

stat

COMING //

- **THROUGH AUGUST 10:** At the Centers for Disease Control and Prevention in Atlanta, the exhibit "Deadly Medicine: Creating the Master Race" features the methods (physical measurements, observations of genetic traits such as eye color) that the Nazis put to terrifying use in deeming people "racially foreign."
- **AUGUST 13:** Arkansas may scale back its program to test the body mass index of schoolchildren. The first of several states to require such testing in an effort to fight obesity, Arkansas has come under fire for potentially injuring students' self-esteem.



FOCUS // CHILD'S PLAY is the unlikely solution to a sub-Saharan public health crisis: the high incidence of disease transmitted by dirty water. With each rotation of a PlayPump's colorful merry-go-round, children draw clean water from 330-foot-deep wells into 660-gallon storage tanks that feature space for advertisements and public health messages about such concerns as HIV/AIDS prevention and proper hand-washing. The ad revenues fund the maintenance of the \$14,000 system.

PHOTOGRAPH BY GIDEON MENDEL/CORBIS



INTERVIEW //

Picturing the Other Side

■ BY CHARLES SLACK

As an award-winning photojournalist for more than 30 years, Max Aguilera-Hellweg has captured street gangs, cowboys and rock stars for Esquire, National Geographic, Rolling Stone and other magazines. But his most demanding assignment was one he gave himself: to understand doctors not by taking their pictures but by becoming one.

Q: What stirred your interest in medicine?

A: In 1989 the women's business magazine *Savvy* sent me to photograph Frances Conley, a neurosurgeon at Stanford. I watched her operate on a man with sudden-onset paralysis. I

was photographing her hands when she stepped aside and said, "Here, take a picture of this." I was arm's length from a spinal cord. I was used to having access to incredible people and places, but this was different: It was the most intimate place I'd ever been. I knew that this was where I wanted to be.

Q: How did you make the leap from photography?

A: By definition a photojournalist is always the voyeur; he always has the secondary experience, never the primary. I'd leave assignments with this emptiness, and it stayed with me for years. I was in a store one day when a man went into cardiac arrest. I had just photographed cardiac bypass surgery the week before, but I couldn't

help keep this person from dying. It was an awful feeling.

Q: So you applied to medical school?

A: First I needed an undergraduate degree, because I had never gone to college. I started by enrolling in an algebra course at the Borough of Manhattan Community College. I began my undergraduate studies at Columbia University School of General Studies in 1995, when I was 39. I got my M.D. from Tulane University School of Medicine in New Orleans in 2004 and completed my internship and residency in internal medicine at the University of Massachusetts Memorial Medical Center in Worcester in 2006.

Q: What was the most trying aspect of your training?

A: In December 2005 I did my first rotation as an intensive-care-unit resident. In my program, the ICU resident carries the code pager for the entire hospital—when a code is called for a life-threatening event, the resident is responsible. You walk into a situation in which you have seconds to figure out what life-support measures to take. There are times when you have to tell a patient he's going to die.

Q: How did you do it?

A: I was straightforward, just as I'd seen my attending physician act with patients when I was a student. The experience taught me that straightforwardness and caring are

often the same thing. Being vague or offering false assurance would have been more painful. Our culture has convinced us that death is unnatural or avoidable, and society tends to consider it vile or repulsive, but it's none of those things. It's a natural

■ The neurosurgeon said, "Here, take a picture of this." I was arm's length from a spinal cord. I knew that this was where I wanted to be.

stage in life, and everyone deserves a dignified passing. Discussing death with patients wasn't easy, but I considered it an honor to help them at this turning point.

Q: After all those years of study, you decided not to enter practice.

A: I had intended to practice medicine. But toward the end of my residency, I found myself wondering what specialty to pursue. Just after my first ICU rotation, I got a call from a friend asking me to lecture at the International Center of Photography in New York City. For six years I had been too busy studying to look at my photographic work. As I went through my photographs to prepare for the lecture, I could see where I had been and where I was going. I'm also a writer and filmmaker, and I became flush with ideas, projects I needed to finish.

