A New Light for Cancer Patients

PHOTODYNAMIC THERAPY EXTENDS LIVES
physical examination will often yield those of the physician’s hands in a skillful about that patient’s illness, but the laying patient. Likewise, a battery of initial labora-

ty studies before the physician arrives. This method is more efficient, perhaps, but be obtained using a computer to interro-

gate a patient before the physician arrives. Certainly, a clinical history can still an art, one that forms in many ways over the past 50 years. Yet there remains tremendous amount: how he gets up from a crutch. Physicians who lack physical diag-

nosis skills tend to order significantly more laboratory studies.

But they’re also equipped with a deep appre-
ciation for the art of medicine, including the elucidation of the medical history and the physical exam that still form a critical basis of our profession.

In my own specialty of neurology, the art of clinical observation was a highly refined skill in the generation of clinicians who were my mentors and role models. Even now, I learn more about a new patient’s problems merely by observing him walking into my office than I do from all the forms he filled out prior to being called into consultation. Before my patient even says hello, I know a tremendous amount: how he gets up from a chair, what his gait looks like, how he carries his arms or how his eyes move. This focuses the history I take and helps me identify whether the primary complaint is the core problem or a symptom of a condition the patient doesn’t know about yet. While a full neurological exam could take hours, like other neurologists with my training, I have picked through the tree of physical diagnoses as applied to what I have seen and heard and can efficiently streamline my interactions without sacrificing clinical accuracy. Physicians with such skills can develop a differential diagnosis in their minds that others might only obtain by ordering layers of tests.

Jefferson has imbued its graduates with wisdom of earlier generations of physicians, not as a romantic notion or historical artifact but as a necessity for accurate and efficient diagnosis and treatment.

At Jefferson, we teach physical diagnosis skills because it’s good medicine.

Sincerely,

Robert L. Barchi, MD, PhD
President
Thomas Jefferson University
In our metric-centric administrative culture, medical schools are too commonly compared on the basis of that which is most readily quantifiable – college grade point averages and MCAT scores of incoming students, and grades and scores of its students. They are reflected in their life experiences. We recruit students who have the broad range of intellectual and personal skills needed for successful and varied careers in medicine. Yes, these are students who routinely emerge from their training as expert diagnosticians and empathic caregivers. But more than this, we are looking to them to become leaders – in dimensions ranging from discovery science to medical education to healthcare reform. Our goal is to generate a cadre of physicians who can function well in healthcare reform. Our goal is to generate a cadre of physicians who can function well in healthcare reform.

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Findings

Could a Tumor Suppressor Also Fight Obesity?

The hormone receptor guanylyl cyclase C (GCC) is a known suppressor of colorectal cancer tumors, but new evidence discovered by Jefferson faculty suggests it may also help fight one of the country’s biggest pandemics: obesity.

Reporting in the Aug. 25, 2011, online issue of the Journal of Clinical Investigation, Scott Waldman, MD, PhD, chair of the Department of Pharmacology and Experimental Therapeutics, and his colleagues found that silencing GCC affected appetite in mice – disrupting satiation and causing obesity. Conversely, mice who expressed the hormone receptor known when to call it quits at mealtime.

Revealing a never-before-known endocrine axis between the intestine and hypothalamus, the research could provide novel therapeutic targets to control appetite, obesity and metabolic disorders that, when occurring together, increase the risk of developing cardiovascualr disease and diabetes. This presents a promising notion given that one-third of the U.S. population is considered obese.

Until now, the role of GCC outside the gut has remained elusive. Waldman and his team have previously shown its role as a tumor suppressor and biomarker that reveals occult metastases in lymph nodes, but GCC’s role in appetite is new and surprising territory.

“We were working with GCC-deficient mice to look at its role in tumorigenesis in the intestine,” Waldman said. “Then the mice grew up, and we noticed something: They got fatter. We couldn’t understand why it was happening, because GCC is expressed predominantly in the intestine. There was no indication that it regulated any function that had to do with metabolism and nutrient uptake.”

To investigate this, Waldman, who also leads the Gastrointestinal Malignancies Program at the Kimmel Cancer Center at Jefferson, and his colleagues raised both normal mice and GCC-deficient mice, tracking their weight, satiation responses, hepatic and serum triglyceride measurements, hormone receptor expression and physical activity.

When the mice digested food, the researchers found that the gut released hormones into the bloodstream – not just into the intestines – and up into the brain, where the hormone receptors were triggered. Mice with GCC knew when to stop, but hormone receptor-deficient mice never got the message that their stomachs were full. They simply kept eating and became obese.

“They got to be diabetic and developed metabolic syndrome, fatty livers and so on,” Waldman said. “We ruled out the usual suspects. Gastroenterology function was normal. They weren’t more sedentary than wild type mice, and they did not have abnormal metabolism. We realized they just had a different appetite.”

The research offers up a new neural-gut axis that explains appetite more. But it still raises some questions. Do obese people possess little to no GCC? And if so, does that mean obese people have a genetic disposition to gain weight? “It’s possible, but it’s still unclear,” said Waldman. “There is the possibility that obese people do not have the receptor or they do not release enough hormones to trigger the receptor. More studies are needed to better explain this.”

“Obesity could be biological, and not behavioral,” said Waldman. “There is no evidence here that confirms that. However, this new information opens that possibility.”

GTP is a fundamental building block in the cell. It is a "cousin" of ATP that is used to build DNA and RNA, as well as other fundamental molecules, in the cell. One of its functions is to serve as the precursor of the signaling molecule cGMP.

Uroguanylin is a type of hormone, or released from the cells of the intestine into the bloodstream via an endocrine process, where it travels to the brain and is cleaved in the hypothalamus by enzymes and turned into uroguanylin. 

