50TH ANNIVERSARY
OF THE WORLD’S FIRST SUCCESSFUL
OPEN HEART OPERATION
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On the Cover
In 1952, WSU physicians made history using a mechanical heart pump built by General Motors.
In 1952, a machine built by General Motors Corp. in Detroit made medical history. Dr. Forest Dewey Dodrill, associate professor of surgery at WSU, used it to perform the world’s first successful open heart operation. The news media and others referred to this mechanical device as the Michigan Heart, because it was built and used in the state of Michigan and because the project was partially funded by the Michigan Heart Association.

There have been a number of books and many articles written about other open heart surgery pioneers who all followed Dr. Dodrill with reports of their own successful open heart surgeries. Almost nothing, however, has been written about Dr. Dodrill since that first case was reported. Now, 50 years later, it is time for that oversight to be corrected.

The First Patient
On July 3, 1952, a 41-year-old male suffering from shortness of breath was about to make medical history. He was the first patient on whom the Michigan Heart, officially known as the Dodrill-GMR (General Motors Research) Mechanical Heart, was successfully used.

The patient had been born in Poland and during World War II had enlisted in the Polish army. “But,” according to Henry Opitek, “when the doctors examined me, they said my heart was too bad for combat or any other [physically active] duty.” He remembered that he had been bothered by chest pains for many years, tired quickly and was short of breath.

When he was admitted to Harper Hospital for the surgery, he recalled seeing dogs romping on the roof of a nearby building. He wondered why each dog had a shaved chest. He later learned that they had been used in the final test of the mechanical heart machine before his surgery. The operation corrected his mitral heart valve, which had become incompetent as a result of the rheumatic fever he had many years before. While he was told he would be the first patient to use the new mechanical heart, he had no idea that the device would eventually be placed on display in the Smithsonian Institution in Washington, D.C.

The patient remained in the hospital about five weeks after the surgery for observation. However, according to Dr. Dodrill’s report, the patient felt he could have been discharged at the end of the second week. In reviewing the actual hospital record, it appeared that Opitek had no complications and likely would have been sent home on about the fourth postoperative day in today’s era of HMOs and DRGs. Incidentally, the physicians on the case donated their services, but Opitek received a bill for $340 (room rate of $14 per day). The Michigan Heart Association and his physicians paid a portion of that bill.

In the published case report, Dr. Dodrill concluded, “The benefits to the patient have not been fully evaluated. The clinical examination, however, indicates there is a definite improvement. To our knowledge, this is the first instance of survival of a patient when a mechanical heart mechanism was used to take over the complete body function of maintaining the blood supply of the body while the heart was open and operated on.”

Twenty-one years after the surgery, a Detroit News article reported that Opitek “has very little physical discomfort and does everything any 62-year-old would do. He takes full advantage of every hour.”
While the medical ethics of those days kept all patients’ names confidential, those same ethical standards also dictated that nothing could be reported or printed about the actual operation itself until a full technical report had been published in a medical journal. When the required report finally appeared in the October 18, 1952 *Journal of the American Medical Association*, newspapers all over the world headlined the story. The nickname for the device, The Michigan Heart, appeared in many newspaper headlines on October 17 and 18, and was also the title of an October 27, 1952 article in *Time* magazine. At the request of the Smithsonian Institution, the Michigan Heart was presented to the museum on September 9, 1954, for permanent exhibition.

**The Historic Operation**

Dr. Forest Dewey Dodrill was the surgeon who performed the historic operation on Henry Opitek for his deformed mitral valve that was predominantly incompetent secondary to fused chordae tendineae. Why isn’t Dr. Dodrill better recognized for performing the first successful open heart operation and why do some folks argue that he was not actually the first to perform a successful open heart operation on a human?

In the first place, Dr. Dodrill did not use a heart-lung machine to perform his first operation. He did use a mechanical heart pump to support the patient’s circulation, but in the first several operations, he used the patient’s own lungs to oxygenate the blood. Therefore, Dr. John Gibbon, Jr., who had one successful case the year after Dodrill’s case, is generally given most of the credit, because he used both a mechanical heart pump and a mechanical oxygenator to oxygenate the blood. Dr. Gibbon performed the first successful open heart operation using a heart-lung machine. Dr. Dodrill had his own mechanical oxygenator and had already reported on experiments with it in a medical journal, but he did not use it on the first several human cases.

