Volume 1 Number 1 Spring 2003

INAUGURAL ISSUE

New Jersey Medical School

CHANGING THE COURSE OF STROKE SAVING SIGHT • CME: MACULAR DEGENERATION • NEW COCHLEAR IMPLANTS



Russell T. Joffe, MD

Message from the Dean



AM VERY PLEASED TO PRESENT the inaugural issue of *NJMS Pulse.* This new magazine embodies the pride that all of us feel for the academic accomplishments of our school. It also serves to highlight our successes in meeting the challenges of today's healthcare environment.

Despite the uncertainties and distractions around us, the faculty, students and staff of NJMS remain remarkably focused and dedicated to achieving our commitment to excellence in medical education, research and clinical care. Within these pages you will read about our innovative biomedical research, exemplary medical care, and forward thinking revisions to our curriculum. You will be reminded of the dedication of our alumni to their patients and to their communities.

Each section of this issue speaks either directly or indirectly to the passionate commitment this school has to its stakeholders, specifically our city of Newark neighbors and their families and the wider northern New Jersey community.

As you glance through these pages, I am confident that you will appreciate, as I do, that NJMS is a vital resource to our community, to our state of New Jersey, and to our nation. Congratulations to all of you: our faculty, alumni, students, staff and community stakeholders for helping our school achieve excellence.

NJMS Pulse

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KEEP IN TOUCH

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insideinformation

New Trial Compares MS Therapies

MRI study monitors lesions of patients taking two medications: Betaseron and Copaxone.

HYSICIANS AT NEW JERSEY MEDICAL SCHOOL (NJMS) have launched a \$3,619,080 clinical trial comparing two FDA-approved treatments for multiple sclerosis (MS): interferon beta 1b (Betaseron) and glatiramer acetate (Copaxone). It is the first head-to-head, randomized study comparing any interferon with glatiramer acetate. The Neurological Institute of New Jersey at NJMS is one of two study sites in the state; the other is the Bernard W. Gimbel MS Center in Teaneck. Principal investigators are Leo J. Wolansky, MD, and Diego Cadavid, MD.

The trial is unique because it uses state-of-the-art magnetic resonance imaging (MRI) technology to detect and monitor brain lesions in patients with MS. These lesions, also known as plaques, are scars in the central nervous system where inflammation has stripped axons of the insulating fatty protein known as myelin. Demyelinated axons do not function efficiently, and these lesions are what cause the symptoms of multiple sclerosis.

MRI has proven to be a valuable tool for diagnosis, management and research of MS. "The 3-Tesla MRI on the Newark campus is state-of-the-art in detecting brain lesions,"

LONG TR, SHORT TE IMAGE OF STUDY PATIENT

The high magnetic fieldstrength of the 3T system produces high signal to noise ratio images, even with thin 3 mm thick sections. Use of thin sections facilitates improved demonstration of small lesions, such as are commonly seen with MS (arrows).





Leo J. Wolansky, MD (left), and Diego Cadavid, MD



says Wolansky. "Within months of FDA approval, we

installed the first 3-Tesla MRI scanner for clinical use in New Jersey. Until now, there was virtually no information about the appearance of plaques using an MRI with a higher magnetic field strength than 2 Tesla."

To further enhance the visibility of the lesions, the study will employ a triple dose of gadolinium, a contrast-enhancing agent used to detect active inflammation. This technique had been described several years ago at NJMS by Wolansky, working with UMDNJ President Stuart D. Cook, MD, who is also director of the MS Center at NJMS. Gadolinium, the 64th chemical in the periodic table of elements, is strongly paramagnetic, meaning that, like iron, it is attracted by magnetic fields, making it particularly useful in MRI.

Participants will be randomized to receive one of the two drugs. "The study is clearly attractive to patients because everyone receives an effective, approved therapy," says Cadavid, who is assistant professor of neurology and neurosciences. "There are no placebos." They receive a baseline scan upon entry, and after that, once every four weeks. All MRIs will be carried out on the 3-Tesla unit, with Wolansky conducting a blinded evaluation of the scans, including visual as well as computer analysis.

"From the scans, we can get feedback that might otherwise take years to obtain," says Wolansky, who is professor of radiology and MRI section chief.

The study is being funded by a grant from Berlex Laboratories, Inc., the manufacturer of Betaseron. A larger study is planned later to compare double-dose Betaseron with Copaxone. "MS is a field full of opinions about these and other drugs, but there is not much hard data to go by," says Cadavid. "This study will give us the first insight into the relative efficacy of these two drugs in a head-to-head trial." •

News about NJMS events, faculty, grants, research and more

Faculty Star in TV Series

HE FIRST THREE PROGRAMS of a cable television series focusing on the most critical health issues facing the state aired in February, featuring several of the medical school's experts. Steve Adubato is the host. The first installment looked at the debate over hormone replacement therapy and included two patients and three physicians, two from UMDNJ: Gerson Weiss, MD, chair of OB/GYN at NJMS, and Gloria Bachman, MD, from Robert Wood

Johnson Medical School. The second installment, examining the potential impact of weaponizing biological agents such as anthrax and smallpox, featured: Nancy Connell, PhD, Director of the Center for BioDefense, NJMS; Peter Wenger, MD, NJMS assistant professor of preventive medicine; and David Perlin, PhD, Scientific Director of the Public Health Research Institute (PHRI). The third show examined the state's and country's level of preparedness for an attack using biological or chemical weapons. William Halperin, MD, DrPH, chair of preventive medicine at NJMS, and Leah Ziskin, PhD, SPH associate dean in south Jersey, participated.

Transcripts of the programs can be accessed at the Healthy New Jersey Web site. UMDNJ is an underwriter of the series.

TB Center Has 10th Anniversary

N THE EARLY 1990S, TB rates were on the rise. The state of New Jersey had the seventh highest rate of TB infection in the country. And to make matters worse, a growing number of TB patients were coinfected with HIV or had a drug-resistant strain of TB, making treatment more difficult and time-consuming. Lee Reichman, MD, decided it was time to take action. And the New Jersey Medical School National Tuberculosis Center was born.

This January, the Center celebrated its 10th anniversary in brand-new, stateof-the-art quarters at the International Center for Public Health in Newark (pictured at right). Its run has been impressive. It has improved medicationtaking compliance in Newark from 62 percent to 98 percent, lowered the TB rates in the city by 62 percent, and achieved National Model Center designation from the federal government. "We now occupy the only clinical facility in the world designed from scratch for safe and effective treatment of TB and multi-drug resistant TB," says Reichman, Executive Director of the Center and a professor of medicine and preventive medicine and community health at NJMS. The TB Center has also demonstrated the effectiveness of a widely used strategy called directly

observed therapy, or DOT, in which public health

workers visit TB patients daily to observe them taking medication.

My My My

In 2001, 23.2 Newark residents per 100,000 had active tuberculosis, down from 71.8 per 100,000 in 1991. Experts believe DOT is the primary reason for the dramatic reduction. TB can be cured, but it requires taking several medications for many months. Unfortunately, once patients begin to feel better, they stop taking the antibiotics, allowing the disease to mutate into drug-resistant strains which can spread.

> Reichman's book, "Timebomb: The Global Epidemic of Multi-Drug-Resistant Tuberculosis" (McGraw-Hill), recently won first prize in the trade category of the American Medical

Writers Association 2002 Medical Book Awards Competition.



Alum Gives \$2 Million for Chair in Orthopaedics

The co-inventor of the New Jersey Knee makes a gift to encourage human joint replacement research at NJMS.

REDERICK F. BUECHEL, MD, a 1972 NJMS graduate and co-inventor of the New Jersey LCS Total Knee Replacement System, has given the school the largest single gift ever received from an alum—a \$2 million endowment to establish a chair in the Department of Orthopaedics. He completed the orthopaedic residency program at NJMS in 1977.

The Frederick F. Buechel, MD, Chair for Joint Replacement will enhance a strong clinical program in total joint replacement at University Hospital with a basic science research program.

"My wish for the chair holder is to push the frontiers of human joint replacement research into practical, clinical applications," says Buechel.

To encourage scientific exchange and research collaborations, the chair holder will work in conjunction with the New Jersey Institute of Technology (NJIT) to establish the Buechel-Pappas Biomechanical Engineering Liaison—a partnership between the NJMS orthopaedic department and the departments of Biomedical Engineering and Mechanical Engineering at NJIT.

This liaison reinforces the importance Buechel places on the value of collaboration. Engineer Michael Pappas, PhD, a professor of mechanical engineering at NJIT, taught biomechanics to NJMS medical students and residents. Buechel, then a surgical resident, was inspired by Pappas' skill at solving complex structural problems. They joined forces when the resident asked his teacher for help in constructing a prosthetic ankle. Since then, they have received more than 100 patents for implants and instruments related to replacement ankles, hips, shoulders, knee and finger joints.



"My wish for the chair holder is to push the frontiers of human joint replacement research into practical, clinical applications." Frederick F. Buechel, MD

The endowment will also establish the Buechel-Pappas Award for Outstanding Biomedical Engineering Research, which will be given every other year to a surgeon-engineering team from the two schools. It will also allow for the development of a clinical research unit on the Newark campus to promote cutting-edge research.

Buechel, who is a clinical professor of orthopaedic surgery at NJMS, was inducted into the New Jersey Inventors Hall of Fame with Pappas in 1998.

Fred Behrens, MD, professor and chair of the Department of Orthopaedics, comments: "This gift, which is a tribute to Dr. Buechel's achievements and his remarkable career, will help to assure that our school remains at the forefront of research and education in orthopaedics."

Treating Complex Head and Neck Malignancies

ead and neck malignancies, including those found in the voice box, throat, mouth, salivary glands and sinuses, account for about 5 percent of all cancers. However, at University Hospital (UH), head and neck malignancies total about 15 to 17 percent of all cancers treated.

What brings these patients to Newark is a multidisciplinary program led by Soly Baredes, MD, chief of the division of otolaryngology-head and neck surgery and associate professor of surgery at New Jersey Medical School. "Head and neck tumors can be difficult to manage in a community setting because of the complexity of treatment," says Baredes. For example, tumors at the base of the skull require the skills of a neurosurgeon, ophthalmologist and plastic surgeon as well as an otolaryngologist. Other head and neck malignancies may







Left and above: The CT scan pictured is that of a parotid tumor.

Below: Soly Baredes, MD, examining a patient

need treatment by oral and maxillofacial surgeons as well.

Baredes says the collaboration among surgeons makes UH's program unique in New Jersey. "For example, our skull base team includes a neurosurgeon, ophthalmologist and otolaryngologist," he explains. "We collaborate on complex tumors that cross the barriers between the nasal cavities, sinuses, and the brain." UH is the only facility in the state, and one of a few in the U.S., with intraoperative MRI technology, pioneered here by neurosurgeon Michael Schulder, MD. It allows surgeons to pinpoint the tumor location and remove it with minimal damage to surrounding tissue. Another special feature of the program is interventional radiology. Preoperative embolization of tumors decreases blood loss during surgery to remove lesions.

A cornerstone of the program are the weekly head and neck tumor confer-

ences, which are attended by representatives of the many specialties on the interdisciplinary team. (In addition to those listed above, these also include medical and radiation oncologists, pathologists, head and neck radiologists, and specialized nursing staff.)

The Head and Neck Cancer Resource Center at UH, funded by a grant from the HealthCare Foundation of New Jersey, provides patients and their families with a variety of rehabilitative services. "This type of surgery affects basic survival skills, such as the ability to eat, breathe and communicate," says advanced practice nurse Ray Scarpa, MA, CNS, AOCN. "Some 40 to 60 percent of patients may have tracheostomies, and many also have laryngectomies." The Center staff, which includes four advance practice nurses, helps with the physical management of supplemental devices, from feeding tubes to breathing aids.



New Company Launched

UNE 25, 2002 MARKED A MILE-STONE for UMDNJ's technology transfer office when BioDelivery Sciences International, Inc. went public using stock ticker BDSI (NASDAQ). It is the University's first spin-off company to go public. Raphael Mannino, PhD, and Susan Gould-Fogerite, PhD, both associate professors of molecu-

lar biology at NJMS, are the company's founders.

Mannino is executive vice president and chief scientific officer of BDSI, and serves on its board of directors. He is a world leader in cochleate technology and an expert in applying artificial lipid-based delivery systems to problems in biotechnology, including drug delivery, vaccine design and gene therapy applications. Gould-Fogerite, co-developer of the cochleate technology, is vice president of innovation/discovery research at BDSI and serves on its board.

The groundbreaking cochleate technology was developed by the partners while at Albany Medical College and NJMS and is licensed exclusively to BioDelivery Sciences International. Cochleate delivery vehicles (Bioral[™]) repre-

Cardiac Surgery At UH Takes Leap Forward

JMS AND UNIVERSITY HOSPITAL (UH) have launched a state-of-the-art cardiac surgery program through a new partnership with Columbia Presbyterian Medical Center (CPMC). Columbia's cardiac surgery program is currently ranked as one of the best in the U.S. Columbia surgeons performed the nation's first robotically-assisted atrial septal defect repair without a chest incision, and

CPMC is also the national training center for two of the three existing FDA trials of robotic cardiac surgery. Its work in the use of LVAD (left ventricular assist device) has helped thousands of patients with end-term heart failure. These and other innovations will now be available at UH.

Several Columbia faculty members have assumed leadership positions in the new program. They include Barry Esrig, MD, chief of the division of cardiothoracic surgery at UH and Douglas Jackson, MD, vice chair of critical care, anesthesiology, and director of the new Cardiothoracic Surgery Intensive Care Unit (currently under construction). They join Michael Banker, MD, director of cardiac surgery at UH. Administration of the new division will be provided by Eric Rose, MD, chair of the department of surgery at Columbia.

Says NJMS Dean Russell T. Joffe, MD: "This affiliation provides enormous opportunity for NJMS as well as University Hospital. The combination of the best of both schools allows us to move quickly in broadening our clinical, education and research capabilities in the entire range of the cardiac sciences."

sent a new technology platform for oral and systemic delivery of molecules with important therapeutic biological activities.

They are stable phospholipid-divalent cation precipitates composed of simple, naturally occurring materials. Their unique multi-layer structure is a large, continuous, solid lipid bi-layer sheet rolled up in a spiral, with no internal aqueous space. Therefore, the interior of the cochleates is essentially free of water and resistant to penetration by oxygen. The structure remains intact, even though its outer layers may be exposed to harsh environmental conditions or enzymes. This includes protection from digestion in the stomach.

The partners hold nine U.S. patents, two Australian, and one issued in the major European countries.