Q: Couldn't you practice medicine and follow your creative ambitions?

A: I considered various medical fields that would offer some flexibility—for example, locum tenens, or filling in for a physician on vacation; or becoming a hospitalist, who treats the hospitalized patients of other physicians. But medicine, however you practice it, is

all-consuming. No specialty allowed the freedom I sought. I couldn't go off for three weeks here, six months there.

Q: So those years were a waste?

A: Not a waste! A great, great adventure. And I accomplished my goal: I am no longer the voyeur; I've been to the other side.

Q: Has becoming a doctor made you a better artist?

A: I can't point to a specific picture and say, "That came out better because I became a doctor." But art is about defining the human condition, which doctors deal with in its most elemental form. I've looked into the face of a grown man fearing his death to his last breath. I've sat with families and told them their loved one passed during the night. I've prescribed medicines that have eased suffering. I haven't just observed these things, I've done them. I've been responsible. How could that not make me a better artist? ■

BY THE NUMBERS //

Quick Fix

400 Number of retail clinics, also known as convenient care clinics, offering walk-in services for basic medical care (such as flu shots, physicals and strep tests) that are typically staffed by nurse practitioners, supervised by off-site physicians and located in chain stores like Wal-Mart

700 Number of retail clinics that industry leader MinuteClinics plans to open by 2008

15 Approximate maximum wait time, in minutes, at a retail clinic (some clinics offer to page shoppers when the nurse can see them)

20.2 Average wait time, in minutes, for a doctor's appointment

90 Percentage of clinic visitors at Target who come for the care but end up shopping as well

\$31 Average amount an insurer saves when a patient visits a MinuteClinic rather than a physician's office or an urgent care facility

\$40-\$70 Average price of services at a retail clinic

200-500 Number of square feet a retail clinic typically occupies, replacing less-profitable departments

60 Percentage of retail clinics that do not accept insurance, making middle-class patients less likely to visit them than higher-income (\$100,000 and more), convenience-craving consumers and the uninsured who cannot afford alternatives

\$77 Amount, in millions, that the chain Take Care Health Systems received from venture capitalists to expand into new geographic markets in 2006 ■

INFOGRAPHIC //

Genes in a Haystack

■ BY RACHAEL MOELLER GORMAN // INFOGRAPHIC BY FLYING CHILLI

More than 99.9% of each person's DNA is identical to that of every other person. It's the less than 0.1% that makes us unique, determining hair color, eye color—and susceptibility to diseases. Many deadly illnesses result from mutations in multiple genes, and scientists have had little idea where in our 3.1-billion-base-pair genome to look. Now, with the completion of the Human Genome Project, the creation of a database of gene variations called single nucleotide polymorphisms (SNPs) and the invention of DNA microarrays that can hold 1 million SNPs, scientists can search for errant genes. Here's how microarrays work, taking the example of schizophrenia research at Harvard and MIT.

