-Brown is communications manager at the Center for Health Policy/Center for Primary Care and Outcomes Research.

Alzheimer's Disease Research Center to be launched

By Bruce Goldman

Frank Longo

Victor Henderson

The National Institutes of Health will fund the establishment of an Alzheimer's Disease Research Center at the School of Medicine. The award, totaling slightly more than $7.3 million, will be dispensed over a five-year period.

"This new Stanford-based center will provide a key mechanism by which our exceptional basic science community can better connect with our translational and clinical neurodegenerative disease research," said Frank Longo, MD, PhD, professor and chair of neurology and neurological sciences. "Many dozens of faculty will be involved."

The center will help scientists conduct interdisciplinary research on Alzheimer's and Parkinson's diseases, as well as on related disorders. An estimated 5 million Americans suffer from Alzheimer's disease, and about 300,000 are living with Parkinson's disease, making these the two most common neurodegenerative disorders nationwide. Moreover, both conditions are rapidly

See ALZHEIMER'S, page 7

Cause of kidney failure key when planning future treatment

By Tracie White

As a new physician in Galway, Ireland, and then as a nephrology fellow at Stanford's School of Medicine, Michelle O'Shaughnessy, MD, began to wonder whether similar treatment plans for all patients whose kidneys had failed was necessarily the best practice.

"I was struck by my patients, who were often young and on dialysis at the age of 23 or 24," O'Shaughnessy said, referring to patients whose kidneys had failed because of glomerulonephritis, a group of rare disorders that damage the kidney's ability to filter the blood.

"I thought there should be other avenues for them," she added. "They were trying to get a career going, to keep their life together. We should be able to treat them better."

Currently, the standard of care is to follow a similar treatment plan for most kidney-failure patients, whatever the initial cause of their kidney failure. The two leading causes in the United States are hypertension and diabetes, followed by the rarer glomerulonephritis, which is also called glomerular disease.

"The cause of the kidney failure and the side effects of prior treatments are often disregarded," O'Shaughnessy said. "All these patients receive the same kind of generic treatment approach: a transplant or dialysis. The original cause of kidney failure is not usually taken into account."

O'Shaughnessy set out to research whether it might be more beneficial to tailor treatment plans individually for kidney failure patients. For example, a patient with a high risk for infections may benefit from a certain type of vascular access for dialysis, or a patient at increased risk for cancer may benefit from more regular cancer screening before and after kidney transplantation.

Subtype of disease matters

In a resulting study, published online June 19 in the *Clinical Journal of the American Society of Nephrology*, O'Shaughnessy and colleagues used big data to determine that mortality rates for patients whose kidney failure was attributed to glomerulonephritis vary significantly according to which subtype of the disease they had. These results suggest that treatment plans should vary according to root causes of kidney failure, she said.

"We showed that a patient's cause of kidney failure is strongly associated with their risk of dying after starting dialysis or receiving a kidney transplant," she said. "This suggests that the cause of kidney failure should not be forgotten even after a patient's kidneys fail; instead, treatment should be tailored toward disease-specific risks, and research should be carried out to determine why these survival disparities exist."

"The cause of the kidney failure and the side effects of prior treatments are often disregarded."

SHUTTERSTOCK

When treating patients whose kidneys have failed, physicians should keep in mind the original cause of the patient's kidney problems and adjust the treatment plan accordingly, a new study suggests.

Researchers examined data from 84,301 patients who, between 1996 and 2011, suffered end-stage kidney disease attributed to one of the six major glomerular disease subtypes.

"We followed these patients to see what their survival was like," O'Shaughnessy said. "We observed quite significant differences in survival."

Results showed that the specific type of glomerular disease determined how long a patient lived after developing kidney failure. For example, mortality ranged from 4 percent per year for patients with the subtype IgA nephropathy to 16 percent per year for patients with the subtype vasculitis. After adjusting for various differences among patients — such as their age, whether they had diabetes or had received a kidney transplant — the researchers found that patients with lupus nephritis were almost twice as likely to die as patients with IgA nephropathy.

"When you divide patients according to their glomerular disease subtype, you actually see a whole spectrum of outcomes," O'Shaughnessy said.

Kidney failure in children

Glomerulonephritis is the leading cause of kidney failure in children. It is most commonly an autoimmune disease that is characterized by inflammation of the glomeruli, tiny blood vessels in the kidneys that remove waste and excess fluids from the body. But each of the many glomerular disease subtypes is unique. In certain subtypes, the immune system attacks the kidneys; in others, it damages the blood vessels.

As a result, the various subtypes are treated using different methods before the kidneys begin to fail. The treatments may include steroids or stronger immunosuppressant medications. The resulting side effects can range from severe infections to diabetes to cancer.

"The rest of the body, apart from the kidneys, has had different degrees of damage from the disease itself and the types of treatments it has undergone prior to kidney failure," O'Shaughnessy said. "When the patients get to dialysis or have a kidney transplant, it's still important for us to remember that" — and to treat accordingly.

O'Shaughnessy thought about this when she was making her rounds as a new physician caring for young patients on dialysis.