Revealing a never-before-shown endocrine signals (here the uroguanylin) into intracellular signals (here the cGMP) is an intracellular messenger molecule that translates extracellular signals that direct the cell's behavior (here the generation of a satiety or "fullness" signal).
That was a high point, but only one of many. Daily phone calls from each of her six grandchildren punctuated the 14 months following her diagnosis with advanced bile duct cancer. Throughout that time, Ariff also inspired a vibrant community of friends at her synagogue with her zest for life and stylish hats, which protected her during a life-extending therapeutic regimen.

“We saw a woman living, not dying,” recalls Ariff’s daughter, Sharon Webb, who shared these memories in the hope that other patients might benefit from the experimental photodynamic therapy that let her mother experience these joyful moments. Ariff passed away in October 2010 at age 83, having outlived the usual prognosis of three to six months.

One month before her death, Gladys Ariff danced until 2 a.m. at her grandson’s wedding.

Ariff refused chemotherapy and radiation, with so little time left, she wasn’t willing to endure their debilitating side effects and limited impact on life expectancy. Her Wilmington, Del., physician referred her to David Loren, MD, associate director of medical endoscopy at Jefferson, who has treated nearly 30 bile duct cancer patients with photodynamic therapy since 2009 – extending their lives post-diagnosis typically by a year or more.

While photodynamic therapy has been the standard of care in Europe for more than two decades, it is not offered widely for bile duct cancer in the United States. The therapy has not yet received FDA approval for this use, though it is approved for some esophageal and lung cancers. Only four medical centers in the United States treat an estimated total of 100 patients annually with photodynamic therapy for bile duct cancer: the Mayo Clinic, Weill Cornell Medical College, Indiana University and Jefferson.

Loren is currently recruiting patients to participate in a multicenter clinical trial expected to begin this year. Pinnacle Biologics, which makes Photofrin®, the photosynthesizing medication used in the therapy, is funding the trial.

By the time symptoms appear, the timeline is virtually the same for bile duct cancer and the more common pancreatic cancer. In the United States, 3,000 patients receive the diagnosis of bile duct cancer annually. Typically they have experienced jaundice, weight loss and itching as tumors block the flow of bile from the liver into the small intestine, where bile plays a key role in digestion. While the disease may be considered curable by surgery in its early stages, most patients don’t find out in time. When surgery is still possible, the odds of extending life expectancy through surgery or photodynamic therapy are often evenly matched.

Currently, more than 70 percent of bile duct cancer patients hear the grim news that their cancer cannot be surgically removed. Their limited treatment options include radiation and chemotherapy that degrade quality of life during a patient’s final months, and stents to keep the bile duct open. Unfortunately, says Loren, these stents typically become useless after tumor regrowth clogs the ends.
Photodynamic therapy offers the prospect of an extra year of life to patients who must suddenly confront their mortality. “What people are looking for is to have extra time with the people they love and to not be burdened by the side effects of chemotherapy and radiation,” says Loren. Photodynamic therapy keeps bile duct tubes open by coring them like an apple. Patients are injected with photosensitizing medication two days prior to the two-hour endoscopic procedure, which delivers tumor-killing light via a 4-millimeter laser fiber threaded carefully down through the intestines and into the bile ducts. The bile ducts are reopened via bursts of laser light focused on tumors, and then stents are placed to keep bile flowing. After treatment, patients typically experience a pain-free three months with no need to visit a doctor, and then return for another round.

For up to six weeks after the therapy, patients must wear hats and protective clothing to block exposure to sunlight and artificial light. These prevent sunburn triggered by the photosensitizing medication. While the treatment can be combined with chemo and radiation, most patients don’t choose this option. In keeping with her upbeat personality, Ariff embraced the restrictions on light exposure with gusto, triggering a fashion phenomenon. Rejecting the hat supplied by the hospital, she asked her milliner to expand her wardrobe of stylish hats. In solidarity, her friends likewise wore their silliest and most colorful hats in her presence. They were a vivid sight at her Wilmington synagogue, where Ariff also inspired a community of volunteers to cater life-cycle events. Her daughter recalls how every woman among the 300 people at Ariff’s funeral wore a hat. “Her style became everyone’s style, which added a touch of fun to that time of sorrow.”

Restrictions on light exposure in the aftermath of this therapy are a deterrent for a significant subset of patients. “For patients who want to be outside, on the beach or gardening, photodynamic therapy would not improve their quality of life,” Loren says. His long-term goal is to develop a multifaceted treatment center for bile duct cancer at Jefferson to treat more bile duct cancer patients with photodynamic therapy and other innovative therapeutics. “We have other novel options available for patients. But they are as yet unproven while we collect data,” he says. Jefferson has one investigative medication, Photofrin®, approved by the FDA for photodynamic therapy. However, adds Kahaleh, “The real challenge is that this is a totally unrecognized and under-diagnosed disease. A lot of people walk around with bile duct cancer unrecognized and then die from obstructive jaundice and infection. If doctors would refer them for an endoscopic evaluation to identify whether their bile duct is constricted, we would be detecting way more bile duct cancer nationally.”

For Ariff’s death, Loren’s clinic planted trees in her memory and mailed a card to her family recalling how “She brought light and joy to everyone.” Inspired by that insight, her family inscribed the phrase on Ariff’s tombstone – just below the outline of a jaunty hat. — Michel Kahaleh, MD, chief of advanced endoscopy, Weill Cornell Physicians

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Everyone knows that a peanut butter and jelly sandwich can be a culinary death sentence for someone with a severe peanut allergy. Yet few people understand the potentially serious health consequences of eating foods with even small quantities of gluten, a protein found in wheat, rye and barley, for people with celiac disease.