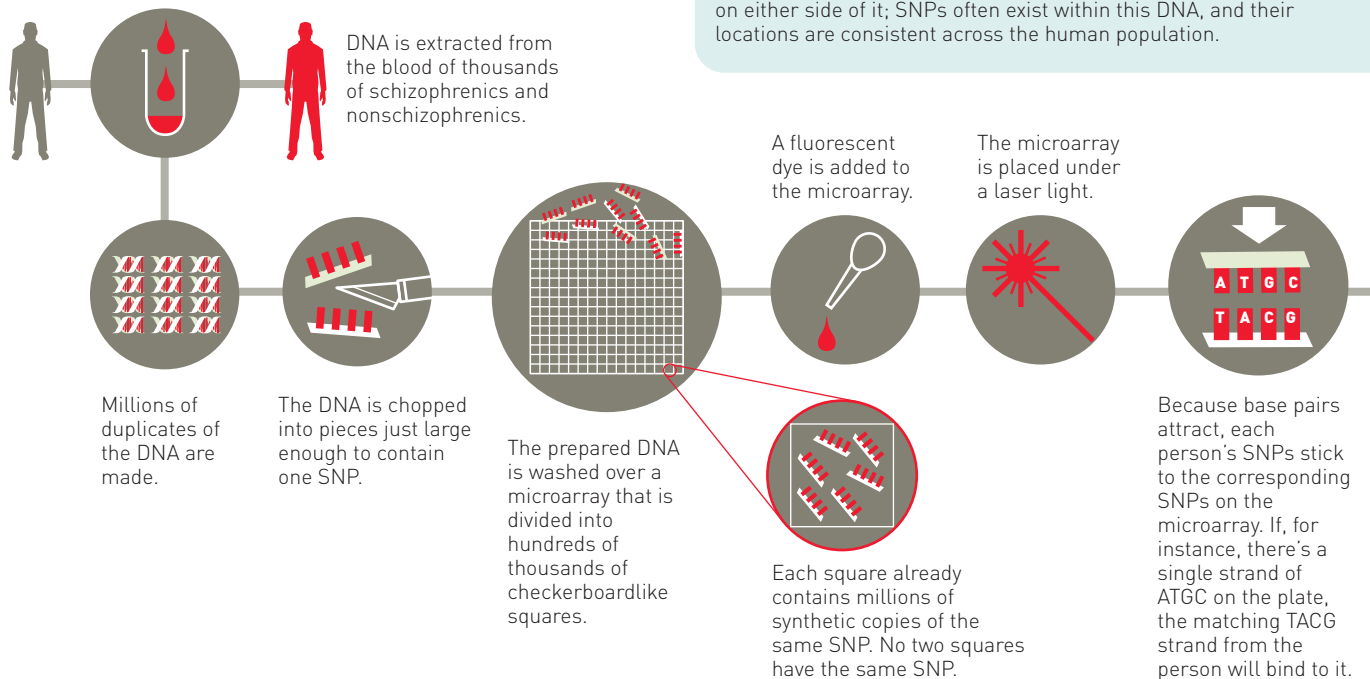
Signposts of disease

Most of the 0.1% differences between individuals occur as single nucleotide polymorphisms. For example, within the sequence of molecular "letters" that constitute our DNA code, 70% of the population might have the sequence ATTG at a particular spot, while 30% might have ATCG.



Although most SNPs don't cause disease, they can point the way to genes that do. Every gene that a person inherits comes with DNA on either side of it; SNPs often exist within this DNA, and their locations are consistent across the human population.

Pattern recognition



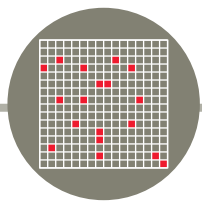
The potential payoff



Once researchers identify suspect SNPs on the chip, they can go back to the original DNA code in the Human Genome Project database and search the genes on either side of each SNP for mutations that could be involved in schizophrenia.



A candidate gene is then thoroughly examined in animal and cell studies to determine what it does and how it might cause disease.



The fluorescent dye, which sticks to the person's DNA, "lights up" only the squares in which a piece of the person's DNA matched a particular SNP.



A computer scans each pattern, then conducts a statistical analysis of the differences between the patterns for schizophrenics and nonschizophrenics.



Eventually, researchers might be able to create drugs targeting the unique networks of proteins in which these genes are involved and tailor treatments according to patients' individual genetic makeups.

MILESTONES // Mobile Aid



Throughout centuries of warfare, soldiers could lie wounded on the field until the battle ended before receiving necessary care. That was bad enough in the era of swords and arrows, but the introduction of gunpowder during the fourteenth century caused the death rate to skyrocket. Still, it took another 400 years and a clever French army surgeon to devise a better system.