"It occurred to me that when I saw those patients, they weren't telling me how they're worried about the fact that they've got glomerular disease," she said. "When I saw them at the clinic or at the dialysis center, they were bothered by the fact that they were getting infections or cancer, or developing other side effects from their medications."

It's important to know why one kidney patient does well and another does poorly, she said. If physicians take into consideration what caused the kidneys to fail in the first place and what types of treatments patients received prior to kidney failure, it could possibly improve the patients' quality of life or increase their life span, she added.

Wolfgang Winkelmayer, MD, a former Stanford faculty member who is now professor of nephrology at Baylor College of Medicine, is senior author of the study. Other Stanford authors are Maria Montez-Rath, PhD, research associate, and Richard Lafayette, MD, associate professor of nephrology.

The study was supported by funding from the ASN Foundation for Kidney Research and the National Institutes of Health.

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

'A mother hen,' early Stanford kidney donor dies at 99

By Kim Smuga-Otto

Twice Inga Goodnight gave her oldest son, Gary, the gift of life: once when she gave birth to him, in 1938, and again, in 1965, when she donated a kidney to him.

Inga went on to lead an active life with Gary and her other three sons, as well as with her grandchildren and great-grandchildren. Gary died at age 60 of a stroke. Inga died April 28 of heart failure. She was 99.

Her long life and the fact that she was 51 at the time of her donation mean Inga was likely one of the oldest living kidney donors. "She was a mother hen. She took care of everyone," recalled one of her sons, Bill Goodnight, a retired wildlife manager for the Idaho Fish and Game Department.

Today, kidney transplants are established procedures; more than 17,000 were performed in the United States last year. Improvements in surgery and immunosuppressive drugs have increased the number of potential kidney matches. Studies have shown that donors have no increased health risks compared with the general public.

COURTESY OF BILL GOODNIGHT

Gary Goodnight, left, received a kidney from his mother Inga Goodnight, right, shown here with his son Torin. Inga died on April 28. She was 99.

Many unknowns

But in 1965, when Gary became the third patient to receive a kidney transplant at Stanford, many things were unknown. Doctors were still determining proper dosages for the immunosuppressive drugs, and they didn't know if Gary's body would reject the kidney or if he would even survive the first year.

While it was known that a person could live with one kid-

Research sheds light on how neurons control muscle movement

OLIVER BURSTON

Studying the brain activity of two patients with Lou Gehrig's disease has given researchers insight into how neurons control muscle movement.

By Barbara Feder Ostrov

Stanford University researchers studying how the brain controls movement in people with paralysis, related to their diagnosis of Lou Gehrig's disease, have found that groups of neurons work together, firing in complex rhythms to signal muscles about when and where to move.

"We hope to apply these findings to create prosthetic devices, such as robotic arms, that better understand and respond to a person's thoughts," said Jaimie Henderson, MD, professor of neurosurgery.

A paper describing the study was published online June 23 in *eLife*. Henderson, who holds the John and Jene Blume-Robert and Ruth Halperin Professorship, and Krishna Shenoy, PhD, professor of electrical engineering and a Howard Hughes Medical Institute investigator, share senior authorship of the paper. The lead author is postdoctoral scholar Chethan Pandarinath, PhD.

The study builds on groundbreaking Stanford animal research that fundamentally has changed how scientists think about how motor cortical neurons work to control movements. "The earlier research with animals showed that many of the firing patterns that seem so confusing when we look at individual neurons become clear when we look at large groups of neurons together as a dynamical system," Pandarinath said.

Previously, researchers had two theories about how neurons in the motor cortex might control movement: One was that these neurons fired in patterns that represent more abstract commands, such as "move your arm to the right," and then neurons in different brain areas would translate those instructions to guide the muscle contractions that make the arm move; the other was that the motor cortex neurons would actually send directions to the arm muscles, telling them how to contract.

But in a 2012 *Nature* paper, Shenoy and his colleagues reported finding that much more is going on: Motor cortical neurons work as part of an interconnected circuit — a so-called dynamical system — to create rhythmic patterns of neural activity. As these rhythmic patterns are sent to the arm, they drive muscle contractions, causing the arm to move.

"What we discovered in our preclinical work is evidence of how groups of neurons coordinate and cooperate with each other in a very particular way that gives us deeper insight into how the brain is controlling the arm," Shenoy said.

He and his colleagues wanted to know whether neurons fired similarly in humans.

Recording human brain activity

To conduct the study, the researchers recorded motor cortical brain activity of two research participants with the degenerative neurological condition called amyotrophic lateral sclerosis, or ALS. The condition, which also is known as Lou Gehrig's disease, damages neurons and causes patients to lose control over their muscles.

The participants, a 51-year-old woman who retained some movement in her fingers and wrists, and a 54-year-old man who could still move one of his index fingers slightly, are participants in the BrainGate2 trial, which is testing a neural interface system allowing thoughts to control computer cursors, robotic arms and other assistive devices.

These participants had electrode arrays implanted in their brains' motor cortex for the trial. That allowed researchers to record electrical brain activity from individual neurons while the participants moved or tried to move their fingers and wrists, which were equipped with sensors to record physical movement. Typically, such mapping in humans can only occur during brain surgery.