Susan Gould-Fogerite, PhD, and Raphael Mannino, PhD



Prestigious Fellowship for Tom Denny

The researcher began his career at New Jersey Medical School in 1983. He's now learning the political "ropes" in Washington and simultaneously managing a multi-million dollar federal appropriation to set up a vaccine reference lab at NJMS. **HOMAS N. DENNY, MSc.** assistant professor of pathology, laboratory medicine and pediatrics at NJMS, was one of seven health professionals named Robert Wood Johnson Health Policy Fellows for 2002–2003 by the Institute of Medicine (IOM) of the National Academies. The fellows are all midcareer health professionals working in academic and community-based settings and were chosen on a competitive basis from nominations.

For three months starting in September, the researcher participated in an orientation designed to familiarize fellows with the public-policy process and government health and biomedical research activities. Denny spent full days learning about current health issues, federal health and research agencies, principal congressional committees active in health affairs and major healthinterest groups.

In December, the fellows moved on to part two of their orientation—organized by the American Political Science Association in conjunction with its Congressional Fellowship Program—to give them a broadened perspective on the range of public-policy issues and the political process. During this time, they interviewed for their work assignments in the offices of senators and representatives in Congress and the executive branch. Denny began working with the U.S. Senate Committee on Health, Education, Labor and Pensions on January 6. His first assignment was to work on a global HIV/AIDS bill, followed by biodefense, and vaccine compensation/liability legislation. As staff to the committee, he works closely with its members to get legislation passed.

Denny, who is also director of the Center for Laboratory Investigation at NJMS, has studied host defense mechanisms in response to tumors and infectious diseases for 20 years. He has served on a number of committees for the NIH-NIAID Division of AIDS as part of the HIV clinical trials program. In 1997, he received a NIH HIV Innovative Vaccine Grant award to study a new method of vaccine delivery. He has authored and co-authored more than 70 peer-reviewed papers.

Denny has also been active in his home town, serving on the Cranford Board of Education, the Cranford Township Committee and as mayor.

In response to the terror attacks of 9/11, Denny established a study on UMDNJ's Newark campus to assess immunologic memory/responses in individuals who had previously received smallpox vaccinations. He is currently analyzing interim data from the study. His next venture will be to set up a reference laboratory at NJMS to support NIH trials for smallpox vaccine and potential vaccines for anthrax and other agents.



Curriculum Changes for NJMS

insideinformation

HINK QUICK: Can you recall three critical points presented during the last fact-driven lecture you attended? If not, take heart. Research indicates that you are more likely to retain material learned in an interactive environment than passive learning in lectures.

Alex Stagnaro-Green, MD, the new associate dean of curriculum and faculty development at NJMS, joined the administration in September, 2002, and has been working to develop and implement a new curriculum by August 2004. His responsibilities also include reviewing the present curriculum to make sure that the school is in compliance with the Liaison Committee on Medical Education (LCME). The LCME is charged by Congress with the accreditation for medical schools in the U.S. and Canada, and has 125 standards all medical schools must meet.

"Different students learn best with different technologies, and certain topics ought to be taught through one modality versus another," explains Stagnaro-Green, who believes in an eclectic approach. "Instead of relying heavily on any one technique, a medical school curriculum must incorporate numerous teaching tactics: lecture, small group, case-based, computer-assisted, and simulated patients." A school wide curriculum retreat was held in January, and more than 100 faculty, students, and administrators participated.

Medical school is a first step in a lifelong journey for the professional. "What we teach will have a lasting impact," he says. "We want to make sure that our graduates are not only well versed in the medical knowledge of 2003, but also "We have a wonderful opportunity and an awesome responsibility to recast the curriculum and learning environment which will shape the physician of the future." Alex Stagnaro-Green, MD

have the skills, intellectual curiosity, and passion for learning to ensure their academic development throughout their careers." To accomplish this, students must be active participants in the learning process and acquire skills they can use forever.

Stagnaro-Green's 3 p.m. session on the endocrine system in "Introduction to Clinical" for 14 second-year students is just one model of the new curriculum already being put into place. In room B-617C of the Medical Science Building, there are no wrong or right answers, just a developing story line for hypothetical patients. Students sit around a wide table taking turns as they read aloud, asking questions and considering case history details. In fact, one of the scenarios concerns an anxious med student who has lost her appetite and is exhibiting other disturbing symptoms. Is it stress? Is it an eating disorder? Could she be sleep-deprived? Is it her thyroid? As more details are offered and the narrative reaches its diagnosis, the case becomes clearer and so do the intricacies of hormones and biochemistry. This woman has Graves disease. Following this, the entire class visits a patient in the hospital who presented with syncope and severe hypocalcemia. During the course of this patient interaction, students became aware of the complex interplay between medical, interpersonal and societal factors which brought this man to University Hospital. These medical students also get a sense of the curricular shifts and interactive learning in store for NJMS.

Streamlining Emergency Care

n terms of timeliness and customer service, emergency departments often earn bad marks. Providing stellar medical treatment quickly in an unpredictable environment poses enormous problems.

But Ronald Bruce Low, MD, MS, believes we should borrow some tricks of the trade from businesses where speed and uniformity of results is crucial. "Computerization is the key," says the newly hired vice chair of surgery and chief of emergency medicine at University Hospital (UH). "Tracking systems used by companies like Federal Express and McDonald's enable companies to meet the needs of their customers. We need to automate an individual's trip through the ER by improving staff access to patient information, ultimately allowing the patient to receive treatment faster."



Low has extensive Level I trauma center experience, coming from Kings County Hospital in Brooklyn and the State University of New York at Brooklyn, where he served as vice chair of the department of emergency medicine. His plans for UH include starting an emergency medicine residency program.

Since the majority of UH's admissions and follow-up appointments result from emergency room visits, improving customer service is essential. "Patient representatives on staff will act as liaisons between the physician and family members,



updating them on the status of their loved ones, assisting with parking issues or even helping to find a pharmacy in the area," says Lowe.

As a Level I trauma center, UH's emergency department is one of the busiest in the state with more than 61,000 visits annually.

New Jersey's Virtual Defense

Tower

EW JERSEY HAS A POTENT NEW MEANS

OF DEFENSE in any potential terror strike using biological, chemical or nuclear weapons. Medtower's Biodefense Knowledge Platform, called INFORM, is likely to become New

Jersey's preferred biodefense information site. The INFORM system is currently available in a scaled-down form at http://inform.medtower.com.

Launched by UMDNJ's Center for Biodefense at NJMS and Medtower, a company that builds Internet-based information systems aimed at targeted audiences, INFORM provides customized content prepared by experts in the field. Among the NJMS content specialists for the site are: biological experts David Alland, MD; Nancy Connell, PhD; William Halperin, MD, DrPH; and Peter Wenger, MD; chemical expert Steven Marcus, MD; response expert Brendan McCluskey, MPA; and radiation expert Lionel Zuckier, MD.

The site posts both daily updates and almost-instantaneous "alerts" and "bulletins" as needed, as well as covering many topics in depth. Material is provided for three levels—the basic (for the general public) is accessible to anyone. Individuals wanting access to the advanced level (for physicians and other healthcare providers) or that for emergency responders will need to register or send an e-mail to the site's manager, and their credentials will be verified.

Also available are educational modules and "expert moderator discussions." Current presentations posted on the Web site include: "Biological Weapons: the Agents and the Threat," "Medical Virology: An Introduction," "Smallpox: An Overview," and "Surveillance and Risk Communication: A Primer." •





Stephen R. Baker, MD

The Full Body Scan Debate: Pros, Cons and Other Cons

HE INTERPLAY BETWEEN the public demand for medical innovation and the introduction of new technology is usually characterized by a dynamic disequilibrium in which wants and resources are often out of sync.

For example, the seemingly achievable cure for a common cold still eludes us. On the other hand, the pharmaceutical industry should be congratulated for introducing powerful drugs that cure a whole host of conditions. These collective achievements have been gained under governmental scrutiny, and with notable exceptions such regulatory efforts have been successful.

In stark contrast, manufacturers of advanced imaging equipment are not subject to the same intense federal inspection and oversight in the United States as the pharmaceutical industry. In fact, nowhere is the tension between public expectations, entrepreneurial expedience and incomplete scientific verification more acutely felt than in the emerging arena of CT (computed tomography) screening. The amazing recent improvements in this technology have made it possible to obtain a comprehensive visual assessment of the body through the generation of narrowly spaced images, painlessly rendered in only a few minutes. CT screening has captured the attention of many individuals eager to know as much about their innards as possible. Screening computed tomography is touted by its adherents to bypass a preliminary visit to a physician. It is so diagnostically incisive, advocates maintain, that the requirement for a physical examination or lab test is obviated because a screening CT can provide manifest evidence of a tumor, an abnormal calcification or an arterial bulge.

No wonder the publicity about CT screening centers is convincing to the worried well. Yet, is this innovation all to the good? It would seem so, according to the testimonials of celebrities who tell the world that their screening exam found a treatable condition before it was too late. Or is there more to this issue?



Colon cancer is the second leading cause of death from cancer in adults over age 40. In most cases, it occurs with the transformation of an initially benign polyp which becomes malignant as it grows beyond one centimeter in diameter. If such polyps are removed when still small, the likelihood of colon cancer is markedly reduced. In a traditional colonoscopic examination, first visual identification and then polyp extirpation can be performed at the same time. As the procedure is often painful, it is most often done under sedation. Screening CT, supporters say, can also discern polyps between 0.5 and 1.0 centimeters in diameter. If none are seen, then a traditional colonoscopy need not be performed.

However, the jury is still out about whether CT colonography is as effective as conventional colonoscopy for the detection of small polyps. The coexistence of feces is one problem, the common presence of numerous diverticula is another. Until definitive proof of CT colonography's efficacy is established, one should be wary about relying on it as the only examination to perform as part of an every 5 to 10 year surveillance for early-stage large bowel cancer.

Cancer of the lung is the most common lethal malignancy in the Western world. Screening CT can certainly find small nodules in the lung. And once detected, a thoracotomy can be performed to remove these tiny tumefactions with the ultimate benefit of making the initially asymptomatic patient cancer-free.

Yet, we do know that a thoracotomy is not necessarily an innocuous procedure. Many benign granulomas appear on CT identical to minuscule cancerous nodules. In individuals who were previously infected by tuberculosis or histoplasmosis, such nodules often remain as a legacy. Thus, a thoracotomy for such patients would be an unnecessary intrusion. What we do not know is the growth rate of lung cancers. Do some stay small and others grow even though all look the same under the microscope? Currently, a multi-center study is underway to answer questions about incipient bronchogenic carcinoma. Until the results are in, one cannot be sure that CT screening creates more mischief than benefit.

The rationale behind calcium scoring

of the coronary arteries is that the presence of calcium salts in the walls of these vessels indicates that the patient, even one who has not experienced chest pain, is at heightened risk for a cardiac event. To be sure, it seems plausible that there is such an association. Yet is it

Why is the **public** so **infatuated** with CT screening? One reason is that a negative screening CT conveys a sense of **immortality.**



An image from a full-body, non-contrast screening CT study. The kidneys are outlined by fat on either side of the spine and the aorta is calcified.

actual? Many studies have suggested that it is not the hardened vascular coat that presages an abrupt arterial occlusion but rather the presence of a soft intimal plaque that is more apt to ulcerate and precipitate a luminal blockage. Even more recent refinements in CT technology have now allowed us, with an intravenous injection of contrast material, to not only observe the calcified vessel wall but also the lumen itself. In effect we can do a virtual coronary arteriogram without invading the arteries directly.

Whether this further advance will be confirmed as effective is still unknown. but it has distinct abnormalities over simple calcium scoring. Moreover, it may also replace diagnostic cardiac catheterization for the recognition of coronary artery disease. The noncontrast CT scan limited only to vessel wall calcification has not yet been proven to be related to a propensity for coronary occlusion. Moreover, with newly realized achievements in CT instrumentation, calcium scoring is probably obsolete with respect to cardiac assessment, because the interior of coronary arteries can be viewed with a noninvasive CT test.

We come now to total body screening. Unlike the other three types of CT evaluation in the asymptomatic individual, there has been no attempt to undertake prospective blinded studies to gauge its efficacy. What does this test assess? In essence, it is a "fishing expedition" looking at all organs in the chest and abdomen for the signs of a tumefaction or an arterial bulge before symptoms ensue. The fact that it entails an unfocused search should not automatically render its dismissal. After all, big fish are sometimes caught in fishing expeditions. So, why not do it? Actually, it is highly unlikely that anything will be found of significance with respect to the saving of a life or even identifying a treatable lesion.

Before proceeding with the assessment of its possible value for each organ under scrutiny we must acknowledge the relevance of the iron laws of testing. When the prevalence of a condition is low, most tests will be truly negative. Of the few that will be positive, most will be falsely positive. Even if the test is

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CHANGING THE COURSE OF

he campaign has been quietly gathering momentum. A small army of stroke specialists is now in Newark to put a stop to the number three cause of death and the leading reason for disability in the United States. "Stroke is life-threatening and 30 percent of people who develop one, die. But quite apart from that, we accept disability from stroke too easily. It really wrecks somebody's future and creates havoc in families. Even physicians don't have the empathy or insight into this. We have the treatment for this," says Patrick Pullicino, MD, PhD, New Jersey Medical School (NJMS) neurosciences chair. Generating millions of research grant dollars, NJMS and University Hospital (UH) have recruited neuro-interventionalists, neurologists, stroke-intensivists, laboratory and clinical researchers, and support staff to help win the race. Within UH, interventional neuro-radiologists and cardiologists are also joining forces to change the course of strokes and improve chances of survival and recovery without disability.

AT THE ACUTE STAGE

S tep into the cerebrovascular angiography suite at UH where the speed stroke demands will send you flying to the center of a patient's brain. According to the National Institute of Health's (NIH) guidelines for acute ischemic stroke, there is a "golden hour" of rapid identification and treatment essential to saving lives. The NJMS-UH team has done this in half the time recommended by the NIH and with more accuracy.

A stroke occurs when blood flow to an area of the brain is interrupted, cutting off oxygen and nutrients to the tissue (ischemic), or when a vessel breaks and spills blood into the surrounding cells (hemorrhagic). Both kinds of stroke create a cascade of biochemical disasters that call for the fastest response possible because the longer brain tissue remains under attack, the more likely the person is to die or suffer serious side effects. If there is one message about stroke that has been hammered repeatedly to physicians and broadcast to the public, it is this window of treatment opportunity: from zero to three hours for intravenous (IV) tPA (tissue Plasminogen Activator). What isn't being stressed is that IV tPA is only one possible answer with limited use. To receive IV tPA, patients must meet strict criteria and candidates are frequently excluded. There are new generations of thrombolytic drugs to open clogged vessels as well as neuroprotective agents under investigation. And in the hands of skilled neuro-interventionalists, some of the miniature mechanical tools that can be placed in arteries-snares, guidewires, catheters, stents, lasers, and neuro-jets-can stage miracle recoveries in minimally invasive procedures. Because of advanced-before, during and after-medical protocols, only a comprehensive stroke center offers real options of survival without disabilities. Paralysis, pain, cognitive, language and emotional deficits aren't every stroke victim's fate.