Dominique-Jean Larrey created relatively lightweight two- and four-wheel horse-drawn wagons to transport the injured in the heat of battle. Larrey called his invention, which he conceived 215 years ago, in 1792, the flying ambulance. (He adopted the name from *ambulancia*, a term for "field hospital" credited to Spain's Queen Isabella and derived from the Latin *ambulare*, "to walk.") Larrey's superiors—including Napoléon Bonaparte, who became commander in chief of the French army in 1795—took notice and charged Larrey with spreading the use of the ambulance throughout the army.

As Napoléon's campaign broadened, Larrey modified his flying ambulance to operate on various types of terrain. Ambulances were drawn by camels in the Egyptian desert and by mules in the mountainous regions of Spain, Poland and Russia. The ambulances' success as well as Larrey's skill as a surgeon—he could amputate an arm in 17 seconds—earned him a promotion to surgeon general.

Although Larrey's invention caught on with other armies, it wasn't until 1869 that the first hospital-based ambulance

service began, at New York City's Bellevue Hospital. The horse-drawn carriages responded to more than 1,400 calls the first year. Thirty years later, Chicago's Michael Reese Hospital introduced a motorized ambulance that could transport patients as quickly as a good horse: about 16 miles per hour.

Larrey, whose wagons were equipped with horsehair-stuffed mattresses, could scarcely have imagined how his invention would evolve. Ambulances today can be outfitted with mobile electrocardiographs that transmit readings over cell phones; defibrillators that provide feedback on the speed and strength of a paramedic's CPR compressions; and pupil-monitoring devices that register the neurological status of an unconscious patient. EMTs can use Web-based data to overlay variables, including weather patterns, traffic jams and hospital bed counts, to decide how and where to take patients, says Robert Bass, an emergency physician and executive director of the Maryland Institute for Emergency Medical Services Systems in Baltimore.

Down the line, Bass foresees greater regionalization of care, as EMTs, using ultrasound images, blood scans and devices that recognize increased intracranial pressure, are able to triage patients en route to the specialty hospital best suited to manage their condition. "It's not unrealistic that ambulances will have these capabilities," Bass says. "It's happening so fast." ■



UPDATE //

A New Step in Scarless Surgery

■ BY CHARLES SLACK

When I wrote about a novel surgical approach for reaching internal organs via the mouth or other natural orifices (“Down the Hatch,” Spring 2006), even the most enthusiastic proponents estimated it would be two to five years or more before the technique might be tried on humans in the United States. Yet on March 21, a scant year after my article appeared, surgeons at New York–Presbyterian/Columbia University Medical Center in New York City inserted instruments through an incision in a woman’s vaginal wall to remove her gallbladder.

The New York surgeons and other champions of this technique, dubbed NOTES (natural orifice transluminal endoscopic surgery), say the advantages include the absence of exterior scarring and significant reduction in pain. (Internal organs are relatively free from nerves, unlike the abdominal wall and parietal peritoneum, which must be cut through in conventional or laparoscopic surgery.)

The New York procedure was in fact a hybrid: To ensure the patient’s safety, the surgeons also created a series of abdominal

incisions for laparoscopic instruments that aided in the operation. But less than two weeks later, on April 2, surgeons at the University Hospital of Strasbourg, in France, removed the gallbladder of a 30-year-old woman through her vagina with the aid of a single laparoscopic incision.

Such developments underscore the excitement surrounding a concept that as recently as the late 1990s was little more than a controversial idea being tossed around by a handful of physicians. They eventually formed a committee that in 2005 outlined both the promise and challenges of NOTES. Yet significant hurdles remain before the technique can gain popular acceptance. Detractors range from those who cite the danger of infections to those who assert that laparoscopy already provides safe, minimally invasive surgery. (Proponents counter that laparoscopy itself was considered controversial

until its advantages became clear.) Still others, including some physicians, find the prospect of removing organs through the vagina or mouth too off-putting.