The participants' implants provided an "opportunity to ask important scientific questions," Shenoy said. The researchers found that the ALS patients' neurons worked very similarly to the preclinical research findings.

Researchers now plan to use their data to improve the algorithms that translate neural activity in the form of electrical impulses into control signals that can guide a robotic arm or a computer cursor.

Other Stanford co-authors of the paper are former research associate Vikash Gilja, PhD; research assistant Christine Blabe; and postdoctoral scholar Paul Nuyujukian, MD, PhD.

The study was funded by the Stanford Institute for Neuro-Innovation and Translational Neuroscience, Stanford BioX/NeuroVentures, the Stanford Office of Postdoctoral Affairs, the Garlick Foundation, the Reeve Foundation, the Craig H. Neilsen Foundation, the National Institutes of Health, the Department of Veterans Affairs and the MGH-Deane Institute for Integrated Research on Atrial Fibrillation and Stroke.

Stanford's Department of Neurosurgery, Department of Neurology and Neurological Sciences and Department of Electrical Engineering also supported the work. ISM

Barbara Feder Ostrov is a freelance writer.

Jaimie Henderson

Chethan Pandarinath

Krishna Shenoy

ney, no one knew if there would be long-term health impacts for Inga. And unlike modern laparoscopic surgery, with its tiny incisions and short hospital stays, the surgery to remove the Inga's kidney involved a large incision that cut through abdominal muscles and required a long recovery.

Despite these uncertainties and obstacles, Inga and her family, much like today's donors, were hopeful and determined.

"There was never a question on her part on being a donor," said Bill.

Gary was born in Indianapolis and spent his early years surrounded by cousins, uncles, aunts and grandparents. As a child, his kidneys shut down and stopped making urine. As a result, his body retained fluid: Bill remembered how his 8-year-old older brother's face puffed up. After Gary was hospitalized for a year, Inga and her husband took the chance that a warm, dry climate might be good for his health. They left their extended family in Indiana, and the six of them drove to Arizona with a camper trailer in tow. Seemingly miraculously, Gary's condition improved.

He remained healthy for over 13 years, during which time the family moved to the San Francisco area. They were aware that Gary's kidneys could fail again, but also hopeful; in 1955, the first successful kidney transplant was reported.

"Gary tracked the news about transplants," Bill recalled. "The first successful ones were all identical twins." Soon, advances in immunosuppressive drugs, as well as a clearer understanding of how to match donors and recipients, led to successful transplants between other relatives. Stanford's second kidney transplant, in 1964, was from a mother to her daughter. When Gary's kidneys failed suddenly, in 1965, he became Stanford's third transplant patient.

"Kidney donors are just incredibly altruistic humans beings."

Tragedy and transplant

Gary's kidney failure arrived on the heels of a family tragedy. Six months earlier, his father had been killed in a car accident. As a result of the accident, Inga and another one of her sons, who had been passengers, were in comas for almost two weeks.

It was a difficult and uncertain time for the Goodnight family. Fortunately, the operation went smoothly, and Gary's new kidney started producing urine right away. The transplant was a success, and the difference for Gary was immediate. "After the surgery, Gary told me he had forgotten how it felt like to be well," Bill said.

It's these recoveries that "make transplantation in general such a wonderful field," said Jane Tan, MD, PhD, associate professor of medicine at Stanford and a physician with Stanford Health Care's kidney transplant clinic for the past 15 years. "It really transforms their lives," she added.

After his surgery, Gary was able to return to his hobby of drag racing and rejoin his team for a National Hot Rod Association-sponsored trip to introduce the sport to Australia. Later he lived in England, where he worked as a Lockheed Martin satellite contractor.

Inga returned to work and cared for her family. She learned to drive — previously she had relied on her husband — and her choice of car, a 1965 Mustang, earned her the nickname "Mustang Sally" from her sons. She took an active role in raising several of her grandchildren.

"Inga lived such a healthy, long life, and that's what we hope for all donors," Tan said.

Today there are more than 100,000 people in the United States on the kidney transplant waiting list, according to the National Kidney Foundation, with someone being added to the list every 14 minutes.

Last year, over 40 percent of the kidney donors were live donors, of whom half were relatives of the recipient. "Kidney donors are just incredibly altruistic humans beings," Tan said. "It's a pleasure to work with them."

Besides restoring Gary's health, Inga's donation has had more subtle effects on the Goodnights. Bill said that his family's experience has inspired him to reach out to others who need transplants. He tells them about Gary's struggles and the difference that Inga's donation made for Gary and for the family.

"Kidney transplants have always been a big thing in the Goodnight family," he said. ISM

Cancer

continued from page 1

cility has been designed with a complete focus on delivering the absolute best in cancer care and compassion to patients and families," said Amir Dan Rubin, president and CEO of Stanford Health Care.

Patients need to check in only once, whether or not they need multiple services during their visit, and each floor is organized by function: Chemotherapy is on the fourth floor; exam rooms, procedure rooms and a branch of the Stanford Health Library are on the third; operating rooms (where same-day surgeries are performed), a pathology lab, a sterile processing unit and specialized radiology rooms are on the second floor; and medical imaging services, as well as a café, are on the first floor.