Jeffrey Farkas, MD, assistant professor and chief of interventional neuro-radiology, worries that too often the standard ER approach to acute ischemic stroke is old medicine. Five years ago, the treatment for every stroke was IV tPA. However, "not

and the

BY MARYANN B. BRINLEY

every patient with a stroke can be approached along one algorithmic pathway. A stroke is actually a host of multiple different disorders. The reality is that you won't find out what's happening to your patient, pinpoint the exact problem, tailor the treatment and do the right thing without delay, within that important window of opportunity, unless you get to a comprehensive stroke center," says Farkas.

Meanwhile, the unique combination of clinical and research expertise on the Brain Attack, or BATeam, has moved beyond the mean, cutting their door-to-drug response on occasion to 15 minutes and doubling the window of time for some patients. The word among BATeam members is that patients in the local Newark catchment area get better treatment for stroke than people living in Manhattan.

Farkas points to his computer and quickly opens images of brains to illustrate successes. Here's an 88-year-old woman who came in three hours after stroke symptoms began and walked out soon after with all of her faculties intact. Here's a 48-yearold police officer who arrived symptomatic and in the back of a squad car. He walked out of the hospital a week later. Here's someone who was 12 hours out, Farkas says. Instead of using tPA, "I opened the artery by advancing a little wire and opening a balloon. See the tip of my catheter. We saved the patient from a drug that could cause him to bleed anywhere in his body." Designed to unclot blood, intravenous tPA can also trigger bleeding elsewhere in the body. "Watch those arteries filling in," Farkas says, pointing to his computer screen. "Now, you can see an area of brain damage but this patient did very well," he adds. By restoring blood flow and oxygen quickly, collateral vessels can take over. "We can turn a bad stroke into a very recoverable one." Every stroke patient is different, however. Depending upon where in the brain the stroke has occurred, warning symptoms can range from paralysis to a full spectrum of sensory and motor difficulties. Thus, to see someone acutely ill with a severe stroke one day and then better the very next is "amazing," he admits. "I've had patients who



Jeffrey Farkas, Charles J. Prestigiacomo, and Adnan Qureshi (clockwise from top)





couldn't move their arms or legs, who were having severe strokes and were just very sick and sympto-

matic, walk away from the table and play tennis the next week." Charles J. Prestigiacomo, MD, assistant professor, Department of Neurological Surgery and Radiology, with specialties in cerebrovascular and endovascular surgery, explains, "The technology in the field of embolization has finally caught up with the ideas." Following the lead of cardiologists who have been opening clogged vessels in the heart and other areas of the body for years, "We manipulate catheters, going up inside blood vessels to take care of problems. We bring catheters to places in the vascular tree in the brain where we just couldn't go before." Being able to speed right to the area of blockage intraarterially can open that NIH window of survival wider than the zero to three hour recommendation because blood flow will begin almost immediately, rescuing cortical tissue from potential neurological damage.

In the angio suite designed for cerebrovascular events, windows along one wall and multiple computers above, behind and in front, allow observation of all the action. More than 10 members of the BATeam—techs, interventional neuro-radiologists, anesthesiologists, nurses, physician assistants—who are ready for strokes 24 hours a day, seven days a week, wear protective lead aprons and vests as well as more traditional surgical garb. Banks of computers display nearly automatic threedimensional images of the vascular anatomy of the male patient on the other side of the windowed wall. What's inside his head does remind you of a tree. This patient has a large, probably congenital, arterial-venous malformation (AVM) and while a stroke didn't bring him to UH, it could have. Seizures and episodes of losing consciousness led him here even after another hospital said nothing much could be done.

The simple use of a computer mouse will turn the tree upside down, inside out, slowly twisting it 360 degrees. By applying a

substance similar to "crazy glue" in specific arteries, the vascular specialists will stop what Farkas calls "a big hose draining blood out of his brain." The images are clear and allow for a look at the AVM, but also permit the physician to scan for other areas of blockage, clots, aneurysms, infarctions or blood that has spilled into brain tissue. "If you can't see it, you can't treat it," explains Farkas. Ischemic strokes, caused by blockages in the vessels of the brain or possibly in the carotid arteries, can be interrupted and ended quickly to save brain cells. If the stroke is hemorrhagic, the cause must be quickly identified and neurointerventionalists can do this. Picking the right patients for the right procedures is key. "You're on a subway system. As long as you know which way to turn and where to get off, you can get anywhere in the brain today," Farkas explains. From a puncture in the femoral artery in the groin, the approach will be up past the heart, through one of the carotid arteries in the neck and right up into the brain, in a minimally invasive technique.

The speed in this race to open a clogged vessel causing an ischemic stroke and reperfuse the nearby tissue, to stop the bleeding in a hemorrhagic stroke, to fix an aneurysm with a stent or coil, or to administer the newest generation of thrombolytic medication directly to the area affected instead of flooding the entire bloodstream intravenously, is faster than ever because of high tech tools. Farkas and his team work closely with industry representatives in designing and testing devices. Imaging modalities are also key. An initial CAT scan can quickly rule out hemorrhage or a brain tumor causing stroke-like symptoms and may even show areas that are in danger of dying but still salvageable. Catching a stroke about to happen, but before damage shows up on the scan, is a coup the BATeam treasures. "This is the most complex anatomy that exists and what we are doing with our equipment is building blood vessel maps right off CAT scans. We started in 1996 at Massachusetts General Hospital. While some literature about CT-Angiography (CT-A) has appeared, not many people are really familiar with the procedure. Current medical literature is now mixed between CAT scans and MRIs, which can be good, but CT-A makes more intuitive sense," says Farkas.

CT-A has become so useful for stroke that it replaces traditional angiograms and MRIs. Even Prestigiacomo was surprised by the reliance on CT-A when he arrived last summer after 11 years at Columbia University College of Physicians and Surgeons. Before any procedure, angiography used to be the gold standard for diagnosis, but Prestigiacomo says, "We can take patients straight to the OR with CT-A and it shows me all the anatomy I am supposed to see." BATeam members work staggered shifts to cover their unit around the clock. Minutes after a page by EMS, other mimicking conditions are ruled out, and the type of stroke is determined, "We are ready to go," explains Michael Lee, angio and X-ray technologist. In the case of an acute ischemic stroke, "We use a local anesthetic and the patient, who is conscious, feels no pain from the procedure." Fast-flowing jets of saline solution at the tip of the catheter and the pumping action of the body's own bloodstream speed the trip.

Inside the angio room, imaging equipment can move along ceiling tracks. Cabinets of devices, long guidewires, catheters and coils for mechanical clot disruption or retrieval and cerebral drug delivery are along one wall. At center stage beneath more computer monitors, the patient is draped in plastic. His body may be nearly invisible on the table but not his brain or the vascular system of highways which feed it. "Embolization has changed how we do AVMs," Prestigiacomo explains. "I always embolize first. You can turn a 12 to 15 hour operation into a 6 to 8 hour procedure and though it's still challenging, it's not the blood bath that it used to be." This man will wake up in good condition, go home in two days and return for further surgery in a few weeks.

Linda Foggie, angiotech supervisor, explains, "Ours is the only hospital around with multiple views of the patient—AP (anterior/posterior) and lateral—at the same time," as well as three dimensional. This AP monitor, a futuristic, big white arc, can swing panoramically around the patient to catch images from inside his head at every angle. "Old cerebral angiograms



Linda Foggie, Mike Lee, and Andrea Hidalgo (clockwise from top)



used to take three to four hours and then diagnostic took two to three hours more," she recalls.

What has pushed UH past the standard stroke medical response is this marriage of radiology and neurology. "The ability to accomplish results so fast takes technology and teamwork," Farkas says. "For years, our team has been led by Andrea Hidalgo, MD, a stroke neurologist, who is still a front-line person. She meets the patient, quickly excludes all other conditions, consults with the family and stretches her responsibilities long into treatment."

As for Farkas, personal experience plays a part, too. As a 24year-old medical student, he recalls, "I watched my grandmother collapse from a stroke. She died even though the EMS arrived within minutes." Back then, there was nothing anyone could do for her. "It was a quick and probably painless way to die, but I always felt that she had more to give me. So now, I spend my time navigating the blood vessels of the brain and spinal cord. Stroke is the most rewarding thing that I could do."

DOWN THE **RESEARCH** ROAD

n the back of a 10 page packet of New Jersey Health Department statistics showing the sad reality of stroke in the state and a belt of even higher numbers for the Newark area, Adnan Qureshi, MD, quickly sketches a brain under attack. A neurologist and researcher trained in both stroke and endovascular work, Qureshi has just arrived from the University of Buffalo Medical School to head the fast-growing stroke unit.

BATeam leaders, like Patrick Pullicino, MD, PhD, and Abutaher M. Yahia, MD, University Hospital's new director of neuro-critical care for stroke (who is also from Buffalo), call Qureshi a stroke pioneer.

With pen in hand, he points to the core of primary cell death being deprived of oxygen (anoxia) because of a thrombus in a vessel. Here's the penumbra, or surrounding tissue, in danger of dying from a secondary wave of toxic chemicals being released by the brain's own cells.

"This cascade of events within the brain is so damaging," he explains, "and we are trying to understand these processes which start immediately in a stroke and can continue for many hours." Brain cell injury will result from this disruption in blood flow at the core. There may be no way to save those first cells at the center from dying within three to five minutes and becoming non-functioning, necrotic, fluid-filled cavities (infarcts). However, just outside that dead zone, this penumbra

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may be salvageable for hours. Yet, without increased blood flow or some form of protection, in a cruel trick of natural brain chemistry, the circle of penumbra cells will come under attack by over-excited amino acids, such as glutamate, in the brain itself. The same supportive neurochemicals, which once carried communication signals and defended against infections and trauma, will turn and kill the normal, neighboring tissue. Cell membranes burst, fill with water and start to trigger brain swelling, the number one cause of death in the first week after a stroke.

Research and clinical teams have been asking questions about the best ways to protect this penumbra. Along with mechanical intervention to reperfuse brain tissue, are there other ways to keep it alive? Antithrombotics prevent formation of blood clots. Antiplatelets decrease clotting capability in blood and so do anticoagulants. To dissolve clots, recombinant tissue plasminogen activator (rtPA), a genetically engineered form of tPA, which is made naturally by the body, was first used in 1996. The bad news: "If you look at the numbers, 58 percent of patients, despite receiving tPA in the recommended window of opportunity, still die or end up with severe disabilities. So there is a lot of room to improve treatment modalities," Qureshi says.

What combinations of medication and delivery technique will improve the odds of preventing death and disability from stroke? (Someone in the U.S. dies every 3.3 minutes from stroke and, for those who survive, the range of frustrating disabilities can be so difficult that suicide becomes a concern.) Most thrombolytic medications employed now for IV or intra-arterial rescue are second generation drugs (citocoline, dizocilpine, nimodipine, tirilazad and others) and improvements on the original rtPA. "We now have approval for clinical, experimental use of third generation thrombolytics," Qureshi says. A thrombus, or embolism, is made of two components: blood cells called platelets and fibrin strands which hold it together. "Thrombolytics only act on the fibrin strands, but what about the platelets?" Qureshi asks. "This is something we've been thinking about all along. If you are going to push clots with only one kind of medication, the platelets are totally unaffected, which may explain why most of the blood vessels are not opening. The third generation of thrombolytics break the fibrin and also have a strong antiplatelet capability."

Another area under investigation is the role of neuroprotectants (calcium channel blockers and other inhibitors) which might extend the window of viability for that penumbra. So far, the trials have failed but, according to Qureshi, the neuroprotectants were unable to get to the area of the brain suffering damage because passage was blocked, so no one really knows whether or not they might work.

And on the top of Pullicino and Yahia's research agenda lists: what is the connection between stroke and the heart? "I'm very interested in developing this new area of neurology and cardiology," Pullicino says. "People doing stroke feel that cardiac care belongs to the cardiologist and cardiologists feel that stroke areas belong to the neurologists." Not thinking across departmental lines is clearly a mistake because stroke is a major complication of heart failure. Investigating these borderlines between the heart and the brain, Pullicino's team has just kicked off a multi-center \$30 million trial from National Institutes of Health (NIH) to study 2,860 patients with cardiac heart failure. "We're going to have 70 sites in the United States and Canada," he says. Cardiac heart failure (CHF) causes 250,000 deaths a year and 75,000 strokes. Among 50- to 59-year-olds, CHF jumps the risk of stroke up four times higher than average.

THE COST OF STROKE

- Total cost of stroke to the United States: estimated at about \$43 billion per year
- Direct costs for medical care and therapy: estimated at about \$28 billion per year
- Indirect costs from lost productivity and other factors: estimated at about \$15 million per year
- Average cost of care for a patient up to 90 days after stroke: \$15,000*
- ► For 10% of patients, cost of care for the first 90 days after a stroke: \$35,000*

Percentage of direct cost of care for the first 90 days*:

initial hospitalization = 43% rehabilitation = 16% physician costs = 14% hospital readmission = 14%

medications and other expenses = 13%

Courtesy of the NINDS * From "The Stroke/Brain Attack Reporter's Handbook," National Stroke Association.

Abutaher M. Yahia, Brian Greenwald, and Patrick Pullicino (clockwise from top right)

IN RECOVERY

A soon as the patient hits the ER, your critical care work has set in," Yahia explains, emphasizing the importance of a comprehensive neuro-intensive care unit (ICU) at all stages and especially in recovery. "You can have a wonderful intervention team quickly fix every blood vessel—intra-arterially, intravenously or mechanically—but that will account for only 30 percent of the patient's chances for survival." Outcome is still going to be determined by what happens afterward.

Blood pressure, oxygen, infection control, body temperature, nutrition, and even management of fluids are critical. Meanwhile, protocols for care may differ from standard ICU strategies. "You need a neuro-intensivist in charge," says Yahia, a trained neurologist who is also an endovascular care specialist. By becoming the patient's advocate, a single neuro-intensivist can manage critically ill neurological patients better.

In the case of a stroke, that calls for special knowledge. For example, stroke patients routinely suffer from cardiac suppression or dysfunction, and while these heart problems may be transient, experience has shown that the need for oxygenation is greater than normal in such complex situations. In addition, "Someone with a stroke cannot communicate easily. Swallowing or breathing coordination can be difficult. Mental status is low." A patient with a small hemorrhagic stroke and impaired swallowing can develop pneumonia, then sepsis and end up in the hospital for weeks.

Swelling after a stroke is a common phenomenon and the first 36 to 72 hours are critical. When the brain swells, it causes pressure on normal tissue and can lead to further cell damage. The main goal for that initial period is to keep normal parts of the brain from being damaged, and to prevent the situation from becoming life-threatening. To get victims safely past the swelling, medication can lower metabolism and oxygen requirement. Hypothermia, or reducing body temperature, also helps. Research on hibernating animals, who exist for months in states of hypothermia, show that slowing the metabolism of the brain and blood flow can give some injured tissue time to recover. However, don't picture a body packed in ice. Yahia and Qureshi have used a catheter with cooling power in the large distal vein. Inserting this special catheter into one of the veins in the groin and sliding it up to the abdomen, they have managed to lower internal temperature and maintain it that way for 24 to 48 hours. Results are encouraging. In critical situations when medical management has been exhausted, temporarily removing part of the skull to allow tissue to protrude is a life-saving option.







Part of every recovery plan must include a comprehensive stroke evaluation workup. "Patients are

going home only to return with another stroke," Yahia laments, explaining the high occurrence of recurrent attacks in the first weeks. Approximately 25 percent of people who have strokes will have another within five years, and that risk is greatest right after the first. Releasing a patient from the ICU, without first determining where the clot originated is an error made too often in hospitals not designed for comprehensive stroke management. "Of all strokes, the carotid artery occlusive diseases contribute 10 percent and the intracranial occlusive diseases contribute another 10 percent. But in the remaining 80 percent of acute ischemic strokes, there are cardiac sources of embolism." Relying only on a carotid Doppler and an MRI scan of the brain, and finding nothing, means "the investigation has not been thorough enough," Yahia says.

"Look at this," he says. The image on his computer of the beating heart of a patient who suffered a stroke earlier, clearly predicts danger. Anyone can see the waxy, gelatinous buildup of plaque right there on the screen. Like a swatch of fabric caught and waving in a stream of water, the fatty deposit actually flutters precariously with each beat of the man's heart. "A piece probably broke off to give him the stroke, but notice how much more is still there on his aorta. Eighty percent of stroke patients have other sources of emboli, and the simplest diagnostic thing that I can do is probe and check."

Under conscious sedation and local anesthesia, using a transesophageal echocardiogram, cardiac sources of clots can be identified. Yahia takes only 10 to 15 minutes with a tool that has been on the market for 10 years. In a few hours, a plan to modify stroke risk factors (hypertension, heart disease, diabetes, blood cholesterol) as well as lifestyle indicators (smoking, alcohol consumption, exercise, diet) can be based on more than

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Through the LOOKING GLASS BY EVE JACOBS

Lenses, lasers, implants and restorative drops are sometimes not a quick fix for aging, or otherwise failing, orbs. While saving sight is often complex, restoring lost vision can be the stuff of research and miracles. As diabetes rates soar and millions of baby boomers make the challenging trek through their 50s and beyond, the incidence of failing eyesight is surging and better answers are desperately needed.

The successes of blind heroes and artists (among the better known—Homer, John Milton and Stevie Wonder) are notable, but for most, thoughts of a sightless life are daunting. A better grasp of the cellular and genetic underpinnings of visual loss is starting to translate into new treatments; and researchers are also developing novel methods for eye repair. Pioneering the state-of-the-art and helping to set the direction of the science are driving forces of academic programs, among them the state's sole residency training program for ophthalmologists at the NJMS Institute of Ophthalmology and Visual Science.

"AS SICK AS AN EYE CAN GET"

The eye is a target for traumatic injury, which can set off a chain of inflammatory responses that produce additional massive damage. Among the aspirations of ocular immunologist David Chu, MD, is halting the cascade of once irreparable impairment inflicted by chemical and thermal burns to the eyes. His newest tools include amniotic membrane and stem cells transplanted to the site of the wounds. What he calls "no magic bullet," nevertheless can stop encroaching blindness and even restore sight.

Take the case of a factory worker whose eyes were accidentally splashed with ammonia. Repeatedly washing out the chemical was the logical first, second, even third step taken by his local hospital. But Chu says that the chemical stripped off corneal surface cells needed to maintain clarity of vision. A wash-out may not suffice as treatment in severe cases. Furthermore, Chu explains that the inflammation caused by chemical or thermal burns is hard to control with drops and pills because of the delicate nature of the ocular surface, leaving scars and seriously impaired vision, which can develop over weeks and months following the initial injury.

Amniotic membrane, which helps to protect fetuses in the womb, improves tissue-healing without scarring. Amniotic membrane is derived from placentas after children have been born. It has been used in burn care for decades, but was not introduced into Western ophthalmology until fairly recently. The use of amniotic membrane as a base for limbal stem cell transplants is a novel idea for repairing scarred corneas. Limbal stem cells—which give rise to new corneal cells—are depleted following certain kinds of eye trauma and disease.

"A combined amniotic membrane and limbal cell transplant is a delicate surgery with complex follow-up," Chu explains. "It's only the beginning of a long battle. This is as sick as an eye can get."

When the cells are taken from the patient's healthy eye, there is no problem with rejection and the chances for success are high. But when the other eye is too badly damaged, cells come from a cadaver or a living relative, and tissue rejection is a significant problem. "It's treated much like a solid organ transplant," says Chu. "The key to keeping the cells alive is to closely monitor the immuno-suppression."

No magic bullet, but when it works, it may appear to be

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nothing short of a miracle. One of Chu's patients—an engineer whose entire body was burned in a chemical accident—had visited many ophthalmologists over a period of years, but was told nothing could be done to restore his sight. His left eye was completely scarred, and the only thing he could see was if the light was on or off. With a limbal cell transplant (cells were donated by his daughter, who is in her 20s) combined with the amniotic membrane transplant, the patient's vision in the left eye was restored to 20/50, and he is now undergoing plastic surgery.

Chu, also a member of the department's Section of Corneal Wound Healing and Ocular Immunology, has been trained in the use of chemotherapy for suppression of the immune system and frequently treats manifestations of autoimmune diseases such as lupus, Crohn's disease, pemphagoid, and rheumatoid arthritis—on the cornea and other visible portions of the eye. Administering chemotherapy, such as cytoxan and methotrexate, for these conditions is not mainstream ophthalmology, he says, but can save sight.

INVENTORS AT WORK

I laucoma can generally be remedied with drugs that either decrease the amount of fluid in the eye or increase the amount of fluid flowing out of the eye. In both cases, the aim is to reduce fluid pressure build-up, which can damage the optic nerve. When drug therapy doesn't do the



trick, lasers are often used to improve drainage and lower pressure.

What happens when the usual methods don't work? According to glaucoma specialist Robert D. Fechtner, MD, 50 percent of glaucoma surgeries fail within five years. That has been his incentive to explore a better way.

Just this past fall, he pulled off a first in this part of the world. A young deaf woman was losing her sight to glaucoma and was not responsive to the standard therapies. Using a 2 ml metal tube fashioned by an Israeli company that manufactures cardiac stents, he implanted the "drain" into her eye employing a needle. The tube passes from the front of the eye (the anterior chamber) into the space between the eyeball and the skin-like covering of the eye (the subconjunctival space). The excess fluid in the eye flows out through the miniature tube, lessening pressure. The young woman's vision has been restored and the outlook is very promising.

Fechtner enjoys wrestling with the unusual problems. He is part of an inventors' alliance, which includes optical technology specialists Richard Greene, MD, PhD, and Gordon A. Thomas, PhD, both at NJIT. Their immediate aim is to devise a means for diabetics to test blood sugar without piercing their skin. The team's concept involves a small device—to be integrated into an eyeglass lens—that uses a type of laser light that will change color when it hits glucose molecules in the aqueous portion of the eye. The device will function as an artificial pancreas, taking constant readings of the patient's glucose levels in the aqueous humour, and triggering insulin release from a pump as needed. The work is underwritten by a grant from the Pfeiffer Research Foundation.

The team also has a \$296,362 grant from the National Medical Technology Test Bed to develop two devices to improve glaucoma monitoring. The "self-tonometer" uses a technology called piezo-spectroscopy to allow glaucoma patients to measure their own intra-ocular pressure (IOP) by touching the device to their eyelids. Currently glaucoma patients have their pressure measured three to four times yearly by an ophthalmologist. More frequent readings will mean less damage to the optic nerve should there be a rise in intra-ocular pressure. Patients will be instructed to call their physician if their IOP rises.

The second device looks and functions like a miniaturized movie camera. For use by physicians, it records "moving pictures" of the inside of the eye, zooming in on areas of the retina damaged by obstructed blood flow. The "retinal mapper" also records changes in the color of the retina, an early indication of glaucoma and other eye diseases. In addition, it will cor-

LEARNING ABOUT DIABETES FROM THE EYES OF THE NEW JERSEY 725

iabetes is disproportionately prevalent and severe among African Americans, and can trigger other complications that are killers. Medical retina specialist Monique Roy, MD, has been following a group of 725 African Americans with Type 1 diabetes since 1993. The participants—now numbering 600—ranged in age from 10 through 70, with the majority being in their 30s, when the study began.

Roy has uncovered some information vital to her study population. Her data shows that African Americans with Type 1 diabetes, particularly women, have more diabetic retinopathy (especially vision-threatening retinopathy) than whites with Type 1 diabetes; and that African American women with Type 1 diabetes are 12 times more likely to die early than African American women in the general population. African American men with the disease are at 6.1 times greater risk of dying early than their peers without the disease, and those with a small amount of kidney disease when they were first seen were more likely to die of renal complications than women. "It looks like many African American men with diabetes start with renal disease," she explains. "It's also what kills them—so protecting their kidneys early on is very important."

Roy says that researchers have looked at the environmental predictors of disease progression, and now need to figure out the causes. "How can we use genes to predict complications?"

relate patterns of colors inside the eye with changes in heartbeat, allowing the inventors to hone in on a relationship between heart rhythms and eye pressure, perhaps yielding new insights.

A NEW STRATEGY FOR "EYE STROKE"

Some evidence suggests that "eye stroke" calls for much the same plan of action as a "brain attack," and time is as much of the essence. More sophisticated diagnostic equipment and a coordinated team approach can frequently halt the progressive cascade of harmful events, radically changing the outcome of a stroke from bleak to bright.

Like a brain attack, eye stroke (central retinal artery occlusion) results from a blocked blood vessel, but its effects are typically localized at the retina and can result in permanent blindness. "It cuts off the blood and oxygen supply to the retina and causes blinding visual loss in the affected eye," says neuro-ophthalmologist and orbital surgeon Roger Turbin, MD.

The newest generation of radiological equipment, that quickly produces clear views of the affected area, and a highly skilled stroke team that is available around the clock mean that complex procedures can be performed shortly after the patient reaches the hospital. In the case of a clot in the ophthalmic artery, a very thin catheter is threaded through the femoral she asks. The retina specialist says that frequently those with Type 1 diabetes have few complications in the first 10 years of their disease. Then some will turn a corner for the worst, and others will continue to do



fine. "We need to determine who has turned this corner after 10 years and try to find out why."

Roy says her research is now focusing on genetic factors, and the interaction between genes and the environment. Investigators are finding that there are many subtypes within the large group of those afflicted with diabetes. There is a small percent of African Americans who have an acute onset of the disease during adolescence or their 20s, become insulindependent, and then go into remission 10 to 15 years later, no longer needing insulin.

The researcher is participating in a world diabetes genetic consortium. The focus is to gather as many families as possible who are affected by diabetes to aid in the hunt for the diabetes gene(s). Roy explains that the researchers would like to collect blood not only from the person with Type 1 diabetes, but from his parents, and affected and unaffected siblings.

artery in the leg, to the carotid artery, and finally into the very narrow ophthalmic artery, so that a clot-dissolving enzyme, tissue plasminogen activator (tPA), can be applied through the catheter to dissolve the clot. The procedure restores ocular circulation and can be highly successful at restoring sight if it is done within four hours of the eye stroke.

Turbin says that the team treated two patients recently who arrived after the prescribed interval—one within eight hours, the other within 24 hours—and that both improved, although vision loss could not be entirely reversed.

New surgical techniques also restore sight in idiopathic intracranial hypertension (pseudotumor cerebri). If left untreated, the condition can lead to visual loss or blindness. Medication generally works to lower cerebrospinal fluid pressure, says Larry Frohman, MD, director of the division of neuro-ophthalmology, who treats many patients with the disorder. But continuing loss of vision may necessitate orbital surgery. According to Turbin, a new variation of the surgical technique called optic nerve sheath fenestration creates a "window" in the sheath-like covering of the optic nerve with better surgical exposure, which permits less tissue trauma and a chance for improved visual outcomes. The optic nerve sheath serves as an escape hatch for the cerebrospinal fluid in the region of the nerve governing vision,

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and by creating an escape conduit, preserves and/or restores lost sight.

Turbin says that there is also a constant influx of very severe trauma that is extremely challenging for the surgical team at University Hospital. The eye trauma surgeons are part of that team. "You need aggressive techniques to put a person back together after high speed car crashes, and penetrating gun and knife injuries, many of which cause serious damage to the eyes," he comments. "These kinds of challenges improve our abilities as thinkers and as surgeons."

LASIK AND BEYOND

The sight restoring Excimer laser wowed doctors and consumers alike when it came on the scene with much fanfare in the mid-'90s. "The initial application of the laser to eye care was a giant leap," says Peter Hersh, MD, professor of ophthalmology at NJMS and the lead author of the clinical study which led to FDA approval of the Excimer laser for correction of nearsightedness in 1995.

LASIK uses the Excimer laser to sculpt the cornea's surface "much like sandpaper works on wood," explains Hersh, who is director of refractive and corneal surgery. LASIK is done under a "corneal flap." In PRK, the cornea is reshaped following the removal of surface epithelial cells. PRK is used if a patient has a thin cornea or problems with the surface of the cornea. In the new LASEK procedure, the epithelial cells are preserved while the laser treatment is done without a LASIK flap.

Over the years, laser technology has become "more dependable and safe," according to Hersh. Wave front technology adapted from astronomy—provides more accurate measurements to use in programming the laser with the hope of improving results still more and minimizing side effects.

Hersh's fascination with new devices is still leading him into uncharted territory. His was one of five sites nationwide selected to perform trials on conductive keratoplasty (CK), which uses radiofrequency energy, rather than lasers, to reshape the cornea for the treatment of farsightedness. The procedure does not require either a surgical flap or removal of surface epithelial cells, and can be done in 5 to 10 minutes per eye in the physician's office. Hersh presented the CK clinical study results to the FDA last year, and the procedure was recently approved by the FDA. This procedure is designed for patients over 40 years old who have farsightedness and need reading glasses.

"We now have a variety of procedures and technologies to use, and we can suggest the treatment option best for that person," he says. "We are also better at picking and choosing who Diabetic macular edema (above).

will do well, so the range of people who can be successfully treated is greatly increasing."

DEVELOPMENT IS SO FAST THAT THE ABILITY TO BE AT THE FOREFRONT OF NEW TECHNOLOGIES IS VERY IMPORTANT."