The NOTES procedure that most intrigues surgeons involves threading endoscopes through the mouth, down the esophagus and through a hole cut in the stomach. With its central location, the stomach offers unsurpassed access to organs in the abdominal cavity. Yet the stomach (and the rectum, another possible avenue) may be prone to complications from infections, should an incision fail to close properly. While surgeons seek surefire methods and more delicate tools to securely close abdominal incisions, most trials continue to be conducted on pigs and other animals.

Still, significant progress is being made toward the day when accessing internal organs via the stomach could be routine. A team at Ohio State University, for example, is already using the gastric route to investigate the spread of pancreatic cancer in patients. And perhaps the best indicator of the rapid growth of interest in the technique is that no fewer than 115 abstracts outlining new research in the field will be presented at an annual NOTES conference to be held in Boston in July. ■

Stops and Starts

CATERPILLAR CELLS may someday replace chicken eggs as the preferred vaccine incubator. Researchers at the University of Rochester Medical Center found that the insects' cells yielded a flu vaccine two months earlier than did embryonated hen eggs. Cells could also shave time off the front end of the process—in the event of an epidemic, vaccine makers could use readily available cells rather than wait for millions of hens to lay eggs.

<http://jama.ama-assn.org/cgi/content/full/297/14/1577>

QUITTING COLD TURKEY might be easier for some smokers, thanks to their genes. It's well established that susceptibility to addiction is at least half hereditary; now the National Institutes of Health and Duke University researchers say the same is true of getting unhooked. The successful quitters shared characteristics within a set of 221 genes that regulate brain wiring, enzymes and neurotransmitters that were not shared by recidivists. Further research is needed to understand how these abstinence-enabling gene attributes stifle the urge to smoke, but perhaps someday doctors will test patients' genotypes to tailor smoking-cessation plans.

biomedcentral.com/1471-2156/8/10

DELAYING THE REGIMEN of insulin injections is a possibility for newly diagnosed type 1 diabetes sufferers who undergo a stem cell transplant, say researchers at the University of São Paulo. The treatment increases the function of insulin-producing pancreatic beta cells, which are destroyed as diabetes progresses. In the study, all but one of the 15 patients given the treatment were able to go from one to 35 months without insulin injections. Follow-up studies are needed to learn how, and for how long, the treatment works.

[http://jama.ama-assn.org; search for "diabetes, stem cell transplantation"](http://jama.ama-assn.org; search for)

FALSE POSITIVES are more likely when radiologists rely on computer-aided detection (CAD) instead of their own eyes to interpret mammograms. Researchers at the University of California, Davis, found that using CAD leads to 32% more unnecessary callbacks and 20% more unnecessary biopsies than traditional detection. For every true positive mark on a mammogram read with CAD, there are 2,000 false ones. The study indicates that systemwide adoption of CAD (which is on the rise since Medicare began reimbursement for the technology) could raise the cost of mammograms by 18% while not clearly improving cancer detection rates.

[http://content.nejm.org; search for "computer-aided detection, mammography"](http://content.nejm.org; search for)

RETIRED PRO FOOTBALL PLAYERS have revealed a possible link between concussions and depression. More than 2,500 former NFL players completed a health questionnaire for the University of North Carolina's Center for the Study of Retired Athletes. Nearly 600 reported enduring three or more concussions on the field; of those, 20.2% said that they had since been diagnosed with clinical depression (versus 6.59% of those who reported zero concussions). The NFL contests the findings and says it will conduct its own study.