For people who have celiac disease, a weekly communion wafer can lead to life-threatening health problems. This autoimmune response to foods with gluten attacks and disrupts basic cellular repair mechanisms throughout the body and blocks the absorption of nutrients from food.

“Celiac disease has a protean and insidious effect throughout the body,” says Anthony DiMarino Jr., MD, the William Rorer Professor of Medicine and chief of the Division of Gastroenterology and Hepatology at Jefferson and co-director of the Jefferson Celiac Center, which opened in early 2011. With 30 physicians, specially trained pathologists and a dedicated nurse practitioner, the center is one of the largest and most integrated providers of care for celiac disease patients in the Philadelphia region. It’s also the only Center City clinic with a full-time registered dietician who specializes in helping patients adapt to the strictly gluten-free diet required to restore their health.

A Stealth Disease

Unfortunately, celiac is a stealth disease. Half of those with the disease are symptom free while they accumulate cellular damage. Those with symptoms typically seek relief for one or more ailments but usually don’t realize they need treatment for the root cause. They may experience miscarriages, stomach pain, weight loss, anemia, migraines, osteoporosis, changes in bowel habits, numbing and tingling in hands and feet and tiny blisters on elbows, arms and knees.

“Anyone with these symptoms, an autoimmune condition or a family history should have a simple diagnostic blood test for celiac,” says David Kastenberg, MD, co-director of the Celiac Center. “Our job is to educate physicians so they know what to look for.”

The blood test measures anti-tissue transglutaminase or anti-endomysial antibodies, indicators of celiac. Even when these antibodies aren’t present, a genetic test can reveal the presence of the disease. A human leukocyte antigen (HLA) serotype of DQ2 or DQ8 will show up among 98 percent of patients with the disease as well as among 30 percent of patients without celiac. A biopsy of the small intestine, obtained via upper endoscopy, confirms the diagnosis.

You Can Never Cheat

Symptoms can be controlled with a strictly gluten-free diet – with the emphasis on strict. Daily limits on gluten consumption are equal to 1/50th of a slice of bread and are easily reached via trace contaminants. “Basically, you can never cheat,” says Emily Rubin, RD, LDN, the division’s dietician. “I try to focus on what patients can eat, not on what they can’t eat, so that it doesn’t seem so overwhelming. Everyone who follows a gluten-free diet should feel better within a couple of weeks and see their numbers come down within six months and normalize within a year.”

The big problem lies with trace contaminants. A hamburger can’t just be plucked off a bun. Eggs can’t be cooked on the same grill as pancakes. Even a peanut butter jar can’t be shared with someone who spreads it on bread; it might contain crumbs. The experience of dining at a restaurant, being a guest at a party or eating a home-cooked meal can be fraught. “This disease is socially challenging,” says Rubin. “Because you feel like it’s annoying to nitpick.”

Currently, celiac disease affects 1 percent of Americans. A Mayo Clinic study found a nearly fivefold increase in celiac disease incidence in current blood samples compared with peer samples collected at Warren Air Force Base in Wyoming during the 1950s. Because the data are grounded in actual blood measurements, the study demonstrates that the increase in celiac disease is not just a reflection of growing awareness and diagnosis. By
assessing mortality rates among servicemen from the 1950s whose frozen blood samples revealed they had undiagnosed celiac disease, the same study revealed a fourfold increase in premature death.

Possible factors in the rising incidence of celiac disease include the increased gluten content of grains due to hybridization and comparable increases in food allergies that some attribute to the hygiene hypothesis (a theory that the modern environment is so clean that the immune system turns on itself). Patients with celiac disease who fail to maintain a gluten-free diet have an elevated risk of developing intestinal lymphoma or bowel cancer. Other serious problems occur when the immune system, responding to proteins in gluten, permanently damages the villi, the hair-like projections that line the small intestine like a shag carpet and help the body absorb nutrients. A condition called refractory sprue afflicts fewer than 1 percent of celiac patients, who then cannot respond to a gluten-free diet because the interior of their intestines has been permanently damaged — rather than a shag carpet, the intestines look more like a tile floor, with no villi present. Poor absorption of nutrients typically leads to a need for long-term steroid therapy and frequent hospitalizations for these patients.

**Disease du Jour?**

In some ways, celiac disease has become a victim of greater visibility. It is sometimes mistakenly associated with gluten sensitivity, a far less serious condition akin to lactose intolerance. People with gluten sensitivity feel better when they eat less gluten — but eating wheat, rye or barley doesn’t affect their health.

People with celiac disease also encounter skepticism because gluten-free eating has joined the ranks of trendy diets — along the lines of South Beach and Atkins. “I actually had a doctor [not from Jefferson] say to me, ‘Oh, you have the disease du jour. Aren’t you in high fashion?’” recalls Alice Bast, who was diagnosed with celiac disease in 1994. By that time, Bast, at 5’9” tall, weighed just over 100 pounds and had suffered a full-term stillbirth, three miscarriages and virtually the full checklist of celiac symptoms. “I tell physicians that celiac disease is one of the most common yet most under-diagnosed autoimmune diseases out there. Please take it seriously. Only 200,000 people in the United States have been properly diagnosed, and almost three million actually have the disease.”

Bast became a patient of DiMarino in 1998. Five years later, she founded a nonprofit, the National Foundation for Celiac Awareness (NCFA), and asked DiMarino to join her scientific and medical advisory board, a role he’s held ever since. NCFA offers free continuing medical education courses to physicians online, facilitates research and initiatives to improve the quality of life for individuals with the disease, and even trains restaurant chefs and food-service managers so that children can eat safely in school cafeterias.

All too often, Bast hears from people who don’t have sufficient medical support for their disease. “It’s not like you get diagnosed with celiac disease and go on your merry way. There is so much follow-up to be done,” she says. “It needs to be carefully managed.”