Patient support services, including those offered by social workers, nutritionists and support groups, are available on the third floor.

"At Stanford Medicine, we are leading the biomedical revolution in precision health — and the new Stanford Cancer Center South Bay represents the intersection of leading-edge technology and science with personalized, precise and compassionate care," said Lloyd Minor, MD, dean of the School of Medicine.

Location, location, location

The location of the center means patients in the South Bay will have easier access to multidisciplinary teams of Stanford Medicine doctors who plan care for complex cancer cases.

"This new center represents the commitment we have to improving patient care," Beverly Mitchell, MD, director of the Stanford Cancer Institute, said. "The new center seamlessly blends state-of-the-art technology with patient-focused design to create an environment of healing and support, and we welcome the opportunity to enhance our growing clinical research program."

The new center's clinicians will include many from the Stanford Cancer Center Palo Alto, and all of those from Southbay Oncology Hematology Partners, where Trillo was treated.

"As more and more people are being diagnosed with cancer, Stanford has wanted to take its expertise beyond the main campus," said Sridhar Seshadri, PhD, vice president of Stanford Health Care's cancer and cardiovascular services. "We saw the Southbay Oncology Hematology group as a perfect marriage: Many of these physicians are Stanford-trained, they've been in practice for many years and they have a strong reputation. And we wanted to learn from them as we bring our practice to the community."

For nearly 20 years, clinical administrative assistant Tracey Laney has been one of the first people whom patients saw at the Southbay Oncology Hematology Partners clinic. She's been fielding questions from those patients for the last several months. "One of the first things our patients have asked us about the new cancer center is, 'Are you going to be there?'" Laney said. "We've developed relationships with patients — and that's an important thing for them."

DNK DIGITAL

NORBERT VON DER GROEBEN

NORBERT VON DER GROEBEN

Clockwise from top: The Stanford Cancer Center South Bay, located in San Jose, opens to patients today. Amanda Thomas, Amir Dan Rubin and Michelle Kenyon stand next to a radiotherapy machine at the center. Stephen Riggio, RN, and Jennifer Friedenbach, RN, in an operating suite at the center.

Unusual hiring process

One of the most unusual aspects of the center is the review process for hiring its employees, said Kate Surman, the center's administrative director. The center's 215 employees, even those who won't work directly with patients, were all interviewed by a patient and family advisory council member as part of their hiring process. Stanford Health Care has 11 such councils, whose more than 100 volunteers partner with administrators, clinicians, nurses and staff to improve the quality and experience of care by sharing their perspective and insights.

"We are making patients and their needs our highest priority," Surman said, "and we are shaping the culture at this new center so that everyone, even those who are not involved in direct patient care, understands the importance of, and is recognized for their role in, patient care."

The center aims to bridge the warmth, familiarity and convenience of a community care model with the advanced care usually found only at academic medical centers. "It's very forward-thinking," said Patrick Swift, MD, a clinical professor of radiation oncology and the center's medical director. "And it will be a dramatic change for patients." ISM

E-cigarettes

continued from page 1

PhD, a postdoctoral scholar in adolescent medicine.

"We're good at delivering messaging that cigarettes are harmful, but we need to do a better job with other products that teens may smoke," added Bonnie Halpern-Felsher, PhD, professor of pediatrics in adolescent medicine and the study's senior author. "We don't want the message kids get to be 'cigarettes are bad, so everything else might be OK.'"

Tripling of e-cigarette use

Halpern-Felsher and Roditis compared teens' knowledge of cigarettes, e-cigarettes and marijuana because they heard from teachers, parents and youth that anti-smoking efforts needed to address more than just conventional cigarettes. The need is borne out by other research: A recent study from the Centers for Disease Control shows that middle- and high-school students' use of e-cigarettes tripled from 2013 to 2014, eclipsing conventional cigarettes as the most common tobacco product in this age group.

Halpern-Felsher and Roditis studied 24 adolescents who attended high school in a Northern California school district known to have high rates of substance use. The students participated in small-group discussions about their perceptions of the risks and benefits of conventional cigarettes, e-cigarettes and marijuana. They also discussed how they learned about these products. The researchers analyzed the themes that emerged in the discussions.

MARC BRUXELLE / SHUTTERSTOCK

A recent study from the Centers for Disease Control shows that middle- and high-school students' use of e-cigarettes tripled from 2013 to 2014.

Students perceived little or no benefit, as well as several detrimental effects, of smoking conventional cigarettes, such as yellowed teeth, bad breath and long-term disease risk. They also said their social norms often discouraged smoking conventional cigarettes. For instance, even smoking marijuana rolled in paper was considered weird because it looks like a cigarette.

Perceptions versus reality

However, students saw getting high as a benefit to smoking marijuana, and perceived it as safer and less addictive than tobacco. They were unsure whether marijuana posed health risks, and also described being under peer pressure to smoke marijuana.

With respect to e-cigarettes, students perceived some benefits, including thinking e-cigarettes looked good, and were unsure of the risks.