[ms-se.com; search for "recurrent concussion"](http://ms-se.com; search for)

HAIR ONCE LOST might actually return. University of Pennsylvania School of Medicine researchers removed skin from the backs of mice, and 19 days later the scientists detected the beginnings of new follicles. Next they pinpointed a set of proteins, called Wnt, responsible for follicle regeneration and found that pumping up Wnt levels yields more follicles. A future route to reversing hair loss, then, might be via the molecular pathway through which Wnt operates.

nature.com/nature/journal/v447/n7142/pdf/447265a.pdf ■

THE CUTTING EDGE //

Gripping New Technology

Most prosthetic arms are clumsy things: Range of motion is limited, and operation can be nonintuitive (for example, a flex of the bicep turns the wrist). But now an international team led by Johns Hopkins University Applied Physics Lab scientists is working to change all of that. Its Proto 1 prosthetic arm features eight motions (such as a grasping hand) and operates using a process called targeted muscle reinnervation, in which nerves from an amputated limb are transplanted to muscles near the amputation site. When the nerves excite the muscles, surface electrodes sense that energy and prompt movement.

Although researchers are still testing Proto 1 on patients, they are already at work on Proto 2 (at left). This prototype will feature more than 25 movements, such as individually bending and spreading the fingers, and as many as 80 sensors on the hand and fingertips that will detect pressure, vibration and temperature. An even more direct connection with the user's residual nerves than that of Proto 1 will control the expanded, more precise motions. Proto 2, slated for completion this summer, will also be a testing ground for various energy sources (electric, hydraulic and pneumatic) to determine which deliver the most power and weigh the least. Whether it will keep its current winning name remains to be seen. ■



POINT/COUNTERPOINT //

Should vaccination against human papillomavirus become mandatory for girls?

POINT: The HPV vaccine will help prevent diseases, which is far preferable to treating them, says Marilyn Tavenner, Virginia's secretary of health and human resources, a registered nurse and former national president of outpatient services for the Hospital Corporation of America.

Earlier this year Virginia's legislature became the first in the nation to require sixth-grade girls to be vaccinated against HPV, a virus that can lead to cervical cancer and whose deadliest strains are transmitted sexually. Although inoculation will cost approximately \$360 per child for a series of three injections over a six-month period, Virginia will likely save health care dollars in the long run: By inoculating preadolescents, thousands will be spared from surgery, hospitalization or premature death. The Centers for Disease Control and Prevention (CDC) estimates that the cost per quality-adjusted life year saved by vaccinating against high-risk HPV types 16 and 18 is as much as \$25,000, which compares favorably with other preventive interventions. (The cost saved by screening for hypertension in 40-year-old men, for example, is at least \$28,000.)

HPV infection is a major cause of cervical cancer. An estimated 11,150 cases of invasive cervical cancer will be diagnosed in the United States in 2007, of which about 3,670 will eventually be fatal, according to the American Cancer Society. The CDC also estimates that 6.2 million Americans are infected annually with HPV via sexual transmission.

Merck's vaccine, Gardasil, helps protect against the two HPV strains—16 and 18—that are responsible for 70% of cervical cancers. Gardasil is also effective against HPV types 6 and 11, which do not lead to cancer but cause roughly 90% of cases of genital warts. In a recent study (published in the *Journal of the American Medical Association* [*JAMA*], Feb. 28) of females ages 14 to 59, 73.2% had no detectable HPV infection, 23.4% had a strain not covered by Gardasil and 3.4% carried the four strains it does cover. Both Merck and GlaxoSmithKline (which produces Cervarix, currently under FDA review) are working on improving their vaccines to cover more types of HPV.

Studies on Gardasil's safety are reassuring. The vaccine contains no potentially infectious live virus. Although safety-



study participants in the youngest category (ages nine to 15) numbered only approximately 1,100, the vaccine was extremely effective in that age group: More than 99% developed antibodies after vaccination. And the four studies analyzed by the FDA prior to approval included 21,000 women ages 16 to 26. Even more safety data will be available by the time routine inoculation begins in the fall of 2009.

To address the concerns of parents who believe the decision to immunize should rest with them rather than the state, Virginia offers a good middle ground: It allows a voluntary opt-out and it provides that parents receive materials describing the link between HPV and cervical cancer.

There is no cure for HPV, only treatments for diseases the virus causes. Mandating the vaccine means it will reach sufficient numbers of young women to make a difference in curbing a cancer that claims too many lives.