Hersh feels that the speed at which laboratory and clinical research findings move into the realm of patient care is one of the greatest advantages of the academic setting. Leading the trials that establish the safety and efficacy of new technologies and devices means more experience and so more skill in handling the complex cases safely. He also does about 120 corneal transplants each year and is research director of the New Jersey Eye Bank, which he says is one of the best in the country.

"Technological development is so fast that the ability to be at the forefront of new technologies is very important," he concludes. "We are helping to lead the development of technologies to restore sight."

THE NJMS INSTITUTE of ophthalmology and visual science

ealing with the unusual, the exceptionally complex, the seemingly unresolvable, the horrific, and disorders and injuries requiring a multifaceted team are what an academic medical program is charged with. Teaching the next generation of eye specialists the state-of-the-art and inspiring in them a devotion to the science demand patience, skill, knowledge, lots of hours, many hands, and more than a few flashes of brilliance. Among the cast:

Marco Zarbin, MD, PhD, Chair • A visionary (no pun intended) who has built up the academic department and led the group to the top of the charts in record time. A retinal surgeon specializing in age related macular degeneration (AMD), his research focuses on sight-restoring therapies for those in the later stages of the disease. During the last eight years, his laboratory has made major progress in transplantation of retinal pigment epithelium (RPE) cells. His research goal for the department is "to cure blindness." He's the author of the CME module on age-related macular degeneration following this story.

Larry Frohman, MD, Vice Chair • A highly respected neuro-ophthalmologist, his clinical focus ranges from the effects of neurological, infectious, and immunological systemic diseases on vision to unexplained visual loss. He has established such a reputation for treating sarcoid, vasculitis, and autoimmune disease affecting the optic nerve and retina, that other medical schools refer patients to him. His interests and expertise also extend to development of Web-based systems for physicians to share clinical resources on neuro-ophthalmological and rare conditions. He is currently President-elect of the North American Neuro-Ophthalmology Society.

Paul Langer, MD • An ophthalmic plastic and reconstructive surgeon who is a valued member of the University Hospital trauma and skull base surgery teams, he heads up the only residency training program in the state for ophthalmologists. The residency recently earned its five-year accreditation with no citations, a feat achieved by only 10 percent of such programs in the U.S. This formerly "unrecognized gem" is attracting the best and brightest, who value: their exposure to a high volume of complex medical and surgical cases; the commitment of the faculty to residency teaching; the high standards of practice in all subspecialties; and the wide spectrum of clinical and laboratory research. Graduates say it is the top program in the tri-state area and among the most elite in the country.

Neelakshi Bhagat, MD • A medical and surgical retinal specialist, and a graduate of the residency program, she is a shining example of the caliber of the training here. When she completed her residency in 1998, there were no women in the surgical retinal field in New Jersey. Twelve-to 14-hour days are the norm. Currently, she spends 25 percent of her day teaching, 55 to 60 percent on patient care, and 15 to 20 percent on clinical research, with some overlap between areas. She is hoping to spend even more of her time teaching. As part of the hospital's trauma surgery team, she now works side-by-side with her role model, Marco Zarbin.

Paul Lama, MD • Associate Director of the Glaucoma Service, Dr. Lama is one of the few glaucoma specialists in the U.S. who is also an internist certified by the America Board of Internal Medicine. His unique medical background has enabled him to become an authority on the systemic complications of medicines used to treat glaucoma.

Ronald Rescigno, MD • Director of the Uveitis Service, Dr. Rescigno is also a principal investigator in the Studies of the Ocular Complications of AIDS, a multicenter study funded by the National Eye Institute. Uveitis refers to a number of infectious and noninfectious diseases that affect the portion of the eye termed the uveal tract. Uveitis patients also include those with diseases such as sarcoidosis, which is particularly prevalent in northern New Jersey.

STROKE

Continued from page 17

general recommendations and carry the weight of concrete evidence: a picture of a heart ready to deliver more clots to the brain.

This stroke recovery plan also includes early rehabilitation. "Within the first day a stroke patient is admitted," explains Brian D. Greenwald, MD, Director of Trauma Rehabilitation, "the team is consulted to hasten recovery of swallowing, speech, motor and cognitive impairments." Though the brain does have great ability to relearn and change (plasticity), rehabilitation therapy is such hard work that specialists like Greenwald are finding important roles for mood altering medications, such as stimulants or anti-depressants. "Psychopharmacology can be used to maximize a patient's participation."

In the best of all possible worlds, the strange, debilitating results that can mar life after some strokes wouldn't happen at all. Recovery would not need to incorporate consideration of paralysis (hemiplegia, hemiparesis, dysphagia), cognitive deficits (apraxia, agnosia), lost language abilities (dysarthria, aphasia), emotional trauma or pain. Neuro-radiologist Jeffrey Farkas, MD, couldn't agree more. Think about the actor Kirk Douglas, he says. "Douglas wrote a book about pulling himself up by the bootstraps after a stroke, and having to relearn everything. The agony of his recovery was so bad that he wanted to kill himself. Had he come here," Farkas poses hypothetically, "and there is no 100 percent certainty ever in life, of course, but, had Kirk Douglas been admitted to University Hospital in that window of opportunity, he wouldn't have had very much to write about."

Contributing researcher and writer: Jill Spotz

FOR PHYSICIANS ONLY!

1-866-27-STROKE (7-8765) is a hotline for physicians' use only, answered by the University Hospital's Emergency Medical System's (EMS) dispatch center and designed to expedite patient transfers from other hospitals or directly from the field in acute stroke situations.



Marco A. Zarbin, MD, PhD • Chair, Department of Ophthalmology

Age-Related Macular Degeneration: Update on Pathogenesis

CHALLENGE TO ALL PHYSICIANS is keeping current in an environment of constant change. There is more information available, but less time to read it. So, to ease the burden, each issue of NJMS Pulse will offer a CME module (worth one credit hour) by a notable NJMS specialist/researcher.

If you would like credit for this course, or just want to finish reading the article, go to the online address on the bottom of page 25. The purpose of this program is to review the cell biology of age-related macular degeneration, and address questions about AMD pathogenesis. The course is designed for all physicians.

Overall Learning Objectives

Upon completion of this course, participants should be able to:

- explain the difference between changes to the eye caused by aging and those caused by age-related macular degeneration (AMD);
- understand the five general concepts relevant to the cell biology of AMD;
- recognize the opportunities for early therapeutic interventions and the potential for later, sight-restoring therapies.

For more information on the Center for Continuing & Outreach Education (CCOE), visit their Web site at ccoe.umdnj.edu.

Accreditation The UMDNJ-Center for Continuing and Outreach Education (UMDNJ-CCOE) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education (CME) for physicians.

UMDNJ-CCOE designates this educational activity for a maximum of one category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

Disclosure In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, all program faculty are required to disclose to the activity participants;

1) the existence of any financial interest or other relationship with the manufacturer of any commercial product or provider of commercial services that relates to the content of their presentation material; or commercial contributors of this activity that could be perceived as a real or apparent conflict of interest.

2) the identification of a commercial product that is unlabeled to use or an investigational use of a product or device that is not vet approved.

Marco Zarbin, MD, PhD, reported no significant relationships.



SUMMARY

Age-related macular degeneration (AMD) is the leading cause of blindness among persons over age 55 years in the United States and Europe. Five general concepts relevant to the cell biology of AMD are identified. First, AMD involves aging changes plus additional pathology (i.e., AMD is not just an aging change). Second, in aging and AMD, oxidative stress causes retinal pigment epithelium (RPE) and, possibly, choriocapillaris injury. Third, in AMD, RPE and choriocapillaris injury result in a chronic inflammatory response within Bruch's membrane and the choroid. Fourth, in AMD, RPE and possibly, choriocapillaris injury and inflammation lead to formation of an abnormal extracellular matrix. This abnormal extracellular matrix causes altered diffusion of nutrients to the retina and RPE, which may precipitate further RPE and retinal damage. Fifth, the abnormal extracellular matrix results in altered RPE biology leading ultimately to atrophy of the retina, RPE, and choriocapillaris and/or CNV growth. In this pathogenetic sequence of events, both environment and genetics can alter any given patient's



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susceptibility to the disease. At this time, it seems likely that multiple genes play a role in determining susceptibility to and resistance from AMD. Manipulation of environmental variables (e.g., antioxidant levels) provides an opportunity for early therapeutic intervention. Gene and/or cellular therapy provide an opportunity for later, sight-restoring treatment. Implicit in this characterization of AMD pathogenesis is the concept there is linear progression from one stage of the disease to the next. This assumption may be incorrect and different biochemical pathways leading to geographic atrophy and/or CNVs may operate simultaneously. Additional experimentation with in vitro and in vivo models will prove or refute the concept of linear progression and will establish the identities of the various pathways that lead to CNVs and geographic atrophy.

INTRODUCTION

Age-related macular degeneration (AMD) is a condition(s) characterized by accumulation of membranous debris on both sides of the retinal pigment epithelium (RPE) basement membrane. Clinical manifestations of drusen (Figure 1), atrophy of the RPE/choriocapillaris, RPE detachment, and choroidal new vessel (CNV) formation (see figure 2 on Web) occur after age 55. In the U.S., AMD is the most important cause of new cases of blindness in patients over 55. Usually, visual loss is confined to loss of central vision with preservation of peripheral vision. Decreased central vision results in loss of the ability to read, to drive, to recognize faces, and, in many cases, to live independently. Approximately 30 percent of patients over the age of 74 have some clinical sign of AMD, and six milFigure 1 • Confluent soft drusen. A. Fundus photograph demonstrating confluent, large soft drusen with overlying foci of RPE hyperpigmentation. These drusen resemble an exudative RPE detachment. RPE hyperpigmentation is a sign of photoreceptor degeneration. B. Late phase fluorescein angiogram of A demonstrating uneven hyperfluorescence and drusen staining. Uneven hyperfluorescence may signify variations in the degree of Bruch's membrane permeability in the macula.

lion Americans have the disease. Over 80% of cases of severe visual loss result from the growth of abnormal blood vessels, CNVs, under the macula. Approximately 600,000 Americans have AMDinduced CNVs.

WHAT IS THE MACULA?

The macula has no histological counterpart, but by convention, most ophthalmologists use the term to refer to the central portion of the area centralis. The area centralis refers to a specialized area of the retina that is ~5500 µm in diameter, comparable to the size of the head of a nail, and contains two or more layers of ganglion cells. The fovea is ~1500 µm in diameter and is a central depression in the macula. The fovea contains the foveal avascular zone, which is ~500 µm in diameter, and the central foveola, which is ~350 µm in diameter. The term macula lutea ("yellow spot" in Latin) derives its name from the presence of a high concentration of yellow pigments, primarily carotenoids, in the foveolar area. These pigments (mainly lutein and zeaxanthin) have antioxidant activity, filter out photic damage-causing blue light, and may be derived from the plasma.

The foveola contains specialized photoreceptors. Photons are captured by the photoreceptor outer segment, a columnar structure consisting of stacks of membranous discs containing the photopigments. The foveola provides high acuity (20/10-20/20) vision necessary for reading, sewing, performing surgery, etc. The extrafoveolar part of the macula provides less sharp vision, ranging from 20/40-20/200. For photoreceptors to function properly, they must be in intimate contact with the RPE. The photoreceptors and RPE exchange nutrients and other materials. The choroid is a vascular layer of the eye wall interposed between the sclera and RPE, and its capillaries, termed the choriocapillaris, provide the blood supply to the RPE and photoreceptors. The RPE is separated from the choriocapillaris by a thin layer of collagenous connective tissue called Bruch's membrane (see figure 3 on Web). Bruch's membrane is composed of an inner and outer collagenous zone separated by an elastic lamina. The basement membranes of the RPE and choriocapillaris line the inner and outer aspect of Bruch's membrane, respectively.

When the macula malfunctions, people experience blurring or darkness in the center of their visual field. AMD affects both distance and near vision, but it results in total blindness only rarely. The condition may hardly be noticeable in its early stages. Sometimes only one eye loses vision while the other eye retains good vision for many years. Some common ways vision loss is detected are: words on a page appear blurred; a dark or empty area appears in the center of vision; straight lines appear distorted.

To finish reading the article and/or take the test, log on to http://ccoe.umdnj.edu/ ccoe/online_learning.html

Supported in part by Research to Prevent Blindness, Inc., the Eye Institute of New Jersey, and the New Jersey Lions Eye Research Foundation.





> ON THE CUTTING EDGE OF COCHLEAR IMPLANT TECHNOLOGY

BY MARYANN B. BRINLEY

Jed A. Kwartler, MD, NJMS '83, likens cochlear implant surgery to "installing the light switch that allows someone to turn on a light." Kwartler is a clinical associate professor in otolaryngology at New Jersey Medical School (NJMS) and a University Hospital (UH) staff surgeon. "It's a small thing to be able to do. But, for a deaf patient, it means all the world. To take someone from the isolation of non-hearing to hearing...well, that is very satisfying."

Close your eyes, he suggests. Keep them closed. "We can continue talking and you are still connected to the world."

Now, put your fingers in your ears. Don't take them out. Try to have a conversation.

"Being deaf can cut you off from the world," Kwartler says. "Even when Helen Keller was once asked if she had a choice of being blind or deaf, she chose blindness."

Sometimes, his patients are as close to home as the Alumni Office on B Level in the Medical Science Building where coordinator Dianne Mink had anguished over her diminishing ability to hear for years. No one knew exactly why this was happening (an auto-immune factor? the residue of childhood ear infections? a genetic connection? hereditary link? hormones? stress?)—and they still don't. Gradually, she went from one hearing aid to two and then suddenly, not even the newest, most sophisticated device helped. That was last year.

"Nothing!" she says, "No improvement. I'd be panicked. Your whole way of life changes. People think you are normal because you look normal but you are out of touch. That isolation is the worst. To be honest, I wanted this cochlear implant so badly that I was just fine, not nervous at all, on that morning of surgery in June," she says. Her three grown daughters "were bananas!" she laughs, "and wondering why I would do this to myself. Yet, the situation had become so stressful and even in terms of connecting to them, I just feel this is a miracle I needed."

Like a complicated melody in a symphony of sounds, a cochlear implant is a complex medical solution with a rich, rocky history and success doesn't begin or end with the surgery. The brain itself may have to rewire the lost or missing neural circuitry which interprets sound waves, not to mention all the high-tech auditory computer mapping required for noise to be understood. "Surgeons get too much credit," Kwartler says. For a patient like Mink, a master student in her own aural recovery, teamwork and timing are certainly factors which promised the best of what this cutting edge technology can bring.

Consider this: Mink even owes her current ability to hear that ice maker in the freezer section of her refrigerator, the directional turn signals clicking in her car, and her daughters' voices on the telephone, to a host of medical scientists dating all the way back to Allessandro Volta, the Italian physicist in the 1880s who invented the electro-magnetic battery, among other things. "Volta," Kwartler explains, "took his electrodes, stuck them in his own ears and created a low level electrical charge. He described the sound as something like gurgling porridge. Obviously, the technology languished a little," he jokes, before emerging in the 1950s in Europe and Australia.

According to the Food and Drug Administration (FDA), approximately 70,000 people worldwide now have cochlear implants and this technology is evolving rapidly. Like the dot

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matrix printers which once produced all of our computer printouts, these auditory nerve prostheses are metamorphosing into clearer and clearer possible answers for 28 million deaf Americans. Advances in our understanding of the central auditory system in the brain, how inner-ear hair cells grow, live and die, as well as breakthroughs in neuroscience, molecular biology, biochemistry and even genetics have revolutionized "what is really a team process," says Kwartler.

As a medical student at NJMS, Kwartler always knew he wanted to be a surgeon and found that microsurgical techniques and miniaturization satisfied the technical demands he loved. After specializing in ear, nose and throat (ENT) medicine, he went west for a fellowship at the House Ear Clinic and Institute in Los Angeles under the legendary Bill House, MD. "I was his last clinical fellow before his retirement and very fortunate to be under his tutelage. Cochlear implants were first performed there in the early 1960s and Dr. House, a godfather of this technology, invented and tried more things than you can imagine."

Kwartler returned to New Jersey in 1990. "One of the reasons we waited to start this intense program at NJMS is that the technology had improved dramatically." While hearing aids amplify sound, cochlear implants, even the early, simplistic versions, aimed to compensate for damaged or non-functioning parts of the inner ear. Every implant system has an internal receiver, or surgically implanted element; an externally worn processor with its battery; and a headpiece with a microphone and transmitter. The processor, worn either behind the ear or on a belt at the waist, is a mini-computer that takes sound information, codes it into electrical signals, transmits the signals to the implanted receiver behind the ear and then sends them further down to an electrode coiled within the cochlea itself.

Most deaf people have lost some or all of the four parallel rows of cochlear hair cells (so-called because of the hair-like cilia on these auditory nerve fibers). Without those 30,000 auditory nerve fibers to get excited enough to change the acoustic energy of sound into electrical energy, the brain can't hear.

"Sound waves are just like ripples on water," explains Kwartler. Normally, these pressure waves vibrate down the ear canal, to the ear drum with its tympanic membrane, and to the three small bones of the middle ear (malleus, incus and stapes) which pick up the vibrations and pass them on into the snail shaped cochlea of the inner ear. "The electrode in an implant, which has been snaked down inside the cochlea, is electrically stimulating the surviving nerve fibers," he explains. Beyond the cochlea, research is also investigating the role of a large bundle of nerve tissue, called the efferent system, which takes the information into the brain to make real sense of the sound.

Uncoiled, the cochlea would break down into discrete sections designed to discern various vibrational energies by frequency. Sound, especially speech, naturally covers a wide frequency, but the early implants had an electrode that delivered only a single, stimulating current and didn't target discrete areas. Thus, the implant user would be alerted to some sound but unable to discriminate speech. "We could show that the patient even identified tones at a normal level but couldn't understand a single word or sentence," he explains. "Technically, the operation would be a success but functionally, the computers weren't powerful enough to code all the information delivered by speech." What scientists have learned is that high pitches are picked up near the base of the cochlea while lower sounds are detected at the apex. Meanwhile, different formulas for trying to determine which was the most important information to deliver to each patient were debated as well as placement of the electrode array. The analogy, Kwartler points out, was like playing Wheel of Fortune. (The TV game show challenges players to guess a word or expression without seeing every one of its letters.) "What 'letters' do you need to know to figure out speech? We couldn't put all the 'letters' into the processor but with the growth of faster and faster, and smaller and smaller computers, we are able to include more information. Our understanding of what patients need to hear, as well as what they can live without, has grown as well as the speed of these processors."

Produced by two licensed manufacturers in the U.S. (Cochlear Ltd. and Advanced Bionics Corp.), cochlear implant

WHAT CAUSES HEARING LOSS?

The reason for Dianne Mink's deafness was never determined. However, experts do know that there are two kinds of hearing loss: *conductive* (caused by middle ear infections, traumatic head injury or birth defects such as otosclerosis) and *sensorineural* (due to heredity, genes, aging, exposure to loud noise or ototoxic medications.)

THE EAR

systems are similar in design, with processors designed to dispatch more than a single shot of stimulation inside. Meanwhile, on the outside, a small ear level microphone can filter, analyze and digitize sound, emphasizing pitch, loudness and timing cues. Audiologists also work with the implant patient for months after surgery to map, set and repeatedly tune these very personal listening programs. They are like musical instruments, Kwartler suggests. And, as this new world of sound travels inside the brain, the neural network is stimulated, reviving, or perhaps, in the case of a baby born deaf, even creating hearing memory. Like a muscle, the brain grows only in response to stimuli. While the architecture of stored memory is still an unsolved mystery, the truth is: in absolute silence, your sensory brain forgets how to hear.

"Remember those first calculators?" Kwartler asks. They were huge by comparison to today's multi-functional minis. Miniaturization in circuitry and science have brought us many smaller, faster devices. "Ideally, the cochlear implant battery should last longer (not just 12 or 6 hours). Ultimately, we'll offer a totally implantable system, like a heart pacemaker."

In the future, physicians may also place devices behind both ears, instead of choosing the ear which has been deaf for the shortest period of time. Clinical trials for bilateral, or double, cochlear implants are taking place and Kwartler's Ear Specialty Group is taking part in the pediatric bilateral implant program, sponsored by Cochlear Ltd. For the moment at NJMS, "We tend to go with the ear which may have some residual hearing and have more surviving nerves to stimulate. That can be hard for patients who fear losing what little bit of hearing they have left because of the surgery itself."

At 9:30 am on Thursday, June 20th, Mink harbored no fears about losing the bare minimal residual hearing in her left ear, the side chosen by Kwartler to implant. She had lost her right ear's function seven years before. After hearing in the left ear first began to decline and aids didn't work, she failed to qualify for surgery. That was in the fall of 2001 and by March, she was back in Kwartler's suburban Springfield office to plead, "You have to test me again." This time, she qualified.

To become a candidate for a cochlear implant, adults must have severe hearing loss in both ears, limited benefit from hearing aids, no medical contraindications, and a strong desire to be part of the hearing world. For children ages 12 months to 17 years, physicians look for lack of progress in auditory skills, supportive families with appropriate expectations, and ask that children be enrolled in educational programs emphasizing auditory skills. "For children who are born deaf, this is a long learn-



ing process," Kwartler says. Controversy within the deaf community about whether cochlear implants are appropriate for babies born deaf, or even if the inability to hear is really a handicap, also exists. Kwartler says, "Some parents expect children to start talking right away." That won't happen, of course. "You have to think of that surgical date as a hearing birthday."

Though the brain is capable of an enormous potential for understanding sound patterns at birth, babbling always has to come before comprehension or real language skills. New tools are being built into some implant processors, like the Nucleus 24, which takes some of the guesswork out of mapping a preverbal human being. With Neural Response Telemetry (NRT), signals are sent to and from the hearing fibers in the cochlea and measure the response. The child isn't asked to provide verbal feedback.

As an adult with a rich hearing history, Mink would be a different story, of course.

Surgery is done on an outpatient basis and can last from two to three hours. "It's no riskier than a tonsillectomy, among the most common procedures done in the U.S.," Kwartler explains. The existing dangers all relate to the structures a surgeon could run into on the way to the cochlea. Though reports last year at a conference in Europe raised the specter of bacterial meningitis following cochlear implant surgery, those risks were dismissed after an investigation and FDA probe. "What's changed is that patients are now being advised to get vaccinated before surgery for pneumoccocal bacteria which causes meningitis," he adds. "The odds now of a patient getting this are about zero."

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The surgery itself, and the approach into the skull, are used for a variety of other problems. Kwartler, one of only a few physicians in New Jersey who perform this procedure, explains that a small area of the head behind the ear is shaved and a curved incision about six to eight centimeters, or three and a half inches, in length is made to expose the mastoid. This bone behind the ear is hollow, like a corrogated cardboard box, and after the top to the box is taken off, Kwartler and his team go deeper. Along the way, they identify structures like the sigmoid sinus, the vein that drains blood out of the head, the lining of the brain which is just to the north of the mastoid cavity, and the floor of the temporal lobe where balance canals sit. During surgery, "you can see them, as well as the nerve which is responsible for movement of the face and cheek sensations. Once we have identified these structures, we know we are in the right spot. We can see the end of the cochlea, an area called the round window, through which the sealed membrane of the cochlea can be entered."

After carving a little seat for the tiny receiver into the mastoid bone and making a tiny—about a millimeter in size opening into the basal, or first, turn of the spiral cochlea, Kwartler slides the electrode into this snail-shape structure. Then, "you're done," he says. "Just coil it down and close up."

Though dizzy and in some pain, Mink was in the recovery area by 11 am and back home by 5 pm with a little help from her children. She stayed close to bed all weekend with her "head bandaged and wrapped in a turban. I don't like to be on painkillers and I remember being in tears at one point. I had no sense of balance." Her instructions were to drink fluids, take Tylenol and not wash her hair. As Kwartler explains, "There is nothing we would be doing in the hospital except mothering her and a patient can get better mothering at home."

By Sunday, Mink felt a little better. Then, energized and anx-

Jed A. Kwartler, MD, and audiologist Christine Hoffman (center) fine-tune Dianne Mink's cochlear implant.

ious to reclaim an ordinary life, "On Tuesday morning, I got into my car and drove to the supermarket to buy blueberries," she says. "The store is only a half mile from my house but I felt as if I had accomplished something." A week later, she went back for a check-up but cochlear implants are never turned on until healing occurs, which can take up to five weeks.

Mink's appointment was set for July 18 and the audiologist Christine Hoffman, her "angel," would do the honors. Kwartler believes that the hardest part of making a

cochlear implant work comes alongside the audiologist and lies with the patient, who must be persistent and fight the urge to turn away from all the sound. Some users describe the first experiences to a clamor of noise, like a pinball game, or the middle of a raucous gambling casino. What is sometimes called "cross chatter," as electrodes jump between fields, can also occur. For sure, implants still can't absolutely restore normal hearing.

Yet, "it was amazing," Mink recalls. Having been warned not to expect perfection, "Christine's voice sounded a little like Minnie Mouse but my brain quickly began to readjust and compensate." She could hear even better after months of dedicated speech processor mapping, practice, and hours of testing. Voices are clear though all three of her daughters still sound the same on the telephone. Music is a bit of a mystery. The beat in a Gladys Knight concert is clear but the melody is missing.

"I have a tiny toggle," she explains from her desk in the Alumni Office, gesturing to the side of her implanted ear, "that can be boosted up or down." The site of the implant incision was sore for awhile and until the fall, she couldn't sleep with her head to her left side. Designed to last forever, the external parts are taken off when she sleeps. She is also careful in the rain. "You can't get it wet," she explains. "So I wear a hooded rain jacket and always keep that umbrella handy." Otherwise, her life is more normal than it has been in years. She even went to the movies, a simple excursion that had become frustrating.

The buzz of students in the hallway, knocks on the door, and telephones ringing are more than welcome intrusions now that she is back in the hearing world.

When two surgical roads appeared in his career path back in the 1980s, Kwartler's instinct to go small has carried no small payback. "I am really able to positively impact people's lives," he says. And Dianne Mink would be the first to agree. highly sensitive and specific, when the prevalence is low the false positive issue cannot be minimized.

njmsvoices

Furthermore, full body CT screening does not take advantage of the added diagnostic capability of intravenous contrast material. Thus, to find a tumor one can only search for a bulge or a hole or a calcification, because without contrast, we cannot assess the sometimes crucial factor of heightened or diminished vascularity.

With that in mind let us first consider the chest. Full body CT screening is incapable of diagnosing cancer of the esophagus at an early, potentially curable stage. If not the thorax, perhaps the real payoff is in the abdomen. Colon cancer detection requires a colonoscopy, either conventional or possibly virtual. The presence of stomach cancer is assessed endoscopically to inspect the mucosa. It is not readily diagnosed by non-contrast CT. Gallbladder cancer is rare except in individuals at risk for it. Cancer of the pancreas has never been recognized as an incidental finding for which removal of the tumor has resulted in a cure. Characteristically, the onset of symptoms precedes CT recognition and by then it is usually too late to extend life by surgery or chemotherapy. Cancer of the adrenal gland is so rare-only 500 cases per year nationwide-that a CT screening would not be likely to find it. Ninety percent of lymphomas appear with non-Hodgkins histology. In this group of neoplasms the cell type rather than the extent of the tumor is the determinant of ultimate survival. Cancer of the bladder typically comes to attention by the presence of infection or blood in the urine, not by the incidental discovery of a mass. Malignancies of the ovary, if detected very early as stage one lesions, are amenable to cure. However,

CT scanning does not reveal these small tumors. Cancers of the cervix and uterus are diagnosed initially by other means. Primary liver cancer is found predominantly in certain at risk populations. Moreover, even the best imaging tests employing a contrast material protocol can only detect two-thirds to threefourths of cases. Non-contrast CT does not play a role here.

This leaves only renal cancer for which the detection of the malignancy in an asymptomatic individual can be crucial, mandating therapy to effect a cure. Here, too, small lesions have a better prognosis than large ones. Yet, small cancers are more readily seen when contrast material is administered. Furthermore, between ages 40 and 60, the chance of developing a renal cancer is only one in 500 in men and one in 700 in women. CT screening, of course, is not done across an interval but at a particular point in time. In any one year in that 20-year period, the chance of finding a renal cancer by non-contrast CT in an asymptomatic individual is only one in 20,000. Hence, it is much more likely that if a CT screening study suggests the presence of a suspicious lesion it will probably be a false positive. Such a distribution of findings was revealed by a study conducted by a leading promoter of CT screening who evaluated nearly 2,000 patients. Twenty renal masses were noted. The author stated that stone disease and simple cysts were excluded from the renal mass group. Of the 20 lesions, two were cancers and one was an angiomyolipoma. What were the other 17? Undoubtedly, they were not tumors at all, but simulations of masses: in other words, false positives.

By the way, CT screening can also identify and measure an aneurysm of the aorta. This is an important finding, because when small, aneurysms can be resected and the condition cured. However, ultrasonography is a valid competitive test which is inexpensive, readily available and deposits no radiation. Hence, it should be the examination of choice.

Why is the public so infatuated with CT screening? For many individuals the test is in accord with their cherished sensibilities about their bodies, even if both the American College of Radiology and the FDA have stated categorically, that full body CT screening has no scientific value. Americans with means are willing to pay for it because they put great faith in new technology, especially if it is relatively pain-free. Moreover, since a screening exam does not require a physician's referral, it is congenial to the fashionable notion of patient empowerment. Moreover, a negative screening CT conveys a sense of immortality.

There are important psychological factors which have helped screening CT become a burgeoning industry. Consumers have a right to know what they are getting for their money because no third party will support screening. They must pay up front. Some patients will get the assurance that comes with a negative scan. However, that does not mean that they are disease-free. CT imaging will not detect hypertension, hypercholesterolemia and diabetes. And if a positive finding is observed, can a consumer be sure without subsequent surgery that it is really real? Unless all these issues are explained to prospective patients, they should beware that while their wants may be served, they are really being conned.

Stephen R. Baker, MD, is Chair of the Department of Radiology at NJMS.

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New Jersey Medical School

Joseph V. DiTrolio, MD '79

A Message to Alumni

S PAST PRESIDENT of the Alumni Association and founder and editor-in-chief of *AlumniFocus* magazine, I am proud to introduce the first issue of *NJMS Pulse*. We have expanded your alumni magazine to keep you up to date on a broad range of clinical and research developments, professional issues and alumni news.

We are keeping the *AlumniFocus* name for the pages with information of particular interest to NJMS alumni, and I am very pleased to serve as editor of this special section.

I hope you enjoy the new look of the magazine and agree with me that the editorial staff has succeeded in launching a fine publication. This is a joint venture between New Jersey Medical School and the Alumni Association. Your support is critical in helping the Alumni Association fulfill its mission, and we encourage your involvement and participation. Let us hear from you.

In past issues of *Alumni-Focus*, you have heard from me on many topics of importance to physicians. Today I have no doubt that the cost of malpractice insurance tops the list and impacts all of us.

How did this issue reach the crisis stage that prompted a doctor walk-out? I believe the process started more than 15 years ago, when cost constraints were first implemented. At first, it didn't seem like much, but slowly the screws were turned. Fees were cut back and doctors corralled into managed care programs. The supposed carrot was that reduced fees could be offset by increased volume.

Healthcare costs continued to escalate, and doctors contributed to some of these increases. The business of healthcare required a new support system, and the expanding expenses to go with it. As a group, physicians have never been known to be good business managers. As collectable fees have decreased over the years, it was just a matter of time until it would be impossible to practice medicine and make a reasonable living.

Remember, the average medical student graduates at 28 with about \$100,000 of educational debt. Ahead is three to seven years of specialty training before new physicians make a competitive salary and start the kind of life many of their contemporaries did 12 years earlier.

Now physicians face the dramatic increase in the cost of malpractice insurance. Are



increased jury awards to blame? Partly, as I have seen cases with no wrongdoing settled for fear of greater losses. The system that sets fee premiums is terribly flawed. Any physician named in a lawsuit—won, lost or dropped—is considered a risk and subjected to increased premiums. One could win every case and still be priced out of existence. This is wrong and unhealthy for our national system.

Could lawsuits be controlled by requiring prior review? I believe those who advocate the "Certificate of Merit" approach are creating a Catch-22 process. Besides the fact that the MD who signs such a certificate does not have to be board certified or even licensed, if the lawsuit is later found to have no merit and is dismissed, malpractice premiums will still go up.

What about patient responsibility? When a physician diagnoses a serious illness, the patient's first reac-

News of special interest to NJMS graduates

tion is often, "Why didn't you find it sooner?" If a surgical procedure does not have the same successful outcome reported on the six o'clock news, the patient wants to know, "Who screwed up?" Sure there are some bad doctors. We all do our best to remove them from practicing to protect the public, and I believe we can do better. However, life is a risk, and bad things can happen. Patient expectations have become totally unrealistic, sometimes encouraged by lawyers.

Now we have healthcare costs increasing, physician incomes decreasing and a malpractice insurance crisis that is the straw breaking the camel's back. If we wish to continue to attract the best and brightest to medicine, we must correct the balance.

Otherwise, the system will spiral out of control. Doctors will pass increased costs on to their patients, who in turn will look to insurance companies. Rest assured, changes would be mandated immediately if the general public had to bear this cost.

A Popular Choice

A 30 percent increase in applications for the coming year puts an emphatic halt to a six-year decline at NJMS and far outpaces an anticipated increase nationwide. According to the Association of American Medical Schools (AAMC), preliminary data for 2003 projects a 4 to 6 percent increase next year, reversing a downward trend since 1996.



Applications at NJMS total 2934 compared to 2248 for last year. The largest number of applicants was 4062 for the entering class in 1995. George Heinrich, MD, associate dean for admissions, suggests that the number of medical school applications reflects job opportunities in other areas. "With the fizzle of dot coms and financial services, applicants seem to be considering medical school more seriously again," he notes.

Despite the drop in submitted applications, the AAMC reports that the number of accepted applicants to U.S. medical schools has remained stable at around 17,000 since 1980.

NJMS CALENDAR of EVENTS

SUMMARY OF MARCH EVENTS

March was a busy month for alumni and students alike. **Career Night** on March 4 was a great success, with 35 physicians telling more than 100 students about their professional experiences. The excitement of **Match Day** on March 20 is still fresh in everyone's mind, as the fourth-year students celebrated their successful residency matches.

In our next issue we will share photos of the **Alumni Association Reunion,** which was held on March 29 at the Dolce-Hamilton Park Hotel.

April 3	Exit interview for 4th year students
April 7, 8, 10, 14 & 15	Phonathons
April 24	Residency Fair—MSB Grand Foyer, 5 p.m.
April 26	Parents Day—MSB Grand Foyer, 8 a.m.
May 2	NJMS Awards and Scholarship Reception
May 16	Alumni Lectures Continental Breakfast, 9 a.m. 15th Annual Stuart S. Stevenson Memorial Lecture—MSB-B610, 9:30 a.m. 8th Annual Benjamin F. Rush Surgical Society Lecture—MSB-B552, 11 a.m. 35th Annual Harold J. Jeghers Memorial Lecture—MSB-B610, Noon Rush Society Luncheon—MSB Grand Foyer, 1 p.m.
May 19	Convocation - NJPAC - 2 p.m.
May 21	Commencement - Sovereign Bank Arena, Trenton, NJ, 10 a.m.
June 4	Alumni Association Annual Board of Trustees Dinner Meeting, MSB B515, 6 p.m. All alumni are encouraged to attend.

Alumni Office at 973-972-6864; from outside NJ, call 800-477-7040.

alumnifocus events













A Memorable Evening for 98 Scholarship Recipients

The Annual Alumni Scholarship Awards Dinner October 17, 2002

The SUPPORT AND GENEROSITY of the alumni and friends of New Jersey Medical School has made it possible for the Alumni Association to award 98 student scholarships totaling more than \$130,000. These awards provide financial assistance to students as they pursue their educational endeavors, including summer research positions, externships and international health elective courses.

The following comments are from John W. Katz, MD'75, President of the Alumni Association, NJMS.

THIS YEAR'S ALUMNI AWARDS DINNER was the best ever, the result of careful planning and hard work. The lion's share of thanks and credit goes to the many large and small benefactors whose generosity swelled the funds, and especially to those endowing the 44 Named Scholarships.

The students applied for the awards with a wonderful combination of scholarship, community and medical school service. Need was also a factor in the selection process. The Scholarship Committee reviewed the applications, referring its recommendations to the Board of Trustees of the Alumni Association for their approval.

This year, many donors attended the dinner, and had the pleasure of awarding their scholarships in person. Following the event, all donors received framed photos of their awardees. It was most gratifying for me to announce the names of those who received scholarships and shake their hands, and I believe a good time was had by all.

Scholarships are the tangible results of giving real help to real students. In the months to come, we will be contacting you to give. Pledge help, the need is great. Please consider endowing a Named Scholarship, or even better, endowing a scholarship to last for perpetuity. For further information, contact the Alumni Office at 973-972-6864.

1. Alumni class scholarship recipients

2. Donor Dr. Richard Pelosi'61 congratulates Chirag Badami'03 on being awarded the Dr. Charles Berry Memorial Scholarship.

3. Dr. Louis Amorosa'69 poses with the recipients of the Anna Amorosa Scholarships, Frank Caputo'03 and George Dakwar'03.

4. Sidney Glasofer'03 and Sarah Lubitz'03, recipients of the Dr. Kurt A. Heinrich Memorial Scholarships, received their awards from Dr. George F. Heinrich'72.

5. Richard Agag'o4 is congratulated by donor Dr. Rene Chalom'89. Richard was awarded the Mayer Chalom Memorial Scholarship.

6. Dr. John W. Katz'75, Alumni Association President, presents the Angelo and Theresa Lina Memorial Scholarship to Omar Akhtar'03. Donor: Dr. John Lina'73.

7. Alumni Named Scholarship recipients

Words of Thanks

The Scholarship Committee would like to share just a few of the many heartfelt thank you notes sent by NJMS scholarship recipients to the donors of their awards.

Dear Class of 1963:

The scholarship is significant to me for several reasons: It offers the peace of mind that added financial support brings, and it implies recognition of my dedication to medicine. Most important, however, it reinforces my belief that people are essentially willing to give of themselves for the betterment of our community. Thank you. *Lee Chadrick Chua '04*

Dear Members of the Class of 1971: This scholarship will certainly help ease the financial burden of medical school. My wife and I especially appreciate this scholarship as she is also a fourth-year student at UMDNJ-New Jersey Dental School. As a student, it means a lot to be recognized, encouraged and supported by alumni of NJMS.

Jason Hade '04

Dear Benefactors of the Class of 1983: In a world and time flooded with reminders of how precious life is and how incomparably commendable it is to give, you are an inspiration for your generosity, kindness and the difference you truly make. As physicians, not only do you heal the pain of a broken and afflicted humankind, but you give even more by your example.

Lori Vales '04

Dear Dr. Amorosa '69: You serve an even more special role than simply as a donor; as a faculty member of UMDNJ, you provide something that cannot have a price attached to it—you provide knowledge and training. These gifts are priceless! You truly are a great role model to all of us.

George Dakwar '03

Dear Dr. Alger '64:

I am humbled to receive the Howard and Edna Alger Memorial Scholarship. It is especially rewarding as you have been a part of my medical education since my first days as a student in the seven-year medical program with the College of New Jersey.

Ricky Madhok '03

Dear Dr. Swerdlin '72:

I cannot thank you enough for this scholarship, particularly at this time, when there is the increased financial burden of residency application, interviews and my rotation abroad. By using the scholarship to further my goals of helping children in the U.S. and overseas, I hope I will honor the individuals for whom the gift was named. *Rashmi Shetgiri '03*

alumnifocus PROFILE

JeanMarie Houghton, MD, PhD

Career Times Two



ARNING TWO ADVANCED SCIENCE DEGREES may be the academic equivalent of climbing the Himalayas. Even with the ultimate tools of the trade in hand, achieving the peak is reserved for the most determined.

Yet, at New Jersey Medical School, the numbers of students currently in dual degree doctoral programs is soaring. This is the question that begs to be answered: Are two advanced degrees really better than one?

Why would medical students overworked, short of sleep and cash, and challenged with absorbing an everincreasing load of complex information—find value in pursuing a PhD? Why dedicate more than a decade (seven years of academic studies plus residency training) to graduate education?

To find answers to these questions, you may want to ask JeanMarie Houghton, MD, PhD. She was the first graduate of the physician-scientist program jointly run by NJMS and UMDNJ's Graduate School of Biological Sciences. New Jersey born and bred, she grew up in Edison, graduated from Douglass College of Rutgers University in 1985, and entered medical school that year. "Initially, my goal was to become a good, old-fashioned practicing doctor," she remembers.

After earning her MD degree in 1989, she completed a residency in internal medicine at University Hospital in 1992, serving as chief resident for one year. This was followed by a gastroenterology fellowship which she finished in 1994. With five years of handson clinical experience, she was ready and looking forward—to hanging out her shingle.

But Buzz Johanson, MD, then the

chair of the Department of Medicine at NJMS, noticed Houghton's tenaciousness and spark. He was convinced that not only would she make a great physician, but sure that she had the smarts and stamina to do original research and make contributions to academic medicine as well. He encouraged her to apply for a K11 Physician-Scientist Training Award from the National Cancer Institute and she was successful, garnering a \$440,000, five-year grant. Winning grant funds is a necessary step to proceeding with this program.

"Training physician-researchers is a national trend," comments Jeff Wilusz, PhD, director of the MD/PhD program at NJMS and GSBS. "It's certainly not something we invented here. The NIH and medical schools across the country believe this is important." Forty percent of U.S. medical schools offer NIHfunded dual doctoral degree programs.

Historically, physicians diagnose disease and administer medical care to patients. Biomedical researchers work in



laboratories to study how cells—and their component parts—function and malfunction. The physician-researcher brings the two together—taking observations from patient care to the laboratory for investigation and more quickly "translating" the discoveries of the lab into actual therapies to combat disease. For Wilusz, the reasoning behind the MD/PhD trend is crystal clear. "Dual training means that future research will be guided by the real clinical issues," he explains.

The desire to do original translational research is often the driving force for those committed to the long haul; and there are two distinct roads to get there. The MD/PhD track takes students through two years of medical school, three to four years of PhD training, then two more years of medical school, followed by residency training. Students earn the MD degree after completion of medical school and the PhD either after completion of the PhD training or when they receive the MD degree. The physicianscientist track takes a fully trained physician with an MD degree, and trains him or her to be an independent researcher, culminating in the acquisition of the PhD.

Houghton spent two years in the lab of mentor Harvey Ozer, MD (then the NJMS chair of microbiology and molecular genetics, and currently the NJMS Senior Associate Dean for Research), participating in his investigation of "gene expression in immortal human cells." Meanwhile, she began her PhD studies at UMDNJ's Graduate School of Biomedical Sciences (GSBS). Back to school was her motto: At age 31, Houghton was sitting in the classroom with students 10 years her junior, many of whom had just graduated from college.

"She was a ball of fire—very dynamic," recalls Wilusz. "We had an MD/ PhD program, but no program for physicians who get their research calling later. We modeled the program to fit Jean."

But even for someone so motivated, the terrain was rough. "I hated it my



"I'm very **stubborn**," says JeanMarie Houghton. "If I start something, **I don't let go."** That seems to be the stuff of **success** in **research**.

first year," she admits. "I went from being in charge to being a first year student sitting in a classroom again, and from being relatively independent to working on my mentor's project." She thought of dropping out of the program, but then "it all started to click."

After two years of work in Ozer's lab, she created her own project focusing on the host response in *Helicobacter* infection. "It gave me autonomy and forced me to take charge of what I was doing," she said. How did she finally know she was on the right track for herself? "I'm very stubborn—exceptionally tenacious," she explains. "If I start something, I don't let go. And if I don't get an answer, I'll try 15 more ways." That seems to be the stuff of success in research.

Houghton says the educational process was long and sometimes painful. But she also uses words like "fantastic"

> and "phenomenal" to describe her classes and the faculty, and credits Wilusz with being a great advisor.

He in turn calls her a "pioneer," saying that it takes guts and stamina to blaze the trail. The dual degree programs are flourishing now, with 15 students enrolled and five or more beginning in the fall. "We've made the leap into being a major national program," he says. "The applicants are all high quality and

some have amazing credentials."

Houghton very happily earned her PhD in May 2001 and was recruited to the University of Massachusetts, where she has new grants, conducts research in her own lab with three people working for her, teaches classes, cares for patients and is involved with the MD/PhD program there. "It was all that training that got me here," she states.

Would she do it this way again? "Yes," she concludes. "Getting the clinical training, then the entire PhD training is the best. You get the experience, knowledge and skills of both."

Along the way, Houghton even managed to find the time to marry fellow NJMS alum Kyung Kim, MD, whom she met during her second year of medical school, and to have three children, Nicole, now 7, and twins, Ashley and Amanda, age 5.

alumnifocus CLASS NOTES

THE **1960**S

Daniel D. Cowell, MD'60

resigned as Chair, Department of Psychiatry and Behavioral Medicine (after eight years) at the Edwards School of Medicine, Marshall University, WV. He remains as Associate Dean for Graduate Medical Education, clinician (Professor of Psychiatry) and educator. His wife, Diana, is a hospice social worker and son Dana is at West Virginia University.

Leo M. Pisculli, MD'60 writes that his youngest daughter, Jenny, is entering her 4th year at Ben Gurion/Columbia University School of International Medicine in Beer Sheva, Israel.

George R. Haddad, MD'61 says his son Jerry and wife Rosemarie welcomed twin boys on July 18, 2002.

Gerald S. Levey, MD'61 is in his ninth year as Dean of the David Geffen School of Medicine at UCLA and Provost for Medical Sciences. His wife, Barbara, is Assistant Vice Chancellor for Biomedical Affairs at UCLA and current President of the Medical Society for Clinical Pharmacology and Therapeutics.

Bill Cantor, MD'62 is still practicing otolaryngology after 32 years in Woodcliff Lake, NJ. He has

IN MEMORIAM

Michael J. Auletta, MD'84 passed away on November 7, 2002. Dr. Auletta received an advanced degree from the University of Michigan in 1987 and completed a fellowship in 1988 at the University of California. He was a dermatologist in Freehold, NJ and an assistant clinical professor at the Robert Wood Johnson Medical School Division of Dermatology.

Franklin Charles Behrle, MD passed away on October 2, 2002, in Grantham, NH. Dr. Behrle served as the executive director for Statewide Perinatal Services and Research Center of NJ. He was an associate professor of pediatrics at the University of Kansas School of Medicine and professor and chairman of pediatrics at NJMS.

Humbert L. Riva, MD passed away at the age of 88 on January 21, 2003. Dr. Riva practiced at St. Michael's Medical Center in Newark for over three decades and was the oldest working obstetrician/gynecologist in NJ when he retired in 1998. He was the chairman of obstetrics and gynecology at UMDNJ, held the same position at the Seton Hall College of Medicine in Jersey City, NJ, and was awarded the title of professor emeritus by both schools.

Robert P. Rossbaum, MD'62 died at his home in South Glastonbury, CT on February 16, 2003, at the age of 73. Dr. Rossbaum, an anesthesiologist, was a partner in the Hartford Anesthesiology Association, Inc., retiring after over 30 years of service. He is survived by his wife Elizabeth, children Robert Ross and Kathleen Vella, and four grandchildren.

William E. Sorrel, MD, PhD, president of the Pan American Medical Association, passed away on November 16, 2002. He is remembered as an inspired leader, brilliant psychiatrist, distinguished educator and humanitarian. taken over the Fifth Pathway Medical Student Program at Pascack Valley Hospital, and enjoys teaching. He is also involved in theater, music and grandfathering. Wife Paula is a watercolor artist. Dr. Cantor is in contact with Frank Blackburn, MD, Karl (Bruno) Brandenberg, MD, and Tony Cuccuzzella, MD, all of the Seton Hall Class of 1962.

William J. Carey, MD'62 is enjoying solo, non-HMO primary care and interaction with house staff at Berkshire Medical Center in Pittsfield, MA.

Joan Bender Cracco, MD'63 is Professor of Neurology, Pediatrics, Physiology and Pharmacology and Director of the Division of Pediatric Neurology at the State University, New York Downstate Medical Center and the Kings County Hospital Center, Brooklyn.

Joseph Cudia, MD'63 retired from ob-gyn practice and is active with family, hobbies and travel.

Donald P. Schwartz, MD'63 is retired from the practice of asthma and allergy, except for three hours a week. He resides in Sanibel Island, FL.

Anthony J. Passannante, MD'66 is Director of Nuclear Cardiology at the New Brunswick Cardiology Group. His son,. A. J. Passannante, Jr., MD, is the managing partner of the group, and daughter, Marian Passannante, PhD, is an Assistant Professor at NJMS.

Andre Vanderzanden, MD'68 is still practicing pediatrics. His daughter Jacqueline, in medical school in NY, will also pursue her father's specialty.

Dennis P. Quinlan, Sr., MD'69 was named Vice-Chair of the Department of Medicine at NJMS.

тне **1970**s

Arthur J. Torre, MD'70 received the Sir William Osler Award for excellence at the American Lung Association's "Breath of Spring" Ball on March 23 at the East Brunswick Hilton. He is the first allergist to receive the award. Dr. Torre is also co-chair of the Pediatric Asthma Coalition of NJ.

Peter J. Kurzweil, MD'71, CMD, was named Certified Medical Director in Long Term Care by the American Medical Directors Certification Program.

Richard H. Steip, MD'73 writes that their oldest son, Brian, 28, is a licensed physical therapist in CA, and they were expecting their first grandchild in December 2002.

Robert M. Carvalho, MD'75 is the Medical Director of the Vista del Mar Hospital in Ventura and Harmony Place in Malibu, CA.

Larry D. Gruenwald, MD'75 and Ann Marie Comandatore, MD'90 are partners in a new pediatric practice at 90 Millburn Avenue, Millburn, NJ.

David L. Isralowitz, MD'75 is an Assistant Clinical Professor of internal medicine at NJMS.

Anthony R. Scillia, MD'75 was named Medical Director of the new in-patient MICA Program at St. Clare's Hospital. He is looking forward to helping with the Psychiatric Residency Training Program with his film lecture series, "Psychiatry and the Cinema."

Audrey Kriegman, MD'76 is Director, U.S. Clinical Development and Medical Affairs for Osteoporosis at Novartis Pharmaceuticals Company. **Paul J. LoVerme, MD'78** is Vice-President of the NJ Chapter of the American College of Surgeons.

Richard Stark, MD'79 is now Associate Chief of Staff, Ambulatory Care, VA New Jersey Health Care System.

THE **1980**S

Linda J. Griffith, MD'81 is Medical Director, Mercy Hospice, Springfield, OH.

Frank L. Kane, MD'82 is the first physician from NJ to be elected to the Board of the American Board of Family Practice.

Robert E. Morrow, MD'83 is Chairman of the Department of Psychiatry at the Pocono Medical Center and was appointed to the Board of Directors of the Physicians Health Programs for the Pennsylvania Medical Society.

Allan R. Tunkel, MD'84 wrote an editorial, "Corticosteroids for Everyone with Meningitis?" which was published in the November 14, 2002 issue of the New England Journal of Medicine.

Douglas R. Mailly, MD'85 wrote that he and wife of 4 years, Mande, were expecting twins.

Louis Potters, MD'85 was inducted as a Fellow in the American College of Radiology. A clinical associate member of the Department of Radiation Oncology at Memorial Sloan-Kettering Cancer Center in NY, he also is medical director for radiation oncology at Mercy Medical Center, Rockville Centre, NY.

James D. Murray, MD'86 is in practice as a vascular surgeon at Kaiser Permanente in Baldwin Park, CA and was recently promoted to the rank of Captain in the U.S. Naval Reserves.

Fred Caruso, MD'87 completed 15 years of Army duty and is now founder and President of All American Imaging, P.A., in Fayetteville, NC.

Lauren D. LaPorta, MD'88, a Clinical Assistant Professor in the Department of Psychiatry at NJMS and Chief Psychiatrist for Consultation Liaison Services at Bergen Regional Medical Center, was elected a fellow in the American Psychiatric Association.

Paul Kovatis, MD'89, who practices orthopaedics, was featured in Best Doctors 2002 in "Better Living Magazine." He is Secretary/ Treasurer of the Bergen County Medical Society and FDA clinical investigator, non-unions in fracture surgery.



James R. Smith, MD'89 is board certified in internal medicine, specializing in sleep disorders. He and his wife share a photo (above) of their three daughters.

тне **1990**s

Sylvie D. Khorenian, MD'91 opened an office for dermatology and cosmetic laser surgery at 630 Palisades Avenue, Englewood, NJ.

Paul J. Molinaro, MD'91 is currently a first-year student at Western State College of Law in Fullerton, CA.

Stay in Touch!

Let us know what you have been doing recently. Mail this form to: Alumni Association of New Jersey Medical School, 185 S. Orange Avenue, MSB-B504, Newark, NJ 07103-2714. Photos are welcome. You can also send your news via e-mail to: njmsalum@umdnj.edu or fax us at (973) 972-2251.

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I would like to be a representative for my class.

Please join the Alumni Association of New Jersey Medical School.

General Dues	\$50.00
Resident in Training	\$15.00
Lifetime Membership	\$1,000.00

Visit http://njms.umdnj.edu/, click on Alumni Association and then On-Line Dues Payment to pay your dues on line.

The Lifetime Membership is now being offered to our alumni as a means to perpetuate the goals of the Alumni Association and enable its members to sustain their support in a more meaningful way. All categories of membership will afford you the opportunity to keep connected with us. You will continue to receive all membership benefits, including *NJMS Pulse* magazine, information about upcoming events and reunions, and library privileges.

Rosanne F. Giannuzzi, MD'93

became a partner with the Montclair Anesthesia Associates, PA, at Mountainside Hospital, Montclair, NJ in October 2002.

James G. Roros, MD'93 and wife Beth welcomed their son Constantinos on September 26, 2001. Dr. Roros accepted a position at Piedmont Surgical Associates, Eden, NC.

Rosaline Ahkami, MD'94, a new mom to baby boy Ryan Kelly Whitworth, practices dermatology part-time in Livingston and Warren, NJ.

Colleen Krol, MD'94 is active in support of The BEAR Group in Hewitt, NJ, and welcomes all inquiries. (See their Web site at http://www.savenjbears.com/).

Stephen Sun, MD'96 works at Organon Pharmaceuticals and is involved in a new startup company called Physician's Discount Book. E-mail him for a copy. **Timothy Kanter, MD'97** completed his residency in internal medicine at Northwestern University. After working with a community health center in Manhattan, he took an academic position at Bronx Lebanon Hospital, where he serves as an HIV specialist.

Brian Valerian, MD'97 is pursuing a fellowship in colon and rectal surgery at Cleveland Clinic Florida in Weston, FL. He and his wife Sharmon are enjoying their first baby, Michaela Rose, born September 20, 2002.

Sonya Strassberg, MD'98 married pediatrician John Welter in April 2001, and started a neonatology fellowship at Westchester Medical Center, Valhalla, NY.

THE **2000**S

Gautam Malhotra, MD'01 and his bride honeymooned in Greece.



New Research Dean for NJMS

HO IS HARVEY LEON OZER, the new senior associate dean for research at NJMS? His colleagues, enthusiastic over his appointment, say that "he is someone who clearly puts the institution and department needs in front of his own personal agenda" and they are "really looking forward to his leadership in this critical position." The accolades go on and on.

He's described as an intellectual, a role model and mentor, honest, fair and supportive. All this and a respected research scientist, too. He attributes these aspects of his character to motivation provided by his parents who stressed that their children do something with their lives.

Ozer graduated cum laude from Harvard College in 1960, and earned his MD from Stanford Medical School in 1965. While there he became interested in genetics research, completing a fellowship in genetics and a year as a visiting research fellow at the Institute for Tumor Biology at the Karolinska Institute in Stockholm, Sweden.

He interned at Boston Children's Hospital Medical Center and served in the U.S. Public Health Service as a research associate and staff fellow at the NIH, and as a senior scientist at the Worcester Foundation of Experimental Biology. His career also includes stints at the University of Massachusetts School of Medicine, Hunter College, the Graduate Center of the City University of New York, the Weizmann Institute in Israel and Johns Hopkins School of Medicine.

In 1988, NJMS recruited Ozer as a professor and chair of the Department of Microbiology and Molecular Genetics. "I made the decision to come here because I knew that the department was good and anticipated that I could possibly make it even better," he comments. He holds a joint appointment at UMDNJ's Graduate School of Biomedical Sciences and also New Jersey Dental School, and considers the recent relocation of the Department of Microbiology and Molecular Genetics into the newly constructed state-of-the-art facilities at the International Center for Public Health in Science Park as one of his major accomplishments.

In his new position, in addition to focusing on research growth, he looks forward to being a spokesperson for the NJMS research community. One of his first recruits, Jeffrey Wilusz, PhD, now professor of microbiology and molecular genetics, and assistant dean of the MD/PhD Program at NJMS, says that Ozer was one of the top reasons he accepted a position here. Wilusz says that the new dean's "knowledge of NJMS inside and out, combined with



his experience as a scientist, a grant reviewer, and an administrator, will help to spearhead the growth of research at this school."

Nancy Connell, PhD, agrees. Currently vice-chair of research in the Department of Medicine, she was also one of Ozer's early faculty appointments. She says that as a department chair he was generous to a fault with his time and energy and support for faculty, staff and students. "He recognized the contributions of all members in the department. He thinks carefully about everything he does and says, and I've never known him to react in haste."

Jant Fant, MS, assistant dean for research, says: "He is a facilitator who brings investigators together to work toward the good of the school."

Ozer's long scientific career means he knows the challenges of the job. To this day, he finds his field of research exciting. For more than 30 years he and his coworkers collaborated in a research program combining the approaches of genetics, viruses, cancer and more recently, aging, supported by grants from the NIH's National Cancer Institute and the National Institute on Aging.

He finds academic medicine rewarding, and also a way to give back something. "I am proud of my personal successes, but I also take pride in my colleagues' accomplishments."

—Carole Walker

Keep in Touch

Our faculty welcomes your comments, suggestions and observations. We have provided email addresses for faculty members featured in this issue and have included patient referral contact information where appropriate. We look forward to hearing from you.

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Patient Referrals

Center for Otolaryngology/Head and Neck Surgery: 973-226-3444 Cardiac Surgery/New Jersey Cardiothoracic Institute: 973-972-5742 Acute Stroke Program at University Hospital (emergencies only): 1-866-27-STROKE (277-8765) Cerebrovascular Disease Management Practice at The Neurological Institute of New Jersey (NINJ): 973-972-2550 Institute of Ophthalmology and Visual Science: 973-972-2065 Cochlear Implant Center of New Jersey: 973-972-0189



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