Secondly, when Dr. Dodrill performed his first case in July 1952, he used his pump to divert the oxygenated blood returning to the left atrium. The blood bypassed the patient’s left ventricle and was pumped back into the patient’s aorta. Dr. Dodrill’s intent was to open the left atrium so he could visualize the patient’s mitral valve and repair it. However, in this patient, the left ventricle was quite large, so he was unable to expose the heart valve as he hoped to do. He therefore placed a purse-string stitch around the left atrial appendage and then, placed his finger through it and...

### Dr. Dodrill: Heart Surgery Pioneer

Forest Dewey Dodrill was born January 26, 1902, in Webster Spring, West Virginia. He received a bachelor’s degree from West Virginia University in 1925 and graduated from Harvard Medical School in 1930. He then served an internship and surgical residency at Harper Hospital in Detroit and became a staff surgeon. In the early 1940s, he served a thoracic surgery residency at the University of Michigan and earned a master’s degree in surgery at the same time. He returned to Harper Hospital and limited his practice mainly to chest and vascular surgery.

He married Ardis Twork, who graduated from nursing school, and worked at Harper Hospital for a while. They had three daughters, one of whom became a physician.

Dr. Dodrill served as clinical associate professor of surgery at the Wayne State University School of Medicine and was chief of thoracic surgery at Harper Hospital during the 1960s. He stopped operating at Harper Hospital around 1972. By then it is estimated that he had performed more than 1,000 open heart operations.

He subsequently developed Parkinson’s Disease and died in June, 1997, at the age of 95.

Presenting the heart machine for display at the Smithsonian are: Edward Rippingille, assistant general manager of research at GM; Calvin Hughes, research biologist and project coordinator who ran the pump and oxygenator during all the procedures; Dr. Dodrill, who performed the surgery; and Charles McCuen, GM vice president and head of research.
performed manipulations on the mitral valve blindly for 14 minutes while the patient’s circulation was supported by the mechanical pump. Some would argue this is not a true open heart operation since he didn’t visualize the defective heart valve. Also, he does not tell us exactly what he did to improve the leaky valve.

With what we know today, none of us would have chosen a mitral valve repair for mitral regurgitation as our very first case. We would have had no training with this technique and not have understood the functional anatomy. Perhaps worst of all, the echocardiogram had not yet been invented! On the other hand, Dr. Dodrill the pioneer did not quite understand the importance of these obstacles. Most of his intracardiac surgical experience was with closed mitral commissurotomies. He knew how to dilate the valve with his finger and separate fused chordae tendineae. He probably thought that if he could see the valve, he could fix it.

In the last eight dogs he tested, where he had used left heart bypass, all had survived and he could directly visualize the mitral valve in each. In the canine experiments, one cannula was placed through the left superior pulmonary vein into the left atrium and connected to tubing running to the Michigan Heart. Tubing coming from the Michigan Heart was connected to a cannula placed through the left subclavian artery into the aorta. After the pump was activated, Dr. Dodrill would place a clamp across the left atrium in such a way that all of the blood entering the left atrium from the four pulmonary veins was returned to the pump. The left atrium on the other side of the occlusive clamp could then be opened, viewing the mitral valve.

The occlusive clamp could not be placed with Mr. Opitek, so Dr. Dodrill therefore went to ‘Plan B.’ He seems to have been lucky with the results he obtained, perhaps very lucky. He also said, “It is probable that such a severe procedure could not be carried out when the left ventricle is maintaining the systemic circulation.”

By September 16, 1953, Dr. Dodrill had performed at least nine open heart operations using the mechanical heart with five or six survivors—an important accomplishment. Meanwhile, Dr. John Gibbon, Jr., in Philadelphia, had developed a heart-lung machine that he used in a series of five patients in attempts to correct various types of heart defects. Only one of those patients survived the operation. Dr. Gibbon became very discouraged by the fact that four of five patients had died and, therefore, declared a moratorium on further human heart surgery at his institution until the problems that were responsible for the deaths could be worked out.