COUNTERPOINT: The vaccine was inadequately tested on nine- to 15-year-olds, and its effectiveness doesn't justify its relatively high cost, says Benjamin Brewer, a family practitioner in rural Forrest, Ill., who writes an online column every other Tuesday for the Wall Street Journal.

During a 10-year-old girl's recent office visit, her mother voiced misgivings about the HPV vaccine. She was aware of the limited safety testing conducted among preteens and couldn't reconcile the risk against the uncertain benefit. Too many medicines have been recalled in recent years, she reasoned, and she would rather wait and see how the HPV vaccine performs over time. Considering that the vaccine was tested on only about 1,100 girls, her point was well taken. The data is simply too sparse to gain a good grasp of the vaccine's safety.

To be truly effective and clinically useful, the HPV vaccine also needs broader coverage against more viral strains. Scientists have identified about 30 types of genital HPV, 15 of them high-risk types that can lead to cervical cancer. Gardasil's coverage of just two of the 15 makes for a tattered safety net.

The vaccine's relatively steep cost—\$360 for three injections—demands a higher level of value. If you spent \$360 on every preteen girl in the United States, you could purchase a lot of primary care and prevention that would do more for their long-term health than an HPV vaccine.

Look at the patients who get cervical cancer. They're often poor women without regular access to primary care, so they aren't getting annual Pap smears. A better use of resources would be to target the highest-risk group and make sure they're being screened for cervical cancer.

Reports on the prevalence of HPV vary, but CDC investigators have found that types 16 and 18 were identified in only a small percentage of the *JAMA* study's participants. A mass vaccination program for such a small group doesn't make economic sense, especially considering the enormous health needs facing our society. Illinois, my home state, is facing a \$2 billion budget deficit. Yet a bill introduced in February calls for vaccinating all 11- and 12-year-old girls in the state, at a cost of about \$4 million to cover the estimated 18,000 uninsured girls in that age group. The question becomes whether we should add millions more in deficit spending for a vaccine with limited results.

A lot of needs are being ignored because the HPV issue is one that grabs headlines and scores political points. It's an easy talking point to say that you voted for an advance that prevents cancer, while conveniently forgetting the price tag.

I'll concede that the economic equation could change. In clinical trials, Cervarix blocks two additional HPV types—45 and 31, the third and fourth most prevalent cancer-causing strains. And time will tell us more about the vaccine's safety.

For now, I'm inclined to side with my 10-year-old patient's mother. Wait and see is wise advice. ■

RANDOM SAMPLING // Feigning Illness

Before turning medical students loose on real patients, most—if not all—schools have them practice on imposters. Standardized patients, or SPs, are trained to simulate medical conditions and histories, undergo examinations and provide feedback about students' bedside manners. The actors below reveal that not only do SPs take great care to create the best learning experience for students but also that such care can yield unexpected returns.

In one final exam, the first-year students told me, "You've got a really funny pulse." My heart was skipping beats, so I drove to the emergency room. The cardiologist said I had an arrhythmia and that "those students may have just saved your life."

—SAM COLEMAN, University of Nevada
School of Medicine, Reno

I once portrayed a pregnant patient who didn't speak English. The medical student explained to my English-speaking "husband," another SP, that there was no fetal heartbeat. While my "husband" pretended to break down, I traveled a spectrum of true emotions in 15 minutes: confusion, fear, frustration, shock, denial, grief. The more humanity you bring to a case, the more real it becomes. And this certainly felt real. I was emotionally spent.

—EVE MULLER, Keck School of Medicine of the
University of Southern California, Los Angeles



I like the students to feel as comfortable as possible while examining me, so I wear men's boxer shorts with designs that correspond to the appropriate major holidays—Christmas, Halloween, Valentine's Day. They really appreciate this type of icebreaker.

—JENNY LIND OLIN, University of South Florida
College of Medicine, Tampa