More than a decade ago, DiMarino counted himself among the skeptics about celiac disease. Then, two of his fellows enlisted his help in a study in which they determined that fewer than 50 percent of obstetricians, gastroenterologists and primary care physicians understood the link between celiac disease and miscarriage. “One of the signs of celiac is a woman who has lost multiple pregnancies,” says DiMarino. “This research has sparked my involvement ever since.”

He vividly recalls one patient, a woman in her early 40s who looked like the picture of good health. Yet she had lost two full-term pregnancies and suffered a series of miscarriages over five years. The woman and her husband had spent tens of thousands of dollars trying to get pregnant. “Someone finally noticed that she had a slightly lowered hemoglobin count and referred her to me,” says DiMarino. “She was one of those folks who had no, or minimal, gastrointestinal symptoms. I put her on a gluten-free diet. She was pregnant within six months and had another baby two years later.”

DiMarino keeps pictures of the two children in his office today.

New Celiac Medication Could Improve Health – and Golf Swing

The extra 15 yards Norm added to his golf drive have attracted even more attention off the links than on.

That’s because he was among six Jefferson patients to participate in a recent multicenter clinical trial for a promising new medication for celiac disease, larazotide acetate. For the prior 15 years, Norm had been unable to get his antibody levels under control. During the trial, he didn’t know whether he was receiving a placebo or the actual medication, but Norm was thrilled with the results: he gained 30 pounds and improved his drive. As soon as the trial ended, he had to stop his medication, which is not yet on the market. Both benefits disappeared.

Six months after the study, Anthony DiMarino Jr., MD, co-director of the Jefferson Celiac Center, was permitted to break the blind. He learned that four out of six of his patients who had participated in the clinical trial had actually received the medication; their antibody counts had improved to normal levels.

“We hope this will be the next big thing,” says DiMarino, who is currently enrolling patients in another clinical trial for larazotide acetate. “What’s so attractive is its safety: it doesn’t get into the bloodstream or alter the immune system, blood pressure or heart rate. You may be able to take it 30 minutes before a meal, and it tightens up the cells in the intestine to block the absorption of accidentally consumed gluten.”

DiMarino, who has no financial connection to the medication or the company that makes it, says, “If you lived in a bubble and never ate gluten again, celiac disease would go away. With this medication, you can stay healthy and live in the real world. It should protect you from the harmful effects of gluten if you’re not sure how food was prepared. The truth is that gluten is so ubiquitous that it’s incredibly difficult to remove from your diet.”

While this medication has potential to become the first FDA-approved drug for celiac disease, it’s not there yet. In the meantime, Jefferson is engaged in a full range of proven diagnostic and therapeutic regimens while also advancing understanding of ways to diagnose and care for patients with celiac disease.

**To reach the Jefferson Celiac Center, call 215-9-CELIAC (or 215-923-5422).**

A symptom checklist for celiac disease is available at www.celiaccentral.org.
LIGHT THERAPY
for a
BLUE PLANET AND BEYOND

Few treatments have emerged in psychiatry that have relatively few side effects, are of minimal cost and alleviate symptoms in less than a week. Fortunately for people who suffer from clinical seasonal affective disorder, or SAD, light therapy is one of those rare treatments. “It’s striking, in the world of psychiatry, how quickly light works as a therapeutic stimulus compared to pharmacological treatments, which may take several weeks to provide relief,” says George Brainard, PhD, neurology professor and director of Jefferson’s Light Research Program.

During fall and winter, 14 percent of the U.S. population experiences some sub-clinical symptoms of SAD, a type of depression; these symptoms sometimes include mild weight gain, modest increased need for sleep, tendency to be less socially interactive and generally feeling worse during the short days of late fall and winter. But for an estimated 2 percent of the population, symptoms can be severe and debilitating and may include feelings of hopelessness and weakness or thoughts of suicide.

Bear-like Behavior
As its name implies, SAD is different from typical depression in that its symptoms recur annually in the fall and winter. People with SAD also tend to crave carbohydrates and may gain 10 to 30 pounds during the darkest months of the year, whereas typical depression is sometimes associated with loss of appetite. Another striking difference is that SAD is associated with hypersomnia, while people with more typical depression often suffer from insomnia. People with SAD tend to sleep from 10 to 14 hours a day. “The weight gain and sleep is similar to bears who store up food for hibernation in the winter,” says Brainard.

Until recently, bright white fluorescent light has been the gold standard for treating SAD. A 1981 study showed that symptoms significantly diminished in seven to 10 days when patients sat by a 2-by-4-foot panel of bright fluorescent light for up to four hours each day. The current standard of treatment is bright white light therapy for 30 to 60 minutes first thing in the morning upon awakening. In the last decade, however, Brainard and colleagues have discovered that specific wavelengths of light corresponding to different colors appear to be more potent than others at alleviating SAD symptoms.

The difference lies not in how we perceive the colors, but on an unconscious level. Light travels from the retina into the brain through two pathways. The more commonly known pathway leads to the occipital lobe, affecting our vision. The other pathway stimulates biological and behavioral responses, in part by triggering the pineal gland, which secretes melatonin, the hormone that affects sleep and has a role in controlling circadian rhythms. A study by Brainard and his colleagues showed the wavelength that has the greatest influence on the pineal gland is 464 nanometers, which corresponds to blue – not coincidentally the color of the sky. Red, by contrast, is least effective.

On the Right Wavelength
In a Phase I clinical trial, just 45 minutes a day in front of a blue light panel was shown to significantly reduce symptoms of SAD, compared with a placebo red light control. Blue light also elicited a 50 to 60 percent remission rate, similar to bright white fluorescent light, but at a much lower dosage in terms of brightness and time. “By getting the wavelength right, you can use a gentler light, which is an important finding for SAD treatment, since it doesn’t cause headaches or eye strain like a stronger white light can,” says Brainard.

Light therapy devices are commercially available in several forms, including light panels, workstations, dawn simulators and head visors. Most light therapy products use white light, but companies like Philips are emerging as leaders in the light therapy marketplace and now offer products with blue light-emitting diodes (LEDs).

At Jefferson, light therapy research is moving beyond SAD treatment. Brainard is working with NASA to create a dynamic lighting system for the International Space Station, with the goal of reducing chronic sleep deprivation among astronauts. “Astronauts are some of the healthiest people in the world, but even the toughest person can collapse from chronic sleep deprivation,” said Brainard. Back on Earth, such research could have significant implications for the 20 percent of the U.S. population that works in jobs that require alertness long after the sun goes down. What began as a treatment for seasonal depression, light therapy is helping even the healthiest among us sleep (and wake) better.
A walk through a village in Indonesia when she was 6 years old set the course of Kathleen Squires’ life. There, she and her father saw a man with bulging legs suffering from a disease she now knows as elephantiasis, a rare lymphatic disorder.

Her compassionate father, whose job with an oil company required the family to move to locations around the world, commented how unfortunate it was that people there didn’t have access to good medical care. “The family legend is that I declared right then that I would become a doctor to help people like that,” recalls Squires.

As director of Jefferson’s Division of Infectious Diseases since 2005, Squires is known for her expertise in HIV clinical care and research, which aligns with her lifelong interest in helping disadvantaged people. “What’s clear is that this infection has settled into a population with few economic resources,” she says.

Jefferson’s clinic treats more than 1,000 HIV patients annually, nearly one-third of whom are uninsured or underinsured and receive care thanks to a grant from the City of Philadelphia. Patients may select established treatment protocols or participate in one of five clinical trials currently open to improve treatment regimens and evaluate new treatment options.

“Many of our patients are among the working poor and can’t afford HIV medications that typically cost $1,000 a month,” Squires says. “This grant enables our clinic to help patients obtain needed services and health insurance. It’s also critical to our research: unless we provide treatment to people with HIV who are impoverished, we won’t be at the forefront of understanding this disease.”

Under Squires’ leadership, Jefferson’s Division of Infectious Diseases provides expert consults to physicians who encounter obscure diseases from the developing world as well as ailments more typically found in the Philadelphia region. This list ranges from pneumonia and Lyme disease to MRSA infections, drug-resistant tuberculosis and endocarditis and osteomyelitis, infections linked to artificial heart valves or bones, respectively.

Squires recently shared her thoughts on her field and career.

Q. What inspired your interest in HIV research and treatment?
A. My career began at the dawn of AIDS, which was first reported in 1981, the year I graduated from medical school. I worked at the epicenter of the epidemic during my fellowship at Weill Cornell Medical College in New York. It has been an incredible journey for me since. AIDS has evolved from a uniformly fatal infection that caused young, vibrant people to wither away and die months after diagnosis into a chronic condition managed with a one-pill-a-day regimen.

I am especially interested in how men and women fare differently with antiretroviral therapy. For instance, I’m trying to tease out whether higher discontinuation rates for antiretroviral therapy among women reflect problems with toxicity, or the reality that most HIV-infected women are single parents who can’t participate in clinical trial schedules.

Q. How has your interest in international travel dovetailed with your work?
A. During my childhood, I lived in Indonesia, Nigeria, Brazil, Puerto Rico and Australia. While I have lived in the United States since high school, my career has enabled me to continue my world travels. Most HIV conferences are held outside the United States.

Q. What do you hope will be the legacy of your contribution to medicine?
A. When I first saw HIV in New York, it primarily occurred among gay men. In the medical and lay communities, there is still pervasive under-recognition that this sexually transmitted disease affects men and women equally. I frequently hear ‘this woman has a false-positive HIV test. Can you help me sort this out?’ In fact, she often does have HIV.

My proudest achievement would be to further contribute to public awareness that HIV affects both men and women, to identify how this disease affects women, especially during child-bearing years; and to define how treatment protocols for men and women should differ.

Q. What advances do you hope to see in HIV treatment?
A. HIV is an absolutely preventable disease – yet its incidence rate hasn’t changed over the last decade. Every year, 60,000 new cases of HIV are diagnosed in the United States. Over the next decade, I would like to see new infection rates drop and more patients receive needed therapies, which would reduce forward transmission.

Most people with HIV live in resource-poor settings. In many parts of the world outside the United States and Europe, this diagnosis is still a death sentence. While global health initiatives are changing that picture, many people share my concern that the economy will slow our progress.

Kathleen Squires, MD:
Working to Make a World of Difference for Patients with HIV
Until Kanani Titchen was in her 30s, she was more likely to portray a physician than to consider becoming one herself. A former actor, Titchen is now a fourth-year JMC student. While her path to Jefferson may have been circuitous, her theatrical experience informs her work with patients today, having taught her how to put herself in other people’s shoes.

After graduating from Tufts University with a dual degree in music and psychology accompanied by a fascination with biology, Titchen, originally from Hawaii, moved to San Diego, where she half-heartedly looked for science jobs. “Something was nagging at me,” she says. “I was 21 years old. It was the only time I felt like I could pursue music and theater without repercussions.”

After a few interviews for entry-level science jobs, she realized she was not yet ready to pursue science. She needed to give acting a shot. Titchen was accepted to the repertory company at the Lamb’s Players Theater, with which she performed and toured for the next four years. In the acting world, being in a repertory company is a coveted gig because of the steady work it provides. Still, her salary was not enough to live on – so, like many actors, she sought other work and taught acting to students in kindergarten through 12th grade.

Despite her busy and unpredictable schedule, she also volunteered at a nonprofit organization working with at-risk youth, teaching them to write, produce and perform plays with positive messages.

After several other acting and teaching jobs in San Diego, Titchen moved to New York City to be a sound technician for a short-run production on Broadway. In New York, Titchen watched artists much older than she still struggling to succeed. It was then that she realized it was time for a change. “I needed to break the rhythm,” she says. “I needed to be bold and start something new.”

Tapping into her love of science and her undergraduate experience in behavioral research, Titchen got a job at an international non-governmental organization doing research on sexually transmitted diseases. The position gave her lab experience and came with an education stipend that she used for a physiology course at Columbia University. She fell in love with the subject matter.

Even though a medical degree was still a distant thought at the time, she enrolled in Columbia’s post-baccalaureate program. “I figured I’d get the basic credits out of the way and then decide what to do,” she explains. A job at an emergency room clinched the idea of medical school. “Finally, my skills working with people and science were coming together,” she says.

Titchen, 36, is among a small subset of older students on campus. As such, she appreciates Jefferson’s size and the vibrant connections formed among peers and mentors who, like her, experienced other careers prior to medicine. Titchen plans to become a pediatrician, a specialty she hopes will allow her to incorporate advocacy and preventive medicine. “I just love pediatrics,” she says. “It’s the greatest feeling to see a kid go from miserable to smiling.”

As a soon-to-be JMC graduate and pediatrician, the stage is set for her career’s second act.

For Former Actor, Pediatrician is the Role of a Lifetime
Schlaff
Menko
Rattan

Dean’s Pilot Programmatic Research Grant Initiative Awards Announced

JMC Dean Mark L. Tykocinski, MD, announced recipients of the Dean’s Pilot Programmatic Research Grant Initiative for 2011 in October. These $50,000 awards are used to provide seed money for the generation of data leading to the submission of successful NIH programmatic grants. In the latest funding cycle, the awardees were:

- Karen Knudsen, PhD, Department of Cancer Biology
- Haisong Liu, PhD, associate professor in the Department of Radiation Oncology, has been named director of radiosurgery physics for the Division of Stereotactic Radiosurgery at Jefferson Hospital for Neuroscience. For the past three years, Liu has worked in the Bodine Center for Radiation Therapy at the Kimmel Cancer Center as a senior physicist.
- Satish C. Rattan, DVM, professor of medicine in the Division of Gastroenterology, was named director of the Division of Stereotactic Radiosurgery at Jefferson Hospital for Neuroscience. For the past three years, Liu has worked in the Bodine Center for Radiation Therapy at the Kimmel Cancer Center as a senior physicist.

Oshinsky Honored by Headache Society

Michael L. Oshinsky, PhD, assistant professor of neurology and a member of the Jefferson Headache Center team, received the 2011 Harold G. Wolff Lecture Award for creating a new animal model of migraine headache. The award is granted annually by the American Headache Society for the best paper on headache, head or face pain and the nature of pain itself. Oshinsky won for his research paper, “Spontaneous Trigeminal Allodynia in Rats: A Model of Primary Headache.”

Rattan Awarded $1 Million NIH Grant

Satish C. Rattan, DVM, professor and chair of the Department of Obstetrics and Gynecology. Schlaff comes from the Department of Stem Cell Biology and Regenerative Medicine and a member of the Kimmel Cancer Center. The findings were reported in the Aug. 1, 2011, issue of Cell Cycle.

Liu Named Director of Radiosurgery Physics at JHN

Haisong Liu, PhD, associate professor in the Department of Radiation Oncology, has been named director of radiosurgery physics for the Division of Stereotactic Radiosurgery at Jefferson Hospital for Neuroscience. For the past three years, Liu has worked in the Bodine Center for Radiation Therapy at the Kimmel Cancer Center as a senior physicist.

Leukemia Drug Could Help Breast Cancer Patients

A leukemia chemotherapy drug may help breast cancer patients who don’t respond to tamoxifen obtain therapeutic benefits, according to a study led by Michael P. Lisanti, MD, PhD, professor and chair of the Department of Stem Cell Biology and Regenerative Medicine and a member of the Kimmel Cancer Center. The findings were reported in the Aug. 1, 2011, issue of Cell Cycle.

New Gene Therapy Ready for Clinical Trials

A promising gene therapy developed in part at Jefferson’s Center for Translational Medicine to prevent and reverse congestive heart failure is on the verge of clinical trials. Reporting in the online July 20, 2011, issue of Science Translational Medicine, cardiology researchers demonstrated the feasibility, long-term therapeutic effectiveness and safety of S100A1 gene therapy in a large-animal model of heart failure under conditions approximating a clinical setting.

“The reversal of cardiac dysfunction in this preclinical heart failure model in the pig – by restoring S100A1 levels in practically the same setting as in a patient – is remarkable and will pave the way for a clinical trial,” said Patrick Most, MD, adjunct assistant professor of medicine at Jefferson and lead author of the study.

“Spontaneous Trigeminal Allodynia in Rats: A Model of Primary Headache.”

Jefferson also ranked in the top 25 percent of hospitals nationally for nephrology, rheumatology and cardiology/cardiac surgery.
**Medical Frontiers**

**Jefferson Offers New Colonoscopy Prep Option**

Jefferson gastroenterologists are offering a new colonoscopy preparation option designed to motivate more people to get colonoscopies and to improve prevention of colon cancer. David M. Kastenberg, MD, associate professor of medicine in the Division of Gastroenterology and Hepatology, and his team found that colonoscopy preparation medication taken in two doses separated by three hours the same day as the procedure is just as effective as typical preparations beginning with medications given the night before. Benefits include less sleep loss, less weekday interference and fewer complaints of side effects. Many people refrain from having colonoscopies to avoid the time-consuming overnight protocol.

**Jefferson Launches Wholly Robotic Cardiac Surgeries**

In September 2011, cardiothoracic surgeons at Jefferson began performing wholly robotic cardiac surgeries, beginning with a mitral valve repair. “This is the next step in the advancement of our robotics program,” said Howard Weitz, MD, director of the Jefferson Heart Institute, the Bernard L. Segal Professor of Clinical Cardiology and chief of the Division of Cardiology. Jefferson is the first hospital in Philadelphia to perform wholly robotic mitral valve repair. The Division of Cardiothoracic Surgery previously conducted partial robotic surgeries using the robotic arm for access and better visualization in and around the heart.

**Longtime Faculty Member Creates Alumni Giving Incentive Fund**

Last spring, Robert L. Brent, MD, PhD, a JMC faculty member since 1965 who has established four endowed scholarships at Jefferson, and his wife introduced the Robert and Lillian Brent Alumni Giving Incentive Fund, which they created to increase alumni giving and inspire generosity in future graduates. The Class of 2011 is the first to be part of this program. The Brents have made a donation to the annual fund in each graduating student’s name for the first five years after graduation. At the end of five years, the class will have an enviable 100 percent giving participation. After five years, it will be up to the class to continue its 100 percent giving record.

Brent has emphasized the importance of giving throughout his lengthy career. In 1974, JMC’s student newspaper published an article, “Eight Degrees of Charity,” that he submitted as a faculty member. He recently revised the piece: "Maimonides, the twelfth century Hebrew scholar, described eight degrees of charity … The highest degree is to provide a means whereby the recipient will become self-sufficient and in turn be able to contribute to society. In all likelihood, Maimonides could not have foreseen the plight of the private university in the twenty-first century – but there is no doubt that he would have considered university support the highest level of philanthropy. Maimonides also said, ‘no one ever becomes impoverished by giving charity.’" "I guarantee you that the gratification and joy of sustaining an institution of education will become a very rewarding part of your life,” Brent has told Jefferson scholars. “For the students that have read the Hippocratic Oath, you know that it states that physicians are responsible for the education of future physicians.”

Brent, a distinguished professor of pediatric radiology and pathology at Jefferson and at Nemours/A.I. duPont Hospital for Children, has received several honors recently, including being named 2011 Castle-Connolly National Physician of the Year in recognition of excellence in clinical care and receiving the William Liey Medal, awarded to pioneers in the field of perinatal medicine.
My modification of Einstein’s Theory of Relativity holds that the older one gets, the faster time moves – especially if you enjoy what you are doing. I’m coming to the end of my term as Alumni Association president, and these two years have flown by because I have thoroughly enjoyed representing the biggest and best medical school alumni in the country.

I would like to thank the people who made this job so much fun, including Phil Marone, MD ’57, MS ’97, and his right-hand staffer, Toni Agnes; the members of the Alumni Association Executive Committee, especially the subcommittee chairs and Marianne Ritchie, MD ’80, who are the bedrock of our organization; and past President John Moore, MD, who showed me the ropes before sadly passing away last fall. And I give special thanks to Vince Armenti, PhD ’79, MD ’82, who will assume the presidency this April. He has always been here for me and will represent us well over the next few years.

And, of course, I thank the thousands of alumni who make up this great organization. I leave you with one last thought: JMC has given us all lifelong gifts: a stellar education, family, friends and an alma mater that is always a source of great pride. Please join your fellow graduates and give back to JMC for a lifetime of career activities that have advanced psychiatry. Field lives in Philadelphia.

Robert E. Rinaldi is working for a weight-loss clinic in Naples, Fla. He reports that he and his wife, Cynthia, are enjoying both work and play in paradise.

Benjamin L. Hoch, associate professor of surgical pathology at the University of Washington Medical Center, has been promoted to director of the school’s residency training program. Residents in the pathology department recently presented him with an outstanding teacher award. Hoch lives in Snohomish, Wash.

Michael A. Baumholtz welcomed his second child, Audrey, in April 2011. He works in Temple University School of Medicine’s division of plastic and reconstructive surgery and lives in Wynnewood, Pa.

Meghan Raleigh recently returned from Tikrit, Iraq, where she served as a U.S. Army battalionsurgeon for the 4th Infantry Division. She reports that she was packing some books from a physical therapy clinic and found one on shoulder injuries in sports written by Phillip J. Marone, MD ’57, MS ’97, associate dean of JMC alumni relations and executive director of the JMC Alumni Association. “It was like a small piece of home to be reminded of Jefferson. All of the sports medicine and physical diagnosis training I had at Jefferson and beyond has helped. And now, while I’m in Iraq, I’m teaching soldiers,” Raleigh writes.

Post Graduate
James Medina, MD, PG, ’02, practices emergency medicine in Lancaster, Pa., and has released an iPhone/iPad application called Coaching Wizard to assist soccer coaches with real-time game management. The app tracks individuals’ playing time, assists with player substitutions, records statistics and assists with email communication.

George Valko, MD ’86
President, JMC Alumni Association

THOMAS JEFFERSON UNIVERSITY AND HOSPITALS
A 16-year-old heir to the inventor of the kitchen blender has just stolen and crashed his father’s Ferrari. When he arrives home after the accident, he collapses on the marble floor of his parents’ mansion.

Hank Lawson, a concierge physician, happens to be on the scene. He rips open the boy’s shirt to find the telltale bruises of hemophilia and quickly diagnoses the boy with a pericardial tamponade. Lawson, who has no supplies, sends the boy’s girlfriend to gather his Factor VIII blood-clotting kit, a razor blade, a Bic pen, duct tape, a plastic bag and a bottle of vodka.

Using the vodka as a sterilizer, he slices into the boy’s chest with the razor and drains blood out of the pericardial sac via the barrel of the pen. Then he seals the wound with the bag and duct tape. The boy survives. Just another day at the office for Hank Lawson – and for Irving Danesh, MD, graduate of Thomas Jefferson University Hospital’s first emergency medicine residency class in 1986.

Danesh, the medical consultant for the USA Network’s show “Royal Pains,” devised the fictional scene above, which appeared in the show’s first episode. Danesh is involved in all aspects of production, including researching bizarre but true medical scenarios; working with the show’s writers to develop medical scenes; assuring medical accuracy; and advising the prop department on such projects as building lifelike chests for Lawson to slice open with razor blades.

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In Memoriam

Joseph P. Kenna, 86, of York, Pa., died Sept. 24, 2010. Kenna served as a U.S. Air Force officer during the Korean War. During his 50-year career, he practiced family and emergency medicine as well as surgery. He was most recently worked at Joseph’s Hospital in Lancaster, Pa. He is survived by his wife of 62 years, Muriel; one son, Joseph, three daughters, Diane, Karen and Denise, MD ‘82, six grandchildren, and three great-grandchildren.

Marvin C. Snyder, 82, of Lehighton, Pa., died July 22, 2011. Snyder was a family physician for 40 years and served on the medical staff of the Gnaden Huetten Memorial Hospital in Lehighton for 35 years. He is survived by his wife of 56 years, MaryAnn; five sons; and two daughters.

Joseph S. Hanr, 86, of Lower Makefield, Pa., died May 17, 2011. Hanr opened a dermatology practice in Philadelphia in 1957. He later helped develop penicilamin to treat severe arthritis and was involved with the development of new uses for diludor, a drug intended for the treatment of tuberculosis that researchers discovered also could be used to treat leprosy and infections in AIDS patients. He is survived by his wife of 59 years, Marvin; two daughters; and three sons.

Donald E. Stoudt died Aug. 14, 2010. Stoudt served in the U.S. Navy from 1956 to 1958 before serving a residency in neurology at Georgetown University. He then ran a private neurology practice in Reading, Pa., until his retirement in 1981. He is survived by his wife, Mary Lu; who completed Jefferson’s diploma nursing program in 1954; four children; and two grandchildren.

James R. Regan, 80, of Bethlehem, Pa., died July 20, 2011. Regan was a physician intern in private practice until he retired. He served his country honorably during peacetime in the U.S. Air Force. He is survived by three sons and one daughter.

Kenneth P. Johnson, 70, of Lutherville, Md., died Sept. 3, 2011. Johnson was former chairman of neurology at the University of Maryland School of Medicine and an internationally recognized expert on multiple sclerosis. His work led to FDA approval of new treatments for multiple sclerosis. Johnson was the founder of the Americas Committee for Treatment and Research in Multiple Sclerosis and was head of the Maryland Center for Multiple Sclerosis, which he also founded. He enjoyed traveling and camping. He is survived by his wife, Jacquil, three sons; a daughter; and two grandchildren.

John A. Kolos, 88, of Philadelphia, longtime clinical professor of psychiatry and human behavior, died Sept. 29, 2011. He is survived by his wife, Nancy; four children; seven grandchildren; and one sister.

Theodore J. Sokowski, 68, of Dresher, Pa., died Sept. 6, 2011. Sokowski worked at Abington Memorial Hospital for 41 years. He served in the U.S. Army during the Vietnam War at Virginia’s Komar Army Health Clinic at Fort Lee. His love for aviation spawned the opportunity to become a flight surgeon, and he made many helicopter trips to Walter Reed Army Hospital. He played the accordion and had a passion for photography. He is survived by his wife, Daria; two sons, Paul and Greg; and five grandchildren.

Jeffrey A. Regan, 79, of Reading, Pa., died Aug. 24, 2011. Descended from Cheng Ch’eng-kung, the pirate who established ethnic Chinese rule over the island of Taiwan in the 17th century, he trained in England prior to coming to the United States to further his neurosurgical acumen. He served a neurological surgery residency at Jefferson. He enjoyed fishing, philosophy, attempting (not always successfully) to fix things around the house and discussing interesting neurological cases. He is survived by his wife, Zen; four children; and two grandchildren.

Raphael Rubin, MD, Professor of Pathology and Cell Biology

Raphael Rubin, MD, 55, of Merion, Pa., professor of pathology and cell biology and a faculty member at Jefferson since 1986, died of brain cancer Sept. 16. Rubin was an expert on liver pathology. His research focused on a kind of cell signaling known as insulin-like growth factor 1—a kind of hormone known to keep cancer cells growing. His research has been published in more than 100 professional journals. He was co-editor of the fifth and sixth editions of Rubin’s Pathology, a medical textbook first published by his father, Emanuel Rubin.

Rubin, who was named physician of the year in 2000 by the American Liver Foundation, headed Jefferson’s liver study unit and worked closely with liver transplant teams. Last April, his portrait was unveiled at JMC. A talented musician who played piano and excelled at the violin, Rubin performed as a soloist with the Main Line Symphony and with the Merion Trio. He played in benefit concerts for Jefferson and for Kehetet Yeshiva High School in Merion, which his daughters attended. He and his wife, Rene Rothstein-Rubin, established a science education fund for the school. In addition to his wife, Rubin is survived by sons Jascha, Saul and Judah; daughters Zipporah, Sophie, Zohava and Batsheva; two brothers; and two grandchildren.

Average number of people hospitalized annually in the United States for flu-related complications: > 200,000

Percentage of people between ages 50 and 64 who have one or more health conditions that put them at higher risk for flu-related complications: 30%

Peak month for influenza: February

Ideal month to get the flu vaccine: September

Recommended age for receiving flu vaccine: over 6 months

Ages at which people are at greatest risk for flu-related complications: < 5 and ≥ 65
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