Dr. John Kirklin, another pioneer in open heart surgery at the Mayo Clinic, referred to this period, stating, “Most people were very discouraged with the laboratory progress. The American Heart Association and the National Institutes of Health had stopped funding any projects for the study of the heart-lung machines because it was felt that the problem was physiologically insurmountable.” Fortunately, General Motors and the Michigan Heart Association continued to fund Dr. Dodrill’s research and he continued making presentations and advancements in the field.
Evolution of the Michigan Heart

Starting as early as the 1930s, a number of groups around the world were working in research laboratories to develop heart-lung machines. In the late 1940s, surgeons, including Dr. Dodrill, were performing shunt operations in children born with certain types of heart birth defects. The operations were “palliative.” None of them corrected the problem, because, according to Dr. Dodrill, in nine out of 10 children, the problem was within the heart. Realistically, at that point in time, there was no way of directly viewing defects inside the heart. But research had already begun to find solutions to the situation. For Dr. Dodrill and his colleagues, that eventually led to 30 months of research and experiments that culminated in building the Dodrill-GMR Mechanical Heart.

In late 1949, Dr. Dodrill approached Dr. Warren Cooksey, who was a cardiologist at Harper Hospital and president of the newly established Michigan Heart Association. Dr. Dodrill discussed the possibility of building a mechanical heart pump to be used for open heart operations. The Michigan Heart Association had just been founded under the auspices of the American Heart Association and one of the goals they were charged with was supporting innovative heart research. Charles E. Wilson, who was then president of General Motors, was also board chairman of the Michigan Heart Association, and was extremely interested in heart diseases.

Dr. Dodrill met with Wilson and showed him many sketches and ideas for building such a pump. Wilson, in turn, called Charles L. McCuen, vice president of GM, who at that time headed the research staff. They agreed that Dr. Dodrill’s idea was worth an engineering try. This project was to be done as a public service, courtesy of General Motors. Incidentally, the very capable Wilson left GM in January 1953 to become the U.S. Secretary of Defense under President Dwight Eisenhower.

In late 1949, Edward V. Rippingille, Sr., was assigned to be consulting engineer for the project. He took charge and traveled extensively, examining various pumps that had been made for such use but had failed for one reason or another. Rippingille summarized the problem: “We have pumped oil, gasoline, water and other fluids one way or another in our business. It seems only logical we should try to pump blood.”

Over about a 30-month period, six to 10 different types of pumps were built and tested by GM engineers. There were eight or nine people from the research laboratories who principally worked on the project and another eight or nine who also contributed.

Dodrill’s heart pump looked somewhat like an old Cadillac V-12 engine. What looked like six cylinders on each side of the engine were actually six separate pumping chambers. Interestingly, Dr. John Kirklin from the Mayo Clinic was also exploring different designs for a heart-lung machine in the early 1950s. As part of his research, he visited Dr. Dodrill’s laboratory on November 13, 1952. They also visited Dr. John Gibbon’s laboratory in Philadelphia. Dr. Kirklin later commented that Dodrill’s pump, built by engineers at General Motors, looked much like a car engine, whereas Gibbon’s machine, built by engineers at IBM, resembled a large computer.

By January 1951, research had progressed to the point that animal studies were needed. Dr. Dodrill got permission from the Harper Hospital administration to use the research laboratories on top of the Buhl
Building, which was one of the buildings within the hospital complex. Eventually, Dr. Dodrill and his colleagues reached the point where eight consecutive dogs that were tested had survived. These, in fact, were the dogs seen through the window by Henry Opitek, who would be Dr. Dodrill’s first patient to use the machine.

Calvin Hughes, a research biologist who was hired by GM to be the coordinator of this project, recalled that the first surviving dog of that group was a German shepherd, which Rippingille subsequently adopted and kept at his country estate. “The dog greeted you in the driveway when you arrived and in Rippingille’s opinion, the dog could do no wrong,” he said.

Ultimately, the GM engineering team built four Dodrill-GMR mechanical heart pumps between 1951 and 1956. Although they all looked similar, refinements were made in the internal workings as the project progressed. The last of the Michigan Hearts used clinically was retired at Harper Hospital in 1957 or 1958 when it was replaced by the latest version of a Gibbon-Mayo type heart-lung machine.

Besides the machine on display at the Smithsonian Institution in Washington, D.C., another is on display at the General Motors World Headquarters in Detroit’s Renaissance Center, and a third is in the lobby at Harper University Hospital in Detroit.

While he was told he would be the first patient to use the new mechanical heart, Henry Opitek had no idea that the device would eventually be placed on display in the Smithsonian Institution in Washington, D.C.

While he was told he would be the first patient to use the new mechanical heart, Henry Opitek had no idea that the device would eventually be placed on display in the Smithsonian Institution in Washington, D.C.
High-Power Medicine Cabinets
SCIENTISTS TESTING medications several decades ago probably had better odds of winning a lottery or finding a needle in a haystack. Methods for studying and testing new pharmacological agents were primitive and often relied on hope, a hunch, or just plain luck. The discovery of penicillin, for example, was a wonderful medical advancement, but it was purely serendipitous, and not the most efficient way to look for cures.

Scientists today employ sophisticated tools like robotic screening, radioactive signal detection, genetic engineering, and three-dimensional molecular modeling to design therapeutic drugs and to understand exactly how they work. Patients obviously don’t want to stumble upon experimental drugs, then cross their fingers and hope for the best. Thanks to technological advances, scientists are designing medications that are targeted to very specific sites, have minimal side effects, and deliver controlled dosages.

The number of new drugs is certainly increasing, but perhaps more important is the quality of these substances. Dubbed “smart drugs,” new therapeutics do more than just get injected or ingested and dispersed randomly throughout the body. They move to targeted areas and deliver appropriate dosages through sophisticated mechanisms that may be activated by heat, light, electrical currents, or magnets.

“New generations of medications will attack diseased cells more forcefully, while sparing healthy cells,” said Dr. Shahriar Mobashery, director of the WSU School of Medicine’s Institute for Drug Design. “In the past, drugs had a primary effect on the problem, but there were so many side effects, that one had to weigh his or her options in deciding whether or not it was worth it.”

In addition to being more effective, new drugs may provide presymptomatic screening for diseases, which could stop people from getting sick in the first place.

Drug design generally begins by examining target proteins that play a critical role in a particular disease or biological process. Drug molecules are then tested to see if they bind to the protein to induce or prohibit important functions. “The power to turn a function on or off could potentially stop the development or spread of a disease or complication. In this way, the idea for a new drug is born,” Dr. Mobashery said.

Rational drug design can only be accomplished if researchers know their enemies intimately. Computer programs and advanced hardware help researchers get the clearest pictures of the viral and bacterial proteins they are fighting, and the drug compounds they are using as weapons. Precisely detailed information about structural formation allows scientists to test compounds electronically, before they are used in any living animal or person.

At the WSU School of Medicine, researchers are combing through proteins, tracking cellular mechanisms, and studying the body’s absorption and metabolism functions to find the keys that unlock the potential of various targets. Current works in progress may provide better antibiotics, tumor inhibitors, vaccines, or new drugs to treat diabetes, cancer and obesity. On the following pages, you will learn about some of the WSU faculty members working on drug design programs and delivery systems to improve our understanding and health.
PHARMACEUTICAL COMPANIES ARE IN CONSTANT SEARCH OF NEW molecular targets to screen their compounds. Three faculty members in the Center for Integrative Metabolic and Endocrine Research (CIMER) are filling that need by studying cells from the inside out. Using a microgenomics approach, they are helping in the search for new drugs to treat diabetes and obesity, both of which are related to the body’s metabolic and endocrine systems.

Dr. Robert MacKenzie, associate professor of psychiatry and behavioral neurosciences, said, “We are using a combination of state-of-the-art techniques to study specific cell types within metabolically important tissues such as muscle, fat and brain. We determine if the genes expressed in those cells could be good targets for new drug therapies.”

As founders of CIMER and former employees for Parke-Davis/Pfizer Global Research and Development, Drs. James Granneman, Robert MacKenzie and Todd Leff conduct industrial and applied research to provide new molecular targets for drug discovery. “During our years at Pfizer, we were on the other side of the research question,” Dr. Granneman said. “We had targets and we looked for new drugs. We know what makes a good drug target from the industry’s perspective, so it’s very useful as we sift through possible molecular targets.”

He explains the process this way: “Disease is caused by dysfunction in specialized cell types. We characterize sub-populations of cells using genomic and proteomic analysis. We determine whether or not the genes expressed in those cells will be good targets, and we validate them. We do the academic work for the drug industry and it makes sense for both institutions to do what they are best at.”

The work of the three researchers is highly complementary. Their collaborations in diabetes and obesity research provide a broad picture of the basic problems involving fat, for example. Dr. MacKenzie has shown how to limit fat intake through appetite suppression and control of metabolic rate. Dr. Leff shows how fat is oxidized in the muscle and Dr. Granneman shows how fat is burned in the cell itself.

More specifically, Dr. MacKenzie traces the genes that regulate body weight through the central nervous system. He has found that animals and humans are obese if they have mutations in the MC4 receptors that are controlled by the hormone leptin. He traces the effects of these mutations on MC4 receptor function.

In related work, Dr. Leff studies gene mutations linked to obesity and diabetes. He examines mutations in the PPAR and HNR4 proteins that cause insulin resistance and problems with insulin secretion in the pancreas. He has made advances in elucidating the transcription signaling and metabolic mechanisms in the liver and fat cells.

Dr. Granneman’s expertise ties together the work done by his colleagues. He investigates the accumulation of fat in and around the muscle cells. If a person stores fat in the muscle cells, he or she will develop diabetes. Dr. Granneman has created a model system to change targeted cells from fat storage units to fat burners. Once the details of this cellular process are understood, pharmaceutical companies may be interested in developing drugs that will trigger this natural fat-burning capability.

The three CIMER faculty members have formed their own company, called NT², or New Targets Technologies, to rapidly translate new targets to commercialization. “It is basic research with a strong view toward translation,” said Dr. Leff.
Magnetic Attraction Pulls Cancer Drugs to Tumor Site

Scott Goodwin, MD

Patients undergoing chemotherapy often endure nausea, hair loss and other side effects because medications are delivered systemically and circulate throughout the entire body in high concentrations. Relief may be in sight thanks to the magnetic field created by a soup-can size magnet combined with iron and carbon particles.

Magnetic targeted drug delivery systems have been under investigation since the late 1970s, and are now becoming more popular as they improve site-specific delivery of drugs. Dr. Scott Goodwin, professor and chair of radiology, is principal investigator for a phase II research trial that will look at the efficacy of a novel magnetically targeted drug carrier (MTC) in the treatment of primary liver cancer. Wayne State University is one of approximately 20 sites across the country and the only site in Michigan to participate in the study.

In this trial, Doxorubicin, a common chemotherapy drug, is mixed with metallic iron—particles that provide a magnetic charge—and activated carbon, which allows the drug, MTC-DOX to be absorbed. The medicine is then infused directly to the liver through a catheter. During the infusion, a magnet is placed on the skin, over the site of the tumor (as determined by CT and angiography) for 15-30 minutes. The magnet draws the MTC-DOX directly into the tumor.

Preliminary studies have shown that the use of magnetic carriers provides a 10-fold increase in the amount of drug in the targeted area of the liver tumor. In addition, MTCs outside the targeted area are barely visible at all, indicating a substantial decrease in the systemic bioavailability of doxorubicin.

“Encouraging results bode well for the use of MTCs as a new and efficacious treatment for liver cell carcinoma, and metastasized liver cancer,” Dr. Goodwin said. Ongoing studies on lung targets also raise the possibility of future treatment for unresectable bronchogenic carcinoma. Furthermore, MTCs can absorb multiple chemotherapeutic agents, immunosuppressive agents and nucleic acids including plasmid DNA. At the moment, Dr. Goodwin plans to actively pursue liver and lung treatments, citing their redundant blood supply and ability to regenerate, which makes them promising targets.

Dr. Goodwin has been presenting this work across the world and recently spent time in China successfully lobbying the State Drug Administration (SDA) to conduct phase II clinical trials of MTC-DOX for hepatocellular carcinoma (HCC). Significantly, this is the first time China’s SDA has approved the clinical trial of an investigative technology that has yet to obtain approval for commercial use in the United States.

“China really needs to begin these trials, since HCC is the most prevalent cancer in the world, and the predominant cancer in Asia due to the endemic presence of the hepatitis B virus,” Dr. Goodwin said. With more than one million cases of liver cancer in China, it accounts for 43.7 percent of the worldwide incidence of the disease.

“If you add magnetic particles to the medicine internally, you can use a magnet externally to draw the medicine to the tumor site.”
DR. DOMENICO GATTI SAID GOODBYE TO BALL-AND-stick models of drug molecules long ago. Thanks to the power of computers and three-dimensional imaging, he can type a few keys and instantly produce clear, dynamic pictures of every atomic composition, chemical bond, folding protein, and molecular interaction imaginable.

The Advanced Laboratory for Macromolecular Crystallography provides powerful equipment for atomic level examination to determine the precise structures of protein drug complexes.

Under the direction of Drs. Brian Edwards, Domenico Gatti and Ladislau Kovari, the lab provides expertise in protein X-ray crystallography. This technique takes a target protein in crystalline form, then sends a powerful X-ray beam through it, diffracting the beam and generating a pattern that is unique to that protein. Complex analysis and calculations then determine the exact three-dimensional structure. With this information, researchers can see how drugs bind to target proteins—and this is the fundamental basis for drug design.

WSU’s lab is one of only five in the world to run a high-power X-ray generator capable of producing an X-ray beam that is 10 times stronger than conventional generators and is almost as strong as that of a particle accelerator. Using equipment like this, researchers can get an inside look at molecular interactions.

Pharmaceutical firms have already taken note of the Advanced Laboratory for Macromolecular Crystallography and have started designing compounds related to drug resistance, blood clotting and other problems, based on knowledge generated by WSU scientists.

‘RATHER THAN WONDER HOW TWO DRUGS MIGHT INTERACT IN THE BODY, YOU CAN PLUG THEIR STRUCTURES INTO THE COMPUTER AND WATCH IT AS IT HAPPENS.’

Domenico Gatti, PhD
Ladislau Kovari, PhD
Brian Edwards, PhD
Cancer Vaccines Offer Possible Alternatives to Chemotherapy

Malcolm Mitchell, MD
Gilda Hillman, PhD

IN THE FUTURE, harsh chemotherapy treatments could be replaced with individually tailored cancer vaccines, said Dr. Malcolm Mitchell, professor of internal medicine and immunology/microbiology and director of the Biological Therapy Program for the Barbara Ann Karmanos Cancer Institute.

The strategy is to enhance the response of the immune system against dangerous cancer cells. By vaccinating patients with their own malignant cells, the immune system recognizes the cancer as a pathogen and activates the lymphocytes to kill off the foreign bodies. In theory, immunotherapy could be used to treat any type of cancer, but vaccines can only work if the cancer is not too far advanced. Furthermore, individual treatments need to be tailored and specially designed for each mutation or genetic cause.

Several researchers are making great headway in designing cancer vaccines. Dr. Mitchell’s discovery of the MG50 antigen, which is involved in the immune response to cancer, could form the basis for a multi-cancer vaccine. The gene is expressed in melanoma, pancreatic cancer, prostate cancer and breast cancer, allowing testing to be done for a “universal vaccine strategy” that could work for any person who expresses the MG50 gene.

“Our goal is to present the antigens to the cancer in a vaccine in a way that the immune system can’t ignore in order to generate a strong immune response to the tumor,” Dr. Mitchell said.

Cancer vaccines and other anti-cancer drugs are also being developed for specific types of cancer. Dr. Gilda Hillman is harnessing the power of interleukin-2 and interferons to treat kidney and prostate cancer. Three major classes of interferons are activated by the body in response to viral infections and other pathogens. Interferons work in complex ways to attack tumor cells through a number of biological mechanisms including upregulation of tumor antigens, activation of T-cells, and expansion of lymphocytes, just to name a few. Dr. Hillman’s current collaborations focus on immunotherapy regimens combined with radiation that have already made it to clinical trials.

Many Wayne State researchers at the Karmanos Cancer Institute are involved in the latest immunotherapy research protocols. Countless clinical trials are underway to test the efficacy of vaccines for cancers of the brain, breast, colon, kidney, lung and skin.

“We hope to stimulate the body’s own response against cancer and reduce the negative side effects that are often associated with traditional cancer treatments,” Dr. Mitchell said. “We’ve made significant progress in the past decade, but there is much more work to be done.”

“By vaccinating patients with their own malignant cells, the immune system recognizes the cancer as a pathogen and activates the lymphocytes to kill off the foreign bodies.”
WHEN BHANU JENA SAYS HE’S CLOSE TO THE SOURCE, HE REALLY means it. While scientists have used light microscopes to look at cells since the 19th century, resolution has been limited by the wavelength of light. Dr. Jena and his research team circumvented this problem with their pioneering studies using the atomic force microscope (AFM) in the mid 1990s. Light microscopy could provide optical resolution of cell structures 300-400 nanometers in size. New AFM technology is capable of imaging biological samples at nanometer and subnanometer resolution.

Nanotechnology provides a most intimate view, allowing Dr. Jena to observe live cells at work in real time and at nanometer resolution. Already, he has documented the discovery of a new cellular structure at the plasma membrane where membrane-bound secretory vesicles dock and fuse to release vesicular contents. These studies have been corroborated and expanded and Dr. Jena’s laboratory recently found similar fusion pores in growth hormone secreting cells of the pituitary and in chromaffin cells.

Results from these and other studies have enabled Dr. Jena to design a way for drugs to be carried and released at target sites, with great precision and efficiency. In this scenario, chemotherapeutic drugs, for example, could be contained within a nanocapsule and released only in diseased cells.

“The drug within the nanocapsule can be released at the target site at 1,000 times more concentration than before,” Dr. Jena said. “The dissipation of the drug throughout the body at extremely low concentration will have little or no harmful side effects. Healthy cells are therefore spared.”

Dr. Jena is very interested in membrane fusion, which has direct implications on viral entry, neurotransmission, release of enzymes and hormones, and drug delivery systems.

“The main research focus of my laboratory is to understand the molecular mechanism of membrane fusion in cells,” Dr. Jena said. “Understanding this vital process will enable us to determine how cells communicate, how neurotransmission, enzyme secretion or hormone release occurs, and how viruses enter and exit cells. This knowledge will help us design and develop drugs to ameliorate secretory defects or regulate the cellular entry and exit of pathogenic viruses.”
Trained as a chemical engineer, Dr. Rod Braun is drawing upon his multidisciplinary knowledge to design better drug delivery systems.

“First, we have to figure out how to get the drug through the blood vessel wall and into the tumor. Then, we have to figure out how to get the drug to penetrate deep into the tumor,” he says. “One way to try to do this is to encapsulate the drug in fat droplets, called liposomes. These liposomes cross the vessel wall and accumulate in the tumor, and they can be triggered to release their contents all at once.”

While at Duke University Medical Center, Dr. Braun was part of a research team headed by Drs. Mark Dewhirst and David Needham. They patented a particular set of low-temperature sensitive liposomes (LTSLs) that are triggered by precise temperature changes to release their contents. Previously, liposomes had to be heated to 42 degrees Celsius; the new LTSLs have a faster release rate at a temperature of only 40 degrees. In the initial studies, heat-activated liposomes were used to shrink 16 of the 19 tumors examined. The studies looked at liposomes carrying doxorubicin, an anