Multidisciplinary clinic offers hope to inner city children suffering from asthma

Asthma in the Air
School of Medicine Administration

Robert R. Frank, M.D.
Interim Dean
Kertia Black, M.D.
Assistant Dean for Student Affairs
Patrick Bridge, Ph.D.
Assistant Dean for Medical Evaluation and Education Research
Joseph Brocato, Ph.D.
Assistant Dean for Community Education
Donna Dauphinais
Chief of Staff
Kenneth Ginsburg, M.D.
Assistant Dean for Clinical Science Education

Michael Herbert
Assistant Dean of Administration and Finance
Matthew Jackson, Ph.D.
Interim Assistant Dean for Basic Science Education
Mark Juzich, M.D.
Assistant Dean for Graduate Medical Education
Stephen Lerner, M.D.
Associate Dean for Faculty Affairs
Helene Lycaki, Ph.D.
Assistant Dean for Health Affairs
John Malone Jr., M.D.
Associate Dean for Medical Center Relations
Silas Norman, M.D.
Assistant Dean for Admissions
Kenneth Palmer, Ph.D.
Assistant Dean for Graduate Programs
David Peper, Ph.D.
Assistant Dean for Continuing Medical Education
J. Edson Pontes, M.D.
Assistant Dean for International Affairs
John Ruckdeschel, M.D.
Associate Dean for Cancer Programs
Basim Dubaybo, M.D.
Assistant Dean for Veterans Administration Affairs
Mary Jean Schenk, M.D.
Interim Associate Dean for Academic & Student Programs
Daniel Walz, Ph.D.
Associate Dean for Research
Charles Whitten, M.D.
Associate Dean Emeritus for Special Programs

Wayne State University Executive Officers

Irvin Reid
President
Nancy Barrett
Provost and Senior Vice President for Academic Affairs
Susan Burns
Vice President for Development and Alumni Affairs, and President for the Wayne State University Foundation
John Davis
Vice President, Treasurer and Chief Financial Officer
Meredith Gibbs
Executive Vice President; Chief of Staff
Harvey Hollins III
Vice President for Government Affairs
Louis Lessem
Vice President and General Counsel
Julie Miller
Secretary to the Board of Governors and Executive Assistant to the President
John Oliver
Vice President for Research

Wayne State University Board of Governors

Tina Abbott
Richard Bernstein
Eugene Diiker
Diane Dunaskiss
Elizabeth Hardf
Paul Massaron
Annetta Miller
Jacquelin Washington
Irvin Reid
Ex-Officio
Julie Miller
Secretary

School of Medicine Board of Visitors

Karen Batchelor
Jan Bertsch
Beth Chappell
Julius Combs, M.D.
John Conway
Steve Ewing
Oscar Feldman
Melvin Hollowell Jr.
Arthur Johnson, Ph.D.
Mary Kramer
Taylor Lewis, M.D.
Robert Lucas, M.D.
W. Ralph Marby
Gwen MacKenzie
Florence Mark
Mariana Noland
William O Neill, M.D.
Jack Ryan, M.D.
Howard Sims
Charly Vickery
Richard Webb

Dean’s Distinguished Advisors/Consultants
Trudy DunCombe Archer
George Dambrach, Ph.D.
Deborah Dingell
Steve Larned, M.D.
David Page
John Schwartz, M.D.
Margaret Smith
Gary Valade

This publication was produced by the Office of the Dean through the Office of Public Affairs and Publications. Your comments are welcome. Feel free to email the editor at adicresc@med.wayne.edu or send your correspondence to the following address:

Public Affairs & Publications
Wayne State University School of Medicine
Public Affairs and Publications
5D University Health Center
4201 St. Antoine
Detroit, MI 48201
(313) 577-1429
(313) 993-4333 fax

Director of Public Affairs and Publications
Kathleen Wedemire, APR
Managing Editor/Senior Writer
Amy DiCresce
Contributing Writers
Andrea Greisko
Leslie Mertz
Design
Midnite Oil Creative
Photography
Robert Stewart Photography Ltd.
Tom Owoc, Biomedical Communications
Contents

02 Asthma in the air
What began as a clinical trial for asthmatic inner city children has become a multidisciplinary clinic offering well-rounded treatment programs to patients and their families. Dr. Elizabeth Secord is providing care to kids suffering from asthma, one of the most common chronic diseases.

05 Neurorecovery and innovation prompt therapies for traumatic injuries
There's no shortage of ambition with Dr. Jay Meythaler. He's found windows of opportunity where none existed for spinal cord and brain injuries. His goal: getting therapeutics across the blood-brain barrier and stimulating the healing of neurons.

08 Shattering the shame of the uninsured
Medical student John Stasko's award-winning photography exhibit, "People of Detroit: A Living Project," features portraits and excerpted interviews from citizens of Detroit sharing their health care experiences.

12 Grad student trades in field journal for flow cytometer
Sarah Krueger celebrates success in the cancer biology Ph.D. program.

14 Smart shunt warns of wear and tear in the brain
Researchers from neurosurgery and engineering are developing an electronic chip that provides a warning signal when a brain shunt needs replacement or retuning.

17 Zebrafish provide pretty model to study ugly bacteria
Dr. Melody Neely learns about deadly strains of strep infections using the 1.5-inch-long zebrafish as a model.

20 Doing the double-take of chemo and radiation
Researchers at Wayne State University and the Karmanos Cancer Institute are helping patients with head and neck cancers live longer lives and avoid cosmetic and functional deformities by using combined chemotherapy and radiation.

24 Think tank spurs action for underserved people
From poverty to homelessness to health care access, Dr. Iltefat Hamzavi advocates for community health issues as co-founder and interim executive director of the Institute for Social Policy and Understanding.

27 Act like a better doctor, be a better doctor
Standardized patients are trained actors who portray a clinical scenario, providing a safe environment for medical students to perfect their clinical skills.

31 Protease knowledge gives Stefanie Roshy bargaining power
Graduate student Stefanie Roshy is on to something big, studying complex proteases that play a role in the progression of breast cancer.
Asthma is one of the most common chronic diseases among children. According to the American Lung Association, an estimated 4 million children under the age of 18 have had an asthma attack over the past year, and many others have non-symptomatic or undiagnosed asthma. Childhood asthma is the chronic disease that causes the most school absences in the United States.

For minority children, especially those who live in the inner city, asthma can cause much more than just a missed day of school. The number of diagnosed cases continues to rise in urban areas and more African Americans suffer abrupt and unexpected death from asthma than asthmatics of any other ethnic group.

Fortunately, a Wayne State University doctor and her multi-disciplinary research team are working to help change and save the lives of children who are most at risk.

For a little more than a year, Elizabeth Secord, M.D., assistant professor in the Division of Immunology, Allergy and Rheumatology within the Department of Pediatrics, has been part of a clinical trial with moderate and severe asthmatic inner city children and their families. She has created a clinic that offers a well-rounded, all-inclusive treatment program to its patients.

“We have approximately 75 subjects enrolled and we’re looking to enroll up to 150. We want it open to the high-risk kids and as many moderate-risk kids as we can accommodate,” Dr. Secord said.

During its study, Dr. Secord’s team has found that a lack of adherence to treatment is a common thread connecting many patient cases, although genetic and environmental factors also come into play.

“There is a high morbidity among children in urban areas. Children who are already asthmatic and are exposed to mold, dust and cockroaches don’t do as well,” Dr. Secord said. “Lack of adherence is a big issue among high-risk asthmatics. Kids that aren’t so bad can get away with not taking their medications once in a while, but...
Dr. Elizabeth Secord understands that children in urban settings may have trouble adhering to asthma treatments because of complicating environmental or lifestyle issues like the presence of mold, dust, cockroaches, smokers or pets in the home.
Dr. Secord's patients and their families often struggle with many stresses of poverty and inner city life, and the additional burden of coping with a chronic illness becomes overwhelming for them. This is why providing a full-range of services is so important.

When entering the study, subjects receive full medical, environmental, psychological, social, and pharmacological evaluations.

The patient’s family then participates in an educational program designed to fit its specific needs. Topics often include making environmental changes in the home, medication education and review, and general information about asthma. The team then formulates an action plan for the family.

Subjects are re-evaluated until their asthma is under control. The patients and families who are considered most at risk are offered additional services including home environmental assessments and motivational enhancement therapy (MET).

MET focuses on the needs of young parents, pre-adolescents, and adolescents, who are often not able to address their children’s or their own health care needs while confronted with many other psychosocial issues.

According to Dr. Secord, the subjects seem very happy with the care they’re being given – with one exception. “They’re not happy with the questionnaires they have to fill out, but we try to make it worth their while because they get more services,” she said.

A distinct facet of the program is the relationship the clinic has with the Family Independence Agency (FIA). A specially trained FIA supervisor, who is familiar with asthma, supervises all referred cases and is part of monthly clinic care meetings.

This allows any FIA workers who report to the supervisor access to clinic recommendations on environmental control and medication management. The ability of FIA workers to recognize lack of adherence to asthma treatments is an added insurance to help protect patients from medical neglect.

Dr. Secord’s study has four specific goals: to reduce the number of asthma-related hospitalizations and emergency room visits; to increase patient and family adherence with asthma therapies; to improve the overall health of children with moderate and high-risk asthma; and to demonstrate a reduction in health care costs.

“Our hope is that we can demonstrate enough of a benefit to Children’s Hospital of Michigan (CHM) and to the insurance companies that it will be worth their while to help continue funding the program. We’ve already shown a decrease in hospitalizations and it’s a significant enough savings that it warrants to pay the extra staff,” she said.

Original funding for the study came from the Children’s Research Center of Michigan. The trial was recently refunded for continuation over several years through a healthcare disparity grant through Medicare.

Dr. Secord feels that a multi-disciplinary approach to health care in an urban setting is a win-win situation for all involved.

“The concept is very simple. We used to have many more multi-disciplinary clinics at CHM and the Medicare reimbursements stopped coming so the hospital cut out the programs,” she said. “Patients would really benefit from the extra care. I think the idea is simple and we’re just trying to show that it’s beneficial to the insurance companies, the patients and the hospital as well.”
There’s no shortage of ambition with Dr. Jay Meythaler. He’s found windows of opportunity where none existed before and he’s breathing fresh air into the research arena for spinal cord and brain injuries.

By Amy Dicresce

Neurorecovery and innovation prompt therapies for traumatic injuries

Picture the injured brain as the hip new nightclub in town, requiring special VIP passes for entry. Most researchers are waiting outside in the cold, trying to figure out how to gain access. More often than not, Jay Meythaler, M.D., J.D., finds himself in the A-list line, getting past the protective guards and slipping through the blood-brain barrier to the hot-spot.

Wayne State University’s new chair of the Department of Physical Medicine and Rehabilitation is slipping new therapies into traumatically injured brains by finding breaks in the barriers that are designed to keep out foreign intruders. Trouble is, some of those foreign substances may be beneficial in healing people with head injuries, spinal cord injuries, stroke, Alzheimer’s and other neurologic diseases.

In developing new therapies for brain and spinal cord injuries, it’s all about access and neurorecovery, Dr. Meythaler said. “We’ve got to get across that blood-brain barrier and stimulate healing of the neurons. We need to know what molecules pass through, and attach ourselves to them; or we can find the weak spots in the wall and take them by storm; but we’ve got to get across it and stimulate neuron recovery.”

With six drug patents and a seemingly endless list of research publications, Dr. Meythaler has sent his compounds into battle a number of times, and they are making substantial headway. His strategy...
is to keep it simple, although that sometimes makes him unpopular. Rather than design a most elegant experiment with a singular focus, he likes to take what is already known and run with it in another direction.

“We are taking off-the-shelf technology and using it in new ways,” he said. Take for example, the drug 4-AP or 4-aminopyrididine. This drug has been known to help with improving nerve conduction through the injured nerves of the central nervous system in multiple sclerosis. Dr. Meythaler has applied it to the peripheral nervous system as well in Gullain-Barre syndrome (GBS).

“At first, I didn’t think it would work in GBS. We tried it and have found promising results,” Dr. Meythaler said.

Another example is baclofen, which has been used to relax muscles that are prone to spasticity in spinal cord injuries or multiple sclerosis. Dr. Meythaler was one of the original researchers to champion a change in the delivery mechanism. For years, baclofen was taken orally, but had only limited usefulness because the medication got dispersed and watered down throughout the body. When Dr. Meythaler delivered it directly to the spinal canal through an implanted intrathecal pump, the results were dramatically better. In addition, he was one of the first to look at its use for head injuries. Again, the results are very good, and a new study is showing that the drug tizanidine may be another alternative to baclofen for reducing spasticity via direct delivery into the spinal canal.

“Our approach is to look at proven compounds, in analogous situations, and then try to parallel that success with a new delivery approach—either through an innovative system or as the result of an add-on molecule—designed to overcome the blood-brain or blood-nerve hurdles,” he said.

Dr. Meythaler’s current research in drug development is operating under two basic tenets. First, he says, there is a window of opportunity for neuroprotection to take place. New animal studies show specific treatment windows for rats with spinal cord injuries. After that brief period, spasticity may start; however, new studies are finding that the spasticity process may be reversed with appropriate therapy interventions and motor function may be enhanced. This time period is an ideal opportunity for interventions by medication and therapy to enhance recovery.

Targeting the exact time and location for therapies in the continuum of complex injuries and secondary symptoms is tricky. Dr. Meythaler points out that you can lose up to 80 percent of your neurons and still be fairly functional for short periods of time. On the other hand, if you lose 90 percent of your neurons, you have only trace functioning that is barely discernable. Somewhere in that 10 percent difference lies a complex area of research.

Current drug trials have indicated that medications may target specific neurons and must be administered in various time windows during the recovery from CNS injury. If these medications are administered outside this window, it
could cause more damage, and result in complications such as convulsions or loss of motor control. “Timing becomes very important as we consider the various neurotransmitters and neuropathways. But as we learn more about chemical composition and complex biological processes, we can try new interventions at just the right time to perhaps find new success where it didn’t exist previously.”

This leads to Dr. Meythaler’s second tenet, which is: “What you use early, you don’t use late and vice versa.” He uses simple logic to explain. “When you have trauma to the head or spine, it sets off a neurochemical cascade of inflammation and the release of glutamate and other excitatory neural transmitters that are released in high concentrations after injury and this may be toxic to neurons that have already been injured. Drugs that block glutamate and these other excitatory neural transmitters should be given early during these high concentration times, but they should not be given later. This is because you learn and have neural plasticity in part due to these very same neural transmitters. Balance needs to be resumed or you’ll have a different set of problems to deal with.”

This early/late principle is violated all the time, Dr. Meythaler said. “Anti-seizure drugs are generally administered early after injury, and they should be. But after the first week, they need to be stopped or they will slow neurorecovery.” Similarly, anti-psychotics are often used for agitation following TBI, but long-term, they interfere with healing.

Also critical to remember is this: the therapy is as critical as the drug, said Dr. Meythaler. “New research shows we may be wrong to get people up and into therapy too quickly in the first few days after injury. The brain and spinal cord need 48 hours of quiet rest, with no therapy, to allow the excitatory responses to calm down,” he said.

These innovative ideas, though questioned by some colleagues, often have successful patients to champion them. In the 1990s, Landon Miller overcame a severe closed head injury and coma with the innovative use of the drug piracetam. This patient inspired Dr. Meythaler to establish Neurorecovery, Inc., a start-up company that develops compounds and devices to aid injuries of the human brain, spinal cord and peripheral nervous system.

Gregory Scott Daniel, who is bedridden and paralyzed after being hit by a drunk driver in Alabama, was the first person in the world to receive a baclofen pump to control his muscle spasticity following a traumatic brain injury. His father, Tommy, said, “When Dr. Meythaler put an injection into Scott’s spine he relaxed and went to sleep. This was the first time I had seen Scott completely relax since he came out of his coma. Due to the assistance of Senator Richard Shelby of Alabama, the procedure was approved through the FDA in about six months.”