Students' sources of information about the three products were varied. The media, families and teachers all warned against the use of conventional cigarettes. Students also got messages from these sources discouraging use of marijuana, but said it was difficult to refuse the drug because its use was so prevalent among their peers. Students received few, mostly informal, messages about e-cigarettes: They said they saw family members using them to try to quit conventional cigarettes, and also saw peers using them.

The findings could help shape future messages about marijuana and e-cigarettes, the study's authors said. For instance, students need to hear about the addictive potential of both products; about the risks of smoking any form of plant matter, which is similar between conventional cigarettes and marijuana; and about the presence of nicotine in e-cigarettes. In addition, flavorants in e-cigarettes may raise the risk of obstructive lung disease.

"Students hear a lot of talk about conventional cigarettes, some about marijuana and very little about e-cigarettes," Halpern-Felsher said. "That gap needs to be filled in classrooms and by health-care providers, parents and the media. We don't want to leave one product behind and leave teens with the impression that, 'Maybe this is the product I can use.'"

Roditis was a postdoctoral scholar at the University of California-San Francisco while the data was being collected. The study was funded by National Cancer Institute.

The Department of Pediatrics also supported the research. ISM

Narcolepsy

continued from page 1

DQB1*0602, which codes for a receptor found on the surface of immune cells.

"HLA variants are associated with a lot of autoimmune diseases," said Steinman, who also holds the George A. Zimmermann Professorship. But by themselves, they don't cause narcolepsy. Rather, the disease seems to be triggered by a combination of genetic predisposition and infection. People with narcolepsy carry more antibodies to pathogens such as strep bacteria or the H1N1 virus, which caused the 2009 swine flu pandemic. Importantly, narcoleptic patients have very low levels of the neurotransmitter hypocretin, which normally helps to keep us awake when it binds to the hypocretin receptors in the brain. They also have fewer of the brain neurons that produce hypocretin. What could explain this constellation of signs?

The answer began to emerge in 2010, soon after the 2009 pandemic, when researchers reported a sharp uptick in the diagnoses of new cases of narcolepsy — but only in some places. Populations that had been immunized with GlaxoSmithKline's Pandemrix vaccine showed an increase in narcolepsy, but those immunized with Novartis' Focetria did not.

The researchers wondered whether this difference could be explained by the fact that Pandemrix and Focetria were made from two different strains of the H1N1 virus. The team found that H1N1 contains a protein whose structure partially mimics a portion of a human hypocretin receptor. This H1N1 protein was contained, as expected, in the Pandemrix vaccine, but at much higher amounts than that found in the Focetria vaccine. Could antibodies normally generated to this flu protein by Pandemrix vaccination also be latching onto hypocretin receptors and causing an autoimmune reaction?

"It was a really exciting moment," Steinman said.

To find out if narcoleptic patients even had such antibodies, the team examined a sample of 20 individuals who developed narcolepsy after Pandemrix vaccination. Seventeen of them had elevated antibodies to the hypocretin receptor. However, among six individuals immunized with Focetria, none had these antibodies.

How H1N1 and Pandremix may cause narcolepsy

The authors propose a hit-and-run autoimmune mechanism for how both swine flu and Pandemrix might cause narcolepsy. They suggest that in genetically predisposed people, high levels of the H1N1 protein stimulate the production of large amounts of antibodies to both the virus and the hypocretin receptor. These antibodies may persist in the blood for months. Either the large numbers of antibodies or inflammation from an unrelated infection could alter the blood-brain barrier, allowing the antibodies to enter the brain. There, the antibodies may latch onto hypocretin receptors, possibly directing the immune system to destroy or suppress brain cells critical to regulating sleep-wake cycles.

Indeed, compared to Pandemrix, Focetria contains 72 percent less of the H1N1 protein and, for this reason, it doesn't appear to have stimulated specific flu antibodies capable of binding to the receptor, according to the researchers.

Because Pandemrix was associated with an increased risk of narcolepsy, it was withdrawn from the market. But Steinman is quick to point out that, even with that risk, the vaccine was far safer than being infected with swine flu. In the United States alone, the 2009 swine flu pandemic resulted in 274,304 hospitalizations and 12,469 deaths.

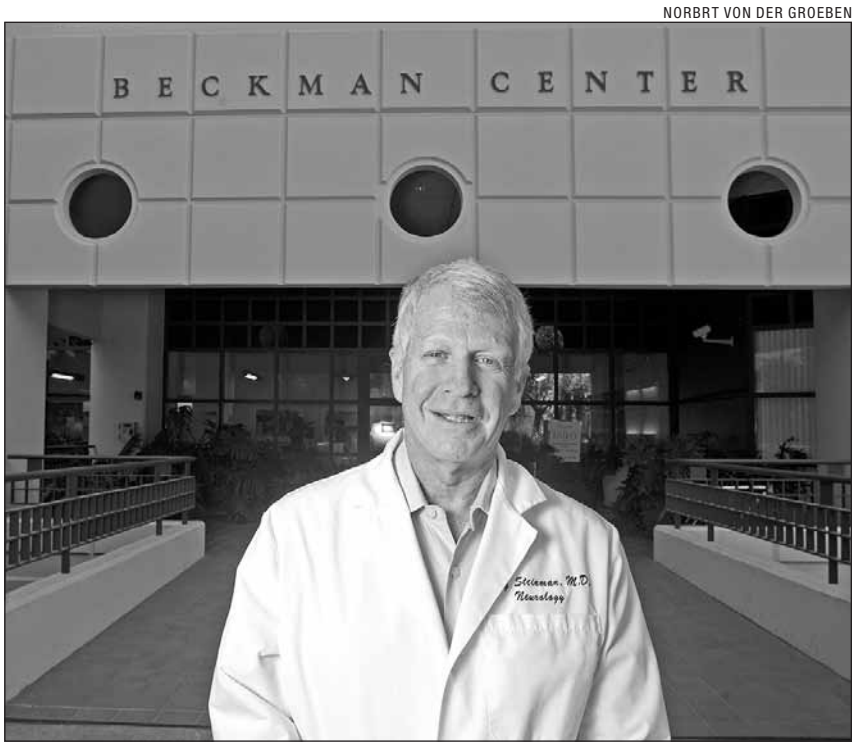
The work advances the understanding of narcolepsy, but Steinman said he isn't claiming they have nailed down the cause. For now, he's calling the proposed mechanism "an inviting possibility." Future work could include comparisons of different vaccines and in vitro studies of banked human blood samples.

Other Stanford co-authors of the paper are senior research scientist Jonathan Rothbard, PhD, and Christopher Adams, PhD, director of proteomics at the Stanford University Mass Spectrometry Laboratory.

A mass spectrometer used in this study was acquired through a National Center for Research Resources award .

Stanford's Department of Neurology and Neurological Sciences, Department of Pediatrics and Department of Microbiology and Immunology also supported the work. ISM

NORBRT VON DER GROEBEN



Lawrence Steinman, and his collaborators believe narcolepsy may be a "hit-and-run" autoimmune disease, meaning that it can cause rapid, pinpoint damage and leave virtually no trace of its work. Narcolepsy is a brain disorder that interferes with normal sleep-wake cycles.

Kennewick

continued from page 1

Rasmussen, PhD. "Due to the massive controversy surrounding the origins of this sample, the ability to address this will be of interest to both scientists and tribal members."

Rasmussen is the lead author of the study, which was published online June 18 in *Nature*. The senior author of the study is Eske Willerslev, PhD, from the University of Copenhagen's Centre for GeoGenetics. Rasmussen initiated the study at the Centre for GeoGenetics and completed the analysis of the DNA sequences at Stanford, working with Carlos Bustamante, PhD, professor of genetics.

Morten Rasmussen

The skeleton, known as Kennewick Man, is called the Ancient One by Native American groups, which believe the bones are those of a long-ago ancestor. In 2004, five Native American tribes of the Pacific Northwest requested repatriation of the remains for reburial, but the proceedings were halted to allow further investigation into the skeleton's origins.

Bits of ancient DNA

Now an exhaustive genetic study of the tiny bits of ancient DNA from a bone in the skeleton's hand refutes the conclusions of the 2014 study. The researchers used the latest in DNA isolation and sequencing techniques to pick out and analyze the skeleton's DNA.

"Although the exterior preservation of the skeleton was pristine, the DNA in the sample was highly degraded and dominated by DNA from soil bacteria and other environmental sources," said Rasmussen. "With the little material we had available, we applied the newest methods to squeeze every piece of information out of the bone."

The researchers compared the DNA sequences from the skeleton with those of modern Native Americans. They concluded that, although it is impossible to assign Kennewick Man to a particular tribe, he is closely related to members of the Confederated Tribes of the Colville Reservation in Washington.

Willerslev and Bustamante are well-known for their studies of ancient DNA. Willerslev and Rasmussen recently published the genome of a young child, known as the Anzick boy, buried more than 12,000 years ago in Montana. That study showed that the boy was also closely related to modern Native American groups, in particular those of South and Central America. In 2012, Bustamante and colleagues used DNA from the 5,300-year-old Iceman mummy called Otzi to show the man likely hailed from the Mediterranean island of Sardinia rather than the frigid Alps, where his body was found.

"Advances in DNA sequencing technology have given us important new tools for studying the great human diasporas and the history of indigenous populations," said Bustamante. "Now we are seeing its adoption in new areas, including forensics and archeology. The case of Kennewick Man is particularly interesting given the debates surrounding the origins of Native American populations. Morten's work aligns beautifully with the oral history of native peoples and lends strong support for their claims. I believe that ancient DNA analysis could become standard practice in these types of cases since it can provide objective means of assessing both genetic ancestry and relatedness to living individuals and present-day populations."

Stanford graduate student David Poznik is also a co-author of the study.

The research was supported by the Danish Council for Independent Research, the Consejo Nacional de Ciencia y Tecnología in Mexico, the National Science Foundation and a Marie Curie Intra-European Fellowship.

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

Alzheimer's

continued from page 3

increasing in prevalence. By 2050, the number of Alzheimer's patients in the United States is expected to reach 13.8 million. The center will home in on common underlying mechanisms occurring in Alzheimer's and Parkinson's.

The center will also provide educational opportunities for community members, patient caregivers, students and health-care professionals.

Victor Henderson, MD, professor of health research and policy and of neurology and neurological sciences, will direct the center. Tony Wyss-Coray, PhD, professor of neurology and neurological sciences, will serve as co-director. Longo and Jerome Yesavage, MD, professor of psychiatry and behavioral sciences, will be associate directors. Michael Greicius, MD, associate professor of neurology, will direct the imaging core of the new center.

"This center's activities will draw on the university's unique strengths in imaging; neuroimmunity; synapse biology; biostatistics and bioinformatics; clinical assessment and research; epidemiology; and caregiver outreach," said Henderson. "We plan to study patients at early stages of illness, as well as healthy older adults, and to follow them over time — in many instances to autopsy. At the same time, we hope to foster new research collaborations that advance knowledge about Alzheimer's, Parkinson's and similar disorders in order to treat them more effectively and help prevent them from occurring."

With this award, Stanford joins the ranks of more than two dozen NIH-funded Alzheimer's Disease Centers at major medical institutions throughout the United States. There are two types of these centers: Alzheimer's Disease Core Centers provide core services in support of research and education, and they support small pilot projects; Alzheimer's Disease Research Centers, in addition, support two to three large-scale research projects.

The Stanford center's two research projects will be led by Nobel laureate Thomas Sudhof, MD, professor of molecular and cellular physiology, and Kathleen Poston, MD, assistant professor of neurology and neurological sciences.

"This is a major accomplishment for Stanford," Longo said. "Our patients will benefit from enhanced trial capability, while their contributions will aid some of the top neuroscientists in the world."

In addition to NIH support, the center's funding was made possible by donations from Stanford supporters and families, the Stanford Department of Neurology and Neurological Sciences, the School of Medicine and Stanford Health Care.

The center's clinical research will be coordinated through the Stanford Center for Memory Disorders. Those interested in participating in research can contact Christina Wyss-Coray, RN, at cwysscoray@stanfordmed.org for more information. ISM

Marcella Alsan, Jason Andrews awarded Rosenkranz Prize

By Beth Duff-Brown

Assistant professors of medicine Marcella Alsan, MD, PhD, MPH, and Jason Andrews, MD, have each won a Rosenkranz Prize for Health Care Research in Developing Countries.

Stanford's Center for Health Policy/Center for Primary Care annually awards the $100,000 prize to young researchers to help them investigate ways of improving access to health care in developing countries.

Andrews is working to identify and develop cheap, effective diagnostic tools for infectious diseases, and Alsan is researching how older girls in poorer countries are impacted by the health of their younger siblings.

The award's namesake, George Rosenkranz, who is now 98, was a pioneer in synthesizing cortisone and progestin, the active ingredient in oral birth control pills. He went on to establish the Mexican National Institute for Genomic Medicine. His family created the Rosenkranz Prize in 2009.

The award embodies Rosenkranz's belief that young scientists have the curiosity and drive necessary to find alternative solutions to longstanding health-care dilemmas.

Getting girls back in school

Alsan, a core faculty member at CHP/PCOR, is analyzing whether medical interventions in children younger than 5 tend to help their older sisters go back to school. More than 100 million girls worldwide fail to complete secondary school, despite research that shows a mother's literacy is the most robust predictor of child survival.

"Anecdotally, girls must sacrifice their education to help out with domestic tasks, including taking care of children, a job that becomes more onerous if their younger siblings are ill," said Alsan, who specializes in infectious disease and has a PhD in economics from Harvard.

Marcella Alsan

Jason Andrews

She said she intends to estimate the impact that illnesses in under-5 children have on older girls' schooling using econometric tools. She will compile data from more than 100 demographic and health surveys covering nearly 4 million children living in developing countries.

Low-cost diagnostic tools

Andrews has been working on ways to bring low-cost diagnostic tools to impoverished communities that bear the brunt of disability and death from infectious disease.

"I began working in rural Nepal as an undergraduate student, and as a medical student founded a nonprofit organization that provides free medical services in one of the most remote and impoverished parts of the country," Andrews said. "As I became a primary physician, and then an infectious diseases specialist, one of the consistent and critical challenges I encountered in this setting was routine diagnosis of infectious disease."

He said those routine diagnostics were typically hindered by lack of electricity, limited laboratory infrastructure and lack of trained lab personnel.

"In my experiences working throughout rural Nepal — and in India, South Africa, Brazil, Peru and Ethiopia — I found these challenges to be common across rural resource-limited settings," Andrews said.

He has been collaborating with engineers to develop an electricity-free, culture-based incubation and identification system for typhoid; low-cost portable microscopes to detect parasitic worm infections; and most recently, an easy-to-use molecular diagnostic tool that does not require electricity.

"The motivation for these projects was not to develop fundamentally new diagnostic approaches, but rather to find simple, low-cost means to make established laboratory techniques affordable and accessible," he said.

Andrews also intends to establish and curate a website to gather open-source ideas and evidence on diagnostic techniques for use in the developing world.

"Stanford is one of the world's greatest hubs for innovation and information sharing as pertains to science and technology and is an ideal home for this venture," he said. **ISM**

Beth Duff-Brown is communications manager at the Center for Health Policy/Center for Primary Care and Outcomes Research.

Stanford Medicine magazine shows some skin — in all its complexity

By Rosanne Spector

Consider your skin. If you're an average-sized adult, you're covered with about 20 square feet of it. By weight, it's your largest organ: about 8 pounds.

So it's no surprise that when your skin has problems, those problems can be hefty.

In the new issue of *Stanford Medicine* magazine, you'll find out how big those problems can be, and learn about new solutions to some of the most distressful skin conditions.

Research on skin is thriving, in large part, because skin is so easy to see said Paul Khavari, professor and chair of dermatology at the School of Medicine.

MATTHEW BANDUSCH

An illustration in the new issue of *Stanford Medicine*, which focuses on skin.

"The accessibility of skin tissue to the application of new technologies, including genomics, proteomics, and metabolomics, make this a watershed moment for progress in alleviating the tremendous suffering caused by global burden of skin disease," Khavari said.

"One of the nice things about skin is that it's amenable to direct inspection," said Stanford dermatologist Anne Chang, MD, in the special report, "Skin deep: The science of the body's surface." "You can look at it. That makes it a great proving ground for evidence-based medicine."

The magazine, produced with support from the Dermatology Department, includes articles not only about new treatments, but also insights into how skin works when it's healthy and how to keep it that way. In a Q&A, actress and playwright Anna Deavere Smith, who is African-American, addresses skin's social meaning, discussing her relationship to her own skin and how, as a writer and actor, she gets under the skin of her characters. The online version of the magazine includes audio of an interview with Smith.

Also in the issue:

- A story about two young men coping with one of the world's most painful diseases — the skin-blistering condition epidermolysis bullosa — including news about an experimental treatment to replace their broken genes. The online version includes a video of a patient at home and interviews with experts on the condition.
- A report on progress being made after years of stagnation in treating the most deadly skin cancer: melanoma.
- A look at one of Stanford Medicine's great accomplishments in dermatology: successful treatment of a rare but dangerous rash — cutaneous lymphoma, a form of blood cancer that spreads to the skin.
- Tips on keeping skin safe from the sun.
- A feature on research seeking to answer the question: Why does skin age?
- The story of a young woman who literally lost her smile and had it restored through surgery.

The issue also includes a story considering the rise in number of castoff donor hearts, despite a shortage of the organs for transplants, and an excerpt from *Jonas Salk: A Life*, a new biography of the polio-vaccine pioneer, written by Charlotte Jacobs, MD, professor emerita of medicine at Stanford.

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

OF NOTE

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

ROSA BACCHETTA, MD, was appointed associate professor of pediatrics, effective May 1. She studies mechanisms of immune regulation and of early onset diseases with immune deficiency and dysregulation. She is currently working to link genetic autoimmune abnormalities with patient phenotypes, with the goal of developing therapies.

BÉRÉNICE BENAYOUN, PhD, a postdoctoral scholar in genetics, was awarded honorable mention and $10,000 in the 2015 Regeneron Prize for Creative Innovation contest. This award acknowledges, rewards and fosters talented early-career biomedical scientists.

ADAM DE LA ZERDA, PhD, an assistant professor of structural biology, has been named a 2015 Pew-Stewart Scholar for Cancer Research by the Pew Charitable Trusts. He will receive $60,000 a year for four years to support his research. He is working to develop a molecular imaging technique that can characterize and monitor individual cells in breast cancer tumors.

MATTHEW FITZGERALD, PhD, was appointed assistant professor of otolaryngology–head and neck surgery, effective Jan. 1. His research investigates how individuals understand speech and sound. He also develops tools and methods to improve the outcomes of cochlear implants and to aid language development in hearing-impaired children.

SANJIV GAMBHIR, MD, PhD, the Virginia and D.K. Ludwig Professor for Clinical Investigation in Cancer Research and chair and professor of radiology, will be awarded the 2015 J. Allyn Taylor International Prize in Medicine. The annual $25,000 prize is given by the University of Western Ontario's Robarts Research Institute, with a focus this year on cellular and molecular imaging in cancer. The award will be presented Nov. 18 in London, Ontario. Gambhir directs Stanford's Molecular Imaging Program.

HOLBROOK KOHRT, MD, PhD, and **PAMELA KUNZ**, MD, both assistant professors of medicine, have been awarded a $100,000 grant from the Caring for Carcinoid Foundation. They will examine 1,031 samples of neuroendocrine-tumor tissue and characterize the tumor-immune phenotype of samples from 20 patients enrolled in a trial of an immunotherapy agent at Stanford.

ED KOPETSKY, chief information officer of Lucile Packard Children's Hospital Stanford and Stanford Children's Health, was honored with a lifetime achievement award at the 2015 Bay Area CIO of the Year awards ceremony on June 18. The annual event is held by the *Silicon Valley Business Journal* and *San Francisco Business Times*. **ISM**

Adam de la Zerda

Matthew Fitzgerald

Holbrook Kohrt

Pamela Kunz

Sanjiv Gambhir

Ed Kopetsky