Currently, Dr. Meythaler is touting the use of adult stem cell transplants to help reverse paralysis. The surgery, called olfactory mucosa transplantation, takes cells from the roof of the nasal cavity and transplants them to the spinal cord, where they transform into nerve cells and help repair injured tissue. Dr. Meythaler and Dr. Steven Hinderer, director of Spinal Cord Injury Recovery at the Rehabilitation Institute of Michigan, are using successful patient cases to speed experimental research like this.

“Our approach is to look at proven compounds, in analogous situations, and then try to parallel that success with a new delivery approach.”
Medical student John Staško says public health

John Staško, a medical student and public health advocate, won an Outstanding Project Award from the American Medical Student Association for his People of Detroit exhibit, which uses photography to raise awareness of the uninsured and underinsured citizens of the city.
Doctors in Detroit know that health care can get a little gritty. Thirty-eight year old Wayne State University medical student John Staško doesn’t shy away from the dark little secrets of inner city hospitals—namely, patients who are homeless, uninsured, impoverished or severely ill. He sits with them, buys them coffee, listens to their complaints about the system, photographs them, and most importantly, gives them a voice.

By Amy DiCresce
A staunch advocate for better public health services, Staško lives in a burned out inner-city neighborhood among the “undesirables” as they are often called and frankly, he is more than a little frustrated at the health disparities and inadequate treatment he witnesses regularly.

Rather than collapse under the weight of the situation, however, he plugs away by competing for small grants, launching art exhibits, hosting conferences and initiating projects that shed light on the problem of health care access. In the meantime, he is earning his medical degree so he can lend more than a voice to disadvantaged citizens. He looks forward to the day when he can lend medical expertise and the clout of medical colleagues who can build a groundswell of support for meaningful change.

“The health care crisis here is huge,” said Staško who has lived in several urban areas during his lifetime, most recently, Dallas, Albuquerque, New Mexico, and Washington D.C. “First of all, Detroit is a very segregated metropolitan city. The lack of a mass transit system and the clear division between the haves and the have-nots means that people aren't forced to interact. The bureaucrats and politicians who make decisions about funding and health care coverage drive in from the suburbs, have their meeting, and get the heck out of the city. They don’t live next door to these people. They don’t ride the bus with them. If they did, I think they'd be a little more concerned about public health, because it would be more personal.”

For Staško, it has become very personal. He recently debuted his own photography exhibit called “People of Detroit: A Living Project.” In it, he features photographs and excerpted interviews in which citizens of Detroit share their experiences accessing health care services. With guidance from Marilyn Zimmerman, associate professor in WSU’s Department of Art and Art History, and Maryjean Schenk, M.D., chair of WSU’s Department of Family Medicine, Staško and collaborating medical student Meegan Green used this exhibit to give a voice to those frustrated and uninsured people whose input is usually left unheard.

“Photography is used to explore and magnify the humanity of these average citizens, making their stories more alive,” Staško said. “We are using photography for societal change.” In doing so, Staško learned that the necessary changes go far beyond hospitals and medicine. A theme echoed throughout the interviews was this: The people who have trouble accessing health care tend to be people who also are unemployed or have menial jobs, lack transportation, have bad credit, endure sub-par housing and dangerous neighborhoods, are chronically ill and are often in pain.

One interviewed citizen summed it up this way. “[They are] spending millions of dollars on stuff we don’t need. It’s as simple as that, you know, because we need education, we need transportation, we need our streets fixed, we need our police officers, and that’s where the issue's coming in at, and that's what my concern is.”

Over and over again, Staško’s project shows the faces of Detroiter’s and the descriptions of their plight. There were many commonalities that went far beyond health insurance.

• “I broke my back three times in three places. I keep respraining it and nobody will cover me.”
• “I can’t go to the doctor because it will cost me money. I keep getting those doctor bills that I can’t pay, got my credit all messed up and I am screwed for the rest of my life.”
• “I have never been more, how do I say, broke and homeless, beat up and robbed.”
• “I have a problem getting to a doctor because I don’t got a driver’s license. I don’t got a car, so I gotta take the bus everywhere or walk.”

Dr. Schenk, research advisor on the People of Detroit project and chair of family medicine, says, “These problems are regularly encountered by WSU physicians. Oftentimes, a patient’s socioeconomic problems are either directly related to or exacerbate the patient’s medical problem. While the physician is able to work with the patient and reduce the professional fee associated with the patient’s visit, there is no such mechanism for a reduced fee for the medical tests and treatments that may be...
necessary to either cure or control the patient’s disease and symptoms. It has been a great privilege and honor to work with the medical students on this project. This project has heightened our awareness of these issues and has brought in other concerned groups.”

In punctuating his point through art, Staško paid attention to every detail. In fact, the easels that were used to display the photographs were made personally by Staško out of rotten wood from abandoned houses in his neighborhood. And whether he knows it or not, his own compassion is seen in the care he shows for his subjects. A former paramedic, auto company worker, scientific research consultant, dabbler in Russian studies, and holder of a Ph.D. in nuclear physics, Staško himself is a study in contrasts.

“I thought initially that this exhibit would show the contrast between the insured and the uninsured. As it turns out, it shows incredible contrasts between the employed and unemployed, the safe and unsafe, and the general disparate condition of those with little or no income,” he said.

As written in his project description, Staško says socioeconomic status is a fundamental cause of disease. “For example, the absence of grocery stores in poor neighborhoods reduces access to food products that are required for good health. Unsafe neighborhood streets and dumped materials influence people to stay indoors and reduce physical activity. Deteriorating neighborhood infrastructures erode social relationships which might help protect against stressful life conditions. Low-income children are exposed to greater levels of violence, family disruption and neighborhood crime.”

WSU School of Medicine Dean Robert R. Frank, M.D., feels that this medical school fills a critical gap in caring for the poor and uninsured. Although he’d love to see more resources made available, he is proud of the school’s longstanding commitment to the community. “When other institutions turned away uninsured citizens, we took care of them. We did not turn our backs on them,” Dr. Frank said. But the bottom line is this: “A kid in Bloomfield Hills should not get more money spent on him than a kid in Detroit.”

The People of Detroit project has garnered much support locally, and public health officials are brainstorming ways to use it as a traveling advocacy piece on a national scale. “Somebody even mentioned that this had potential to grow like the AIDS quilt, where people in cities throughout the country would add their photos and personal experiences, and eventually, we’d have this massive volume of personal experiences that could not be ignored,” he said.

“The project is timely and urgent. National debate merely simmers over universal health care, yet just as the debate seems to start percolating, the field shifts and the public is bewildered and must regroup. Solutions seem long in coming and weak in effect. The city of Detroit itself tries to assemble its own Public Health Authority, yet is foiled by the unknown. Our project will be a catalyst for change.”
Grad student trades in field journal for flow cyometer

Sarah Krueger celebrates success in the cancer biology Ph.D. program

By Amy Dicresce
Sarah Krueger’s day job is a far cry from just a few summers ago when she found herself snorkeling with stingrays in the Florida Keys and calling to frogs in mid-Michigan forests in the dead of night. As an undergraduate biology major with an interest in marine biology, Krueger has since found practicality and application in a less outdoorsey, but equally fascinating area of study—cancer and radiation biology.

Although canoeing and kayaking were her real summer calling, she took a seasonal research assistant position in the lab of Dr. Kaladhar Reddy, upon the urging of her brother who completed his doctoral degree in that lab in 2002. Joseph Krueger knew that his self-described mildly obsessive-compulsive and highly motivated sister would get caught up in academic research. She did, of course, and was accepted into WSU’s Ph.D. program the same year her brother finished.

“I just became fascinated with the breast cancer research we were doing and I knew that this was a more broad-based and practical career path for me. I’m still a naturalist who’s interested in oceanic warming and protecting the environment, but I feel I can make a positive impact in turning cancer patients into cancer survivors through my work,” she said.

Now Krueger works exclusively as a graduate research assistant in the Karmanos Cancer Institute’s Radiation Biology Department led by Dr. Michael Joiner. Her research project concentrates on defining a link between overall cell survival and cellular proliferation following low-dose radiation exposure. With mentoring from Brian Marples, Ph.D., Krueger is helping to find the mechanism and proteins involved in the phenomenon that makes cells more sensitive to radiation therapy when they are exposed to lower doses.

“Low-dose hyper-radiosensitivity is a response in which cells die from a greater than anticipated sensitivity to small single doses of ionizing radiation, generally at doses less than 0.5 Gray. We believe this happens because of a three-component system of damage recognition, signal transduction and damage repair,” Krueger said.

Interestingly, the Joiner group has found cells are most sensitive to low doses of radiation during G2 phase, just before mitosis, which is the key element of low-dose hypersensitivity under investigation by Krueger. For a brief window of time, there seems to be a delay in the cell cycle whereby DNA repair is allowed to occur, but in certain cells this response appears to be defective, which leads to reduced survival at low doses of radiation. Much of Krueger’s time in the lab is spent getting cells into G2 phase in an effort to try and inducing the defined low dose response and subsequent repair mechanisms for critical investigation.

“Elucidating these processes will provide a more complete understanding of low-dose radiation sensitivity. We hope that one day this research will allow for design strategies to overcome the activation of radiation resistance, which may impact the evolution of clinical radiotherapy.”

Krueger has already presented key findings at research meetings in France, St. Louis and Toronto, and was awarded first-place in the 2004 Graduate Student Research Day at the WSU School of Medicine. In recognition of her research, she has received a travel award, allowing her to attend additional meetings for the American Association for Cancer Research (AACR) and the joint meeting of the Radiation Research Society (RRS), American Society for Therapeutic Radiology and Oncology (ASTRO). In fact, she has applied for an RRS scholar-in-training award and is expected to be a front-runner.

Dr. Marples can attest to the work ethic and talent of Krueger. “Sarah is a self-motivating student with an affinity for experimental research. She has a passion for excellence that is evident in all her academic endeavors. On a more personal level, Sarah’s well-developed sense of humor and sharp wit make her a pleasure to work with.”

Krueger is expected to complete her Ph.D. in 2006 and is considering several career directions. She says she’s very interested in an academic career, because she enjoys the teaching and learning symbiosis of a university.

“In any case, I see myself near water,” she said. With her kayak and canoe strapped to the roof of her car, you may see her between experiments somewhere in Michigan or California or beyond. ☮
By incorporating advanced technology with a traditional medical treatment, a multidisciplinary team of researchers hopes to offer a much-improved prognosis for children and older adults living with hydrocephalus, or “water on the brain.” The team is developing a device that will sense increases in pressure within the brain, control a valve in a shunt to drain the excess cerebrospinal fluid (CSF) as necessary, and provide warning when the shunt needs replacement or an electronic “tune up.”

The proposed device, called a smart shunt, will be useful in treating the well-known infantile/children’s hydrocephalus as well as the less-familiar condition called normal pressure hydrocephalus, which mainly affects older adults and mimics some of the symptoms of Alzheimer’s disease. Both forms of hydrocephalus can cause brain damage and sometimes death, said Pat McAllister, Ph.D., who is the principal investigator of...
The research project and WSU professor of neurological surgery. The research team, with guidance from Drs. Steve Ham (chief) and Sandeep Sood, pediatric neurosurgeons at the Children's Hospital of Michigan, is in the process of creating a smart shunt equipped with a tiny, pressure-sensing electronic chip built right into the shunt's wall. It is also testing a number of novel, neuroprotective materials that will discourage the body's typical inflammatory response, dissuade infection, and prolong the shunt's lifespan.

"Children need the smart shunts for a couple of reasons," said Dr. McAllister, who has studied the pathophysiology of hydrocephalus for more than 20 years, and holds joint appointments in WSU’s physiology, anatomy and cell biology, and ophthalmology departments. First, the currently used shunt frequently becomes obstructed when brain tissues grow over the device and into its draining holes. "This blockage usually leads to dangerous increases in intracranial pressure (ICP), which if not treated quickly, can lead to escalating neurological deficits and sometimes death. The problem is that we do not have pressure sensors that can detect these changes continuously and warn the physician in time to prevent brain damage," he said. A solution is the implantable sensor and electronic chip under development by Gregory Auner, Ph.D., of the Department of Electrical and Computer Engineering and a key member of the research team. Dr. Auner is also professor and director of the WSU Smart Sensors and Integrated Microsystems Program.

The researchers hope to embed this tiny, 1.0 mm x 1.0 mm x 0.25 mm electronic device in the wall of the shunt where it can detect rising pressure early on when it is the least dangerous, Dr. McAllister said. Neurophysiologist Paul Finlayson, Ph.D., of WSU’s otolaryngology department, is assisting the project by directly measuring ICP in the brain and comparing these findings with measurements reported by the prototype implantable sensors.

Once a blocked shunt is identified, the typical treatment is its replacement, also known as revision, Dr. McAllister said. In many patients, the revisions and associated surgery cause the normally compliant brain to become stiff and inflexible, and therefore even less able to absorb excess fluid or to withstand ICP spikes. WSU chemical engineer Dr. Simon Ng and post-doctoral fellow Dr. Anfeng Wang are working on the root of that problem by coating the shunts with specially designed polymers. These materials discourage the tissue adhesion that makes the revisions necessary in the first place.

Dr. McAllister’s lab is currently conducting 30-, 60- and 90-day in vivo studies to determine the biocompatibility and biostability of the polymers. “Our preliminary results show that some of these coatings diminish the inflammatory response in the brain as well as the amount of tissue build-up on samples,” he said. The researchers, lead by postdoctoral fellow Dr. Xuemei Liang, are also exploring the possibility of adding slow-release antibiotics to the coatings or to the silicone wall of the catheter to resist infection, a common problem with shunts. Together, these actions would prolong the life of the shunt, thereby reducing the number of revisions, he said.

On a day-to-day basis, the smart shunt’s sensor would be able to monitor intracranial pressure constantly and control the shunt’s valve to meet changing demands.

Dr. Pat McAllister (left) is working with engineers to design better shunts for people with hydrocephalus or “water on the brain.”

Figure one is the normal or control aqueduct. Figure two is the aqueduct in an animal with hydrocephalus; notice lots of red astrocytes. Figure three is the shunted animal aqueduct. Notice more green microglia and reduced red astrocytes, indicating signs of recovery.
meet changing demands. He explained that plane trips, travel to areas with different elevations and therefore different atmospheric pressures, and simple shifts in posture from sitting to standing can increase or decrease ICP levels and pose problems for patients with currently used shunts. A smart shunt, on the other hand, would give the patients newfound freedom, he remarked, as well as a bigger safety margin.

Older adults who develop normal-pressure hydrocephalus would benefit, too. In this condition, the patient has a normal ICP for all but a few minutes a day, Dr. McAllister said. “These patients will spike a pressure in the middle of the night, maybe for three minutes, and then it will go back to normal, which makes it very difficult to detect. What we now believe is these spikes in pressure are just like some little guy with a hammer banging on the roof of the cerebral ventricles (the chambers within the brain that house CSF). Over time, that gradually causes brain damage.” Some researchers believe three of every 50 patients with dementia actually suffer from normal-pressure hydrocephalus, and Dr. McAllister suspects the rate may be much higher. At any rate, he said, “It’s a significant problem.”

The transient nature of the ICP increases in this condition has presented obstacles for its treatment. “It’s very difficult to design a CSF shunt system for people with normal-pressure hydrocephalus, because you don’t know what their pressure is at any particular moment,” Dr. McAllister said. “If, however, we could have a pressure sensor in the shunt that’s draining the CSF, and that sensor was feeding information back to the valve, then we should be able to manage their pressure changes much, much better.” Some members of the research team are also considering the possibility of adding pressure-sensitive proteins or other particles to the shunt’s walls, perhaps in lieu of a sensor chip.

Another potential addition to the shunt is one of drug-delivery. “The main drug that we’re investigating is called minocycline, a derivative of tetracycline that has been shown in stroke models and in some neurodegenerative disorders, like Parkinson’s disease, to inhibit inflammation,” he said. “It’s never been tried in hydrocephalus, but it’s a very attractive candidate for inhibiting the brain’s inflammatory response, and in particular the accumulation of glial cells. During her graduate studies, Dr. Janet Miller, now a postdoctoral fellow in the lab, showed that glial cells increase during hydrocephalus, and we suspect this is one of the major reasons that the brain becomes stiff,” he said. The research team is working on new drug-delivery implants, possibly in conjunction with the shunts, that can convey medications on an as-needed basis and directly to targeted tissues in the central nervous system.

The research team’s work will likely have applications beyond hydrocephalus, he added. “The drug-delivery system and, in fact, all of the technology developed for hydrocephalus can also be used to improve the treatment of many other medical problems, including stroke, cardiovascular disease, bladder and bowel dysfunction, and other neurological disorders, such as infections, tumors, and brain trauma.”

Dr. McAllister credits the research group’s successes so far to its multidisciplinary nature. “I had been thinking about a way to improve shunts for many years, but it was only a year ago when I started talking to engineers that I realized it could actually be done,” he said. “Now, with this multidisciplinary approach, we can go all the way from the neurosurgeons who are putting these things in the patients to the engineers who are designing the implants. It has certainly allowed us to build a better team and make a meaningful clinical impact.”

Dr. McAllister and postdoctoral fellow Dr. Janet Miller are working on new drug-delivery implants that can convey medications on an as-needed basis and directly to targeted tissues in the central nervous system.
The small, striped fish in Melody Neely’s four aquaria flash iridescent blue-green colors when the light hits them just right. They may also hold the answers to some of the most common and deadliest of human pathogens.

Dr. Neely, assistant professor of immunology and microbiology, is using the 1.5-inch-long zebrafish as a model to study two streptococcal bacteria: *Streptococcus pyogenes*, which the media has publicized as the “flesh-eating bacteria”; and *Streptococcus iniae*, which once only infected fish.

The zebrafish in Dr. Melody Neely’s lab (above) provide a window into the progression of streptococcal bacteria in humans.
but has recently jumped the species barrier to humans. “Streptococci are the causative agents of a large group of diseases, a lot of them being fatal,” Dr. Neely said.

*Streptococcus pyogenes* affects more than 20 million people a year in the United States alone, she said. Most of the infections result in strep throat, a usually short-lived condition that patients typically describe as a severe sore throat, but sometimes the infections lead to dangerous diseases, including necrotizing faciitis, or flesh-eating disease, and streptococcal toxic shock syndrome, or STSS. Both have mortality rates approaching 50 percent, she noted. Necrotizing faciitis spreads very quickly and results in massive tissue destruction accompanied by fever and excruciating pain, often ending in death within 24-48 hours. STSS can lead to an extreme drop in blood pressure, organ failure, and other symptoms, and can result in death in as little as 24 hours. “We want to determine which pathogenesis mechanisms allow this to happen so rapidly,” Dr. Neely said. “If there were a way in which we could modulate one of the mechanisms through either the pathogen or the host, we might be able to develop a new therapy to combat these very fatal diseases.”

*Streptococcus iniae* is troubling for another reason. It was considered strictly a fish pathogen until 1995-1996, when four people in Canada became ill after handling infected fish. The infection led to meningitis, septic arthritis, cellulitis, fever, confusion, and/or endocarditis in the patients.

Dr. Neely believes an understanding of the mechanisms used by the two bacteria to infect and proliferate in zebrafish will also provide a window to their progression in humans. “There are lots of reasons we’re using zebrafish,” Dr. Neely said. “First, the genome for the zebrafish was recently sequenced. Now that we know all of the genes that are in the organism, we found that zebrafish have a very similar genetic makeup to mammals, which is quite interesting. These fish also have a very well-developed immune system, including all of the immune-type molecules that humans do, so they respond (to bacterial infection) in the same way.” For many diseases, including those she is studying, the fish’s symptoms even parallel human symptoms. In addition, zebrafish are inexpensive, easy to keep, and the perfect size for study. “One of the biggest advantages is that they’re about 1.5 inches long, which means you can take an entire transverse or longitudinal section of a zebrafish and put it on a single microscope slide. Since we can then look at the whole body in a single animal, we can see the site of the initial infection, as well as where and how it spreads throughout the body at different time points.”

Dr. Neely’s team is studying 1) how the bacteria initially colonize a host; 2) what genes are involved in causing different outcomes, such as systemic vs. localized necrotizing disease; and 3) which interactions occur between the pathogen and the host tissue. The last is particularly challenging, she said. “We look at it this way. In infection, bacteria
find themselves in a new environment once they come inside the host. They sense the environment and based on that new environment, they change their gene expression so they can survive. The host then senses the presence of the bacteria and upregulates its own defenses, such as cytokines, oxygen radicals and lysozymes, to combat the invading pathogens. "The battle doesn’t end there," she said. "Now the bacteria have to fight off all these other molecules that are trying to kill them, so they have to change their gene regulation again to survive that onslaught."

Neely’s in vivo system captures all the subtle steps in this complex, back-and-forth exchange. "In our live system, we not only get to look at that dynamic interplay between the host and pathogen, but we also have the opportunity to look at multiple tissues, and that’s particularly important in systemic pathogens like these that can disseminate from the site of infection to multiple organs and tissues within the body," she said.

To determine the role of host and pathogen in disease progression, Dr. Neely’s research group, which includes four graduate students and a technician, makes a random or a targeted mutation to shut down genes in the bacteria, and then screens the mutated bacteria through the zebrafish to find those that no longer cause disease. This way, they can deduce which genes are essential to disease progression. “Then we look at what’s known about the gene or about the protein that it makes to determine what role it plays in the disease process.” She and her research group have already identified several genes with this method and are now doing additional in vitro experiments to home in on their specific mechanisms.

On the host side, the researchers are concentrating on immune factors and their effects on the course of the disease. One method involves placing the fish under a stress condition, which is known to dampen the immune response in fish and in humans, and testing whether the fish are more susceptible to disease even when disease-related genes are knocked out.

An understanding of the mechanisms of S. iniae and S. pyogenes infections may have implications beyond flesh-eating disease and STSS, she remarked. “S. iniae has shown similarities to another set of human pathogens, called group B streptococcal bacteria, which cause meningitis in human newborns and have a similar effect on zebrafish. This makes zebrafish an excellent animal model — and one of the few animal models available — to study the progression of meningial disease. In addition, these bacteria have gained notoriety the last 10 years for causing systemic and bacteremic infections in the elderly and in immunocompromised human patients.”

The work will also likely extend to other gram-positive bacteria, such as Listeria and Staphylococcus. “We’re hoping that by using the zebrafish and our in vivo model, we can look at general infection pathways that all of the gram-positive pathogens use. Since these pathways seem to be highly conserved, we’re hoping that we can use the zebrafish and our in vivo model to determine how the general infection pathways work. If we can determine what the mechanisms are, we would be able to devise strategies to combat multiple species.”

Streptococcus pyogenes affects more than 20 million people a year in the United States alone. Most of the infections result in strep throat, but sometimes the infections lead to dangerous diseases.
No cancer is pretty, but head and neck cancers are literally in your face, so there is greater potential for the problems to become downright ugly. Continuing a long-history of medical innovations, researchers at Wayne State University and the Karmanos Cancer Institute are helping cancer patients live longer lives and avoid cosmetic and functional deformities by advancing new treatment standards.

Organ preservation and combined chemoradiation therapies form the core philosophy of the WSU/Karmanos head and neck cancer team which includes Drs. John Ensley, professor of internal medicine/oncology, John Jacobs, professor of otolaryngology, and Harry Kim, assistant professor of radiation oncology. The team is a research powerhouse that gets published in the most prestigious medical journals, challenges dogma with their presentations at national research meetings and sets new agendas for treatment standards with their research protocols. Most importantly, they bring their work directly to cancer survivors, significantly improving the way they look, talk, eat, breathe and live.

Head and neck cancers are hard to ignore. They can affect the oral cavity (mouth and tongue), oropharynx (the middle of the throat), salivary glands, larynx (voicebox), nasopharynx, (air passageway at the upper part of the throat), the nose, or the paranasal sinus cavities around the nose. This disease set is particularly uncomfortable because it aggravates sensitive areas that are used for base functions like eating, swallowing and breathing.

For decades, WSU and Karmanos researchers have tested new therapies in an area of cancer that has gone largely ignored. “In the past, conventional therapy consisted of the surgical removal of the cancer-ridden organs as primary treatment. Many people lost their voice boxes, or other organs important for swallowing such as the tongue and throat tissues,” Dr. Ensley said. As director of the medical oncology portion of the head and neck cancer multidisciplinary team, he is championing new treatment standards and urging clinicians to use chemotherapy and radiation in combination to stop cancer growth and to preserve the organs whenever possible.
cancer growth, and to preserve the organs whenever possible.

"Take breast cancer, for example. It took 20 years to stop doctors from performing mastectomies as primary treatment for breast cancer. With the help of Dr. Bill Powers, in fact, from our own Radiation Oncology Center, we got state laws passed requiring surgeons to provide non-surgical radiation options that would treat the cancer and preserve the breast. We are undergoing similar battles now as we have defined alternative, non-surgical therapies to treat squamous cell carcinomas of the oral cavity, pharynx and larynx. These treatments are being accepted as new standards and are slowly being instituted in cancer clinics across the country."

These regimens have also improved the outcome for patients who still undergo surgery as the primary treatment for their cancers. In May 2004, Drs. Ensley, Jacobs and Kim co-authored a New England Journal of Medicine report establishing a combined regimen of chemotherapy and radiation following surgery as the gold standard for high-risk, advanced-stage squamous cell carcinoma of the head and neck. This national phase III trial enlisted the participation of 459 patients through the U.S.A. Head and Neck Cancer Intergroup and was administered by the Radiation Therapy Oncology Group. The need for aggressive treatment has been critical, because even after surgical removal of affected areas, these high-risk cancers in the head and neck frequently recur in the original tumor bed. Patients who had chemoradiotherapy (combined treatment) post-operatively did better than those with only radiotherapy in local and regional control (no recurrence) and disease-free survival.

We have defined alternative, non-surgical therapies to treat squamous cell carcinomas of the oral cavity, pharynx and larynx. These treatments are being accepted as new standards and are being instituted in cancer clinics across the country.

According to Dr. Jacobs, they believed concurrent radiation and chemotherapies would make cancer cells more susceptible to radiation and destroy more tumor cells. The results of this post-operative Wayne State regimen were first presented in 1989 at the American Society of Clinical Oncology meeting. This concurrent regimen has been tested at the cooperative and now the intergroup levels in the past decade in esophageal cancer, larynx and pharynx, and tongue cancer as well as nasopharyngeal tumors. In each large scale study, this regimen has provided improved survival and/or organ preservation.

“These chemotherapy regimens were first identified and tested right here at WSU. They were subsequently taken to national cooperative groups where, based upon the WSU data, phase III trials were conducted resulting in new national and international standards for the treatment of all groups of advanced stage head and neck cancers. These studies have resulted in WSU being internationally recognized for its expertise in head and neck cancer,” Dr. Jacobs said.

In November 2003, Dr. Ensley was senior author on another New England Journal of Medicine study using the WSU cisplatin-radiation regimen for laryngeal preservation and regional control. The results of the trial showed a 20 percent reduction in the number of advanced-stage patients requiring removal of their voice box compared to radiation alone. Most recently, the Southwest Oncology Group, using Wayne State/Karmanos Cancer Center regimens, reported successful organ
preservation for advanced cancer of the tongue (70-80 percent) and hypopharynx (50 percent). "This is significant because we are making strides in improving patients' quality of life and avoiding dysfunctional surgery," Dr. Ensley said.

Although these trials have resulted in new standards of therapy, Dr. Ensley said, challenges still remain. The combined therapy presents high levels of toxicity and can produce severe adverse effects ranging from dry mouth, pain, and taste dysfunction to serious infection of the mucosal lining and fatal toxicity. The people who benefit most from chemoradiation are those with late-stage, high-risk cancer for whom the benefits of aggressive therapy generally outweigh the risks. Dr. Ensley said that these head and neck cancers are usually discovered late and therefore run a high risk for problematic cosmetic and functional consequences from both the tumor and conventional treatment. In these cases, aggressive treatments, both surgical and non-surgical, are the only hope.

"Advanced head and neck cancer remains a therapeutic challenge and the collaboration of multidisciplinary teams is, more than ever, essential," Dr. Jacobs said. "The technological development of new radiological and biological tools, coupled with the introduction of new cytotoxic and non-cytotoxic compounds offer encouraging possibilities."

Dr. Kim, the radiation oncology expert on the team, is trying to overcome tumors that respond poorly to the cisplatin-based chemotherapy. "In some tumors, pre-exposure of head and neck squamous carcinoma cells to photon radiation increases resistance to subsequent cisplatin treatment. Similarly, cisplatin-resistant tumors also respond poorly to subsequent photon radiation treatment. We are trying to learn more about the molecular basis underlying cisplatin and photon radiation resistance and hope to design more multimodality protocols to answer these questions," Dr. Kim said.

The Radiation Oncology Center offers state-of-the-art photon radiation treatment techniques such as intensity modulated radiation therapy (IMRT), interstitial brachytherapy, gamma knife radiotherapy, and neutron radiotherapy, which is available in only two centers in the U.S.

"With such unique therapeutic capabilities, the Radiation Oncology Center is not only a major referral center throughout the state of Michigan, but also from out of state for many difficult-to-treat, advanced and unusual cancers in the head and neck," Dr. Kim said.

The head and neck multidisciplinary team is leading some of the national clinical research cooperative groups such as RTOG and SWOG, and is pioneering innovative treatments such as perioperative p53 gene therapy and a new chemotherapy of cisplatin and taxotere with radiation therapy.

The team continues to build upon head and neck cancer treatment developments that have advanced at WSU and Karmanos through the decades.
Dr. Hamzavi believes physicians should be more active in combating poverty and inadequate health care access for their patients; otherwise, they're just leaving the situation for the next generation of young doctors with no end in sight.
“Our dermatology clinic takes 25 percent of the uninsured in Michigan. There were days when we would have 120 patients during a three-hour clinic and we would have to pick which ones to treat. I had to wonder, is this the United States or is this sub-Saharan Africa?” said Illefat Hamzavi, M.D., WSU clinical assistant professor of dermatology. He is also a co-founder and interim executive director of a Michigan-based think tank, known as the Institute for Social Policy and Understanding (ISPU). “Physicians need to engage in discussions of why these patients show up at our doorsteps. We need to take the initiative to do more than put a Band-Aid on what is a systemic problem.”

Toward this end, Dr. Hamzavi and the ISPU have partnered with WSU’s Paul Toro, Ph.D., an internationally known expert in homelessness issues, to raise awareness of the plight of this large segment of society and to spur policy changes.

Dr. Toro summarized the problem: “On the one hand, we as health care professionals can complain about how (people who are homeless) are underinsured or uninsured, and they’re difficult to deal with, and they cost us money, but from my standpoint, they’re underserved. I don’t care that they’re uninsured. They are people in our society who are dramatically underserved.”

His recent study of homeless adults in Wayne County illustrates the problem. “If you look at this representative sample of how many health problems they have on average, you will be quite amazed,” said Toro, WSU associate professor of clinical psychology. “About two thirds of these people report at least 10 health problems in the last six months. This is out of a checklist of 50–60. Half of those people have 10 to 19 health problems, another third have more than 20, and 13 percent have 30 or more health symptoms.” Just one or two of the milder symptoms on the checklist would be enough to send most people to the doctor’s office, he noted, but homeless people typically lack that option. “Their health problems stem from extreme poverty, living on the streets, not eating well, and a lack of access to health care. They have a very hard life.”

Dr. Toro is now compiling his findings into a series of policy briefs which will be publicized by the ISPU, Dr. Hamzavi said. The first, which is now available through the ISPU website
The ISPU originated a few months after the fall of the World Trade Centers in September 2001, when Dr. Hamzavi and 10 other concerned individuals, including then-Congressman and now WSU professor David Bonior, began discussing perceptions of Muslims in the United States and particularly in Michigan, where many live. The dialogue soon expanded to U.S. policy and how well it reflects the issues facing its Muslims, as well as Americans of other minorities. “I’m a native Michiganian, and a lot of the people I know are native Michigarians, but we’re not all Caucasians or all African Americans. We come from different backgrounds, and we want a voice in the way the country and the community are shaped. We simply want to provide ideas about how we can possibly live in the future, and that’s what a think tank does,” Headquartered in Clinton Township, the ISPU defines itself as an independent, nonprofit, research organization committed to studying U.S. domestic and foreign policy. It now collaborates with about 30 scholars, including Dr. Toro, on issues ranging from politics and religion to genetically modified foods.

One of the ISPU’s first major efforts was a national conference, called “Islam in America,” which was jointly hosted by the ISPU and the WSU College of Liberal Arts and Sciences. “We got a lot of scholars as well as policy makers to come down, and we had a simultaneous press conference in Washington, D.C., and Detroit. That conference brought a lot of international recognition for the university,” Dr. Hamzavi said. Afterward, college dean Robert L. Thomas and development officer Susan Emfinger approached Dr. Hamzavi about working with Dr. Toro to disseminate his research findings and recommendations to key policy makers. The idea struck home, Dr. Hamzavi said. “We have always talked about how ISPU could encourage a policy of inclusion in our country, and Detroit especially, and that theme was continued with the poverty/homelessness issue. Now, Dr. Toro writes these policy briefs based on his research, and we create the forums for him to express himself and tell policy makers what’s happening.”

While Dr. Toro is working on additional briefs for the ISPU in the hopes of swaying national policy, he encourages the medical community to do its part, as well. During a recent presentation to first- and second-year medical students at Wayne State, Dr. Toro reminded them of their obligation to society. “The reality is that all people who go to medical school are subsidized, and those at a public university, like Wayne State, are heavily subsidized. They get a pretty low tuition for what the training costs,” he said, adding that he also reaped the rewards of subsidization through his doctoral program in clinical psychology. “I don’t want to guilt-trip people too much, but the reality is that we owe society. We should give back to society in some way, and we should do pro bono work. Perhaps we can give free care every month to help indigent people, like Dr. Hamzavi does. It’s a good thing, and I think all physicians should do it.”

Dr. Hamzavi also urged medical professionals to become active advocates of policies that will solve or at least reduce poverty and homelessness. The long-term benefits are many and include improved medical care overall.
practice makes perfect is a fine motto for some professions. Baseball players take batting practice before the big game. Chefs sample and taste recipes before serving them in restaurants. But where is the practice field for doctors to treat sick people? How do they rehearse breaking bad news to loving families? How do they learn to interpret the pumping and breathing sounds they hear through a stethoscope? And how many patients are willing to see a doctor at the practice stage of their training rather than the expert phase?

Approximately 300 people at Wayne State University have proven that they are happy to be practice patients for novice doctors. In fact, they even get paid for it through an innovative Standardized Patient Program, directed by Ron Spalding and coordinated by Maurice Kavanagh in the School of Medicine's Conjoint Teaching Program.

By Amy DiCresce
Services. Spalding and Kavanagh train people to play patient roles with specific sets of symptoms and specific medical histories that are presented to medical students for discussion and diagnosis. The program ensures that all students have uniform training and acquire the necessary clinical skills.

Lori McParlane was an office manager and nursing student when she was turned on to a new part-time job at WSU: a standardized patient (SP). One of her first assignments was to play the part of Ms. Cooper, a fast-living woman with multiple risk factors for heart disease. The lighter sticking out of her pocket was a dead giveaway that she was a smoker, and it served as a planted cue to prompt medical students to ask questions about her health behaviors and health history.

“The students are grateful that they have a safe place to practice and get out of their third year. This exam not only tests the students’ clinical abilities, but also prepares them for the Step 2 Clinical Skills Exam they are required to pass as part of the United States Medical Licensing Exam. Through the mid 1990s, standardized patient experiences were formally integrated throughout the medical curriculum to teach students information gathering, diagnostics, clinical medicine, interpersonal communication skills, physical exam techniques, compassion and professionalism. Now, Spalding, Kavanagh and McParlane tailor a variety of SP programs for training residents, genetic counselors and other health care workers throughout southeast Michigan, in addition to their work with medical students.

In fact, Spalding and Kavanagh have built a true academic research and medical education specialty out of the SP program. They are among the founding members of the Association of Standardized Patient Educators (ASPE), an international group that publishes research on the validity and methodology of such training programs. The demand for this reliable teaching tool is continuously growing, particularly as core clinical competencies are required and assessed by the Accreditation Council for Graduate Medical Education and other accrediting agencies.

Spalding said SPs enhance student education, because you can’t always count on the full spectrum of learning when you observe patients in a hospital setting. “The SPs are not actually sick or worried about their care. They won’t get whisked out of the room for an x-ray or feel too groggy from surgery to undergo an evaluation. Teaching efforts can be concentrated more on student learning rather than the side effects of the sick patient’s condition. And the situation is a little more comprehensive and predictable,” he said.

Student David Edwards said it didn’t matter that the SP wasn’t a “real patient” he examined during the musculoskeletal portion of his training. “It’s a body you’re examining. That’s what counts most. It doesn’t matter if it’s in a hospital or a simulated doctor’s office. I just need to learn the range of motion tests, the anatomy and the techniques. I see this as a way to learn the mechanics of doctoring.”

Andrea O’Boyle agreed saying, “In the hospital, you see what’s wrong with patients, but it’s hard to see what’s right. This helps us learn how a normal physical exam should be.”

From a bank of video monitors down the hall, Dr. Michael Stellini, professor of internal medicine, can watch the student-patient interactions and jot down notes for discussion and feedback after the encounter. Whether they are being evaluated on their interviewing skills or technical clinical skills, each student has a checklist of things he or she must complete. If the faculty member sees that a student is weak in a particular area, the student can get access to “master clinicians” through extra time spent in training situations. And, because the interactions are videotaped, the student can review his or her own skills.

“This interactive learning experience is valuable for the students and the faculty. In the hospital, students generally just observe and report what they learn to the residents. Here, they practice, they feel a

The students are grateful that they have a safe place to practice and get out their jitters and anxiety. For me, it is really enriching to know that I am helping to train the next generation of physicians.
person’s joints to check for inflammation, they learn to take a proper blood pressure, they listen to heart sounds, they examine the body from head to toe, and they begin to learn how the systems of the body work together,” he said. “They begin to assess the difference between what a normal baseline is and what might be suspicious.”

There are many indications that the training works. In fact, this semester, a particularly observant student heard a murmur or abdominal bruit in an SP that could be indicative of an aortic flow problem. “After listening to these normal sounds a few times, he discovered something that just didn’t sound right,” Dr Stellini said. “I went over to take a listen and the student was right on.” While SP exams are not meant to be diagnostic or to take the place of professional medical care, this is an instance where discovery really benefited the SP and it was a true indication that the training worked for the student.

Another advantage of standardized patients is the predictability of the training experience, regardless of geographic location. Beginning with academic year 2002-2003 a new course called Clinical Medicine was introduced into the first year curriculum. As part of the course, 10-12 students are assigned to a small group to get an introduction to the knowledge, skills and attitudes needed in clinical practice. Course facilitators are made up of faculty and volunteer community hospital physicians. This means, faculty members are training WSU students in more than 20 sites from Ann Arbor to Pontiac. SPs can go to these off-site locations and accommodate training. This cadre of SPs, known colloquially as the Parachute Club, are assigned to rotate between sites and “parachute” into the teaching setting as needed.

SPs in the Parachute Club bring rating forms and other supplemental materials as needed to aid with the exercises. “Both faculty and students have reacted favorably to these interactions, citing as most beneficial the opportunity to practice interviewing skills and techniques in a safe non-threatening environment. And they value the patient generated feed-

From a bank of video monitors down the hall, instructors can watch the student-patient interactions and jot down notes for discussion and feedback after the encounter. The Standardized Patient Program, directed by Ron Spalding and coordinated by Maurice Kavanagh, ensures that all WSU medical students have uniform training and acquire the necessary clinical skills.

Could you play the role of standardized patient?

WSU’s pool of standardized patients include people from all walks of life—teachers, auto workers, nursing students, aspiring actors, volunteers, and a host of other part-time job seekers who feel like doing something interesting and valuable to the community while earning $10-$14 per hour. No medical expertise is required and all training is done by qualified WSU faculty.

If you would like to learn more about participating in the Standardized Patient Program, please call (313) 577-1414 or visit www.med.wayne.edu/conjoint/sp_programs/index.asp.
“In the hospital, you see what’s wrong with patients, but it’s hard to see what’s right. This helps us learn how a normal physical exam should be.”

Professor Anne Greb in the Center for Molecular Medicine and Genetics has incorporated SP methodology into the curriculum of the genetic counseling program to help monitor students’ progress in developing the nationally defined practice-based competencies. The first SP encounter, a pregnant woman at risk of carrying a gene mutation for Duchene Muscular Dystrophy, occurs at the end of the first semester. The second encounter, which occurs at the end of the second semester, involves having the same patient return to review her carrier results. Students are expected to present “bad news” genetic test results, provide appropriate information on risks and management, and address psychosocial, coping, support, and disclosure issues as appropriate. The complexity of psychosocial and other confounding factors incorporated into the SP portrayal, is increased with each encounter.

In a pilot study to test the program, Greb found the following to be true.

“In the hospital, you see what’s wrong with patients, but it’s hard to see what’s right. This helps us learn how a normal physical exam should be.”

“The results from the first encounter showed that students’ communication skills were on target. However, their skills related to taking targeted family history, understanding the importance of confirming a diagnosis, and nondirective counseling were not, prompting specific curriculum adjustments. Overall, the use of SP encounters has been valuable in helping us determine if our curriculum goals, with regard to clinical skills development, are being met,” Greb said.

The Standardized Patient Program is a true test of our curriculum, Spalding said. “We can make sure our future doctors are getting the right messages, the right information and the right training.”

Students say patient actors help them learn the mechanics of doctoring.

Back,” Kavanagh said. “In fact, the students who don’t get an SP experience and have only ‘real’ clinic or hospital patients have commented that they are at a disadvantage. Clearly, the SPs play a necessary role in education. Our students and faculty are requesting them regularly now.”

Medical Education Commons to house SP program

The new Richard J. Mazurek, M.D., Medical Education Commons to be built adjacent to the Shiffman Medical Library will house the expanding Standardized Patient Program. With more than 20 rooms equipped with audio and video equipment, students will be able to practice their clinical skills and later review them with advisors and faculty members. Eventually, all students will create their own learning portfolios that will contain video footage of the work they’ve accomplished and the skills they’ve learned. This will be one of the largest clinical skills labs in the country and will be a teaching tool for medical educators and health care workers across the state.

The new Education Commons will also house other educational tools including computerized patient simulators similar to those in the pharmacy program, and life-like models that allow students to perfect basic skills like suturing, intubation, giving injections, CPR, etc.

If you’d like to support this program with a contribution to the Education Commons, please contact the School of Medicine’s Office of Development and Alumni Affairs at (313) 577-1495.
Graduate student Stefanie Roshy is on to something big. In the past, scientists wondered about the importance of proteases; but now their complexity has been validated and Roshy is part of the exploration.

“We know now that proteases are more than just housekeeping genes. My particular work has elucidated their importance in the development of the normal mammary gland and the progression of breast cancer,” Roshy said. This work won her first place in the 2004 Graduate Student Research Day and it fuels multiple career opportunities when she completes her Ph.D. later this year.

Under the tutelage of Bonnie Sloane, Ph.D., professor and chair of pharmacology, Roshy is learning her trade thoroughly and is being recruited by several members of the proteolysis research societies across the country. Research on proteolytic enzymes, their inhibitors, and their substrates has grown to the point where it has become difficult to keep up to date, and new researchers like Roshy are being welcomed into the field.

Roshy uses a 3D in vitro system to look at the roles of cysteine proteases, specifically cathepsin B and matrix metalloproteinases (MMPs), in the malignant progression of cancer in the mammary acini, or parts of the breast glands where milk and fluid is produced. By learning more about selective inhibitors, she and her colleagues hope to find ways to block cancer progression.

With the supportive and assertive Dr. Sloane guiding her research, Roshy has already made more than a dozen research presentations from Colorado to Slovenia to Japan. She has co-authored a Cancer Research article, a review article in Cancer Metastasis Reviews and a handful of abstracts, and has been honored as a young investigator several times by her peers.

“I was scared to death the first time I had to present my research in front of all these senior investigators, but now I am very comfortable with it. I’ve learned a ton about my field based on input and feedback from colleagues and I’ve learned new and interesting avenues to pursue with this work,” Roshy said.

Roshy is exploring opportunities for post doctoral positions and interviewed at a few labs at the National Institutes of Health. Newly married to a patent lawyer, Roshy said she and her husband would love to live in the Washington D.C. area for both of their careers, but they are open to new opportunities.

“Stefanie is a bright student and an outstanding scientist with much to contribute,” said Dr. Sloane. “It has been delightful seeing her develop into a skilled and innovative researcher. We will all miss her when she moves on to her postdoctoral position, yet we look forward to watching her career evolve and to spending time with her again at national and international meetings.”

Nationally acclaimed colleagues have honored Stefanie Roshy as an outstanding young investigator. She expects to complete her Ph.D. later this year.

By learning more about selective inhibitors, Roshy hopes to find ways to block cancer progression.
When health professionals are immersed in a powerful academic environment, the result is an astonishing pace of life-saving discoveries. Developments that used to occur once a decade have accelerated into continuous breakthroughs and they are happening here, in the heart of the Detroit Medical Center/Wayne State University system.

The DMC is the only health care center within Metro Detroit with this crucial research affiliation. Direct access to state-of-the-art research at Wayne State Medical School creates the difference between the care you’d find at any hospital and the advanced care you can only find at the DMC.

Gateway to the DMC
I-75 at Mack
One exit north of the stadiums

**BREAKTHROUGHS HAPPEN WHERE RESEARCH HAPPENS.**

**RIGHT HERE**

**CHILDREN’S HOSPITAL OF MICHIGAN:** where the first successful pediatric bone marrow transplant in Michigan occurred.

**DETROIT RECEIVING HOSPITAL:** where Michigan’s first Level I Trauma Center was established.

**HARPER UNIVERSITY HOSPITAL:** where the world’s first open-heart surgery was performed.

**HUTZEL WOMEN’S HOSPITAL:** home of the nation’s only National Institutes of Health Perinatology Research Branch.

**KARMANOS CANCER CENTER:** developed the first human breast cancer cell lines, facilitating worldwide breast cancer research.

**KRESGE EYE INSTITUTE:** where the first radial keratotomy procedure in the U.S. was performed.

**SINAI-SINAI GRACE HOSPITAL:** established the nation’s first comprehensive program for sickle cell anemia.

**WAYNE STATE UNIVERSITY:** the Center for Urban African-American Health is one of only eight sites in the nation designated by the National Institutes of Health to address racial disparities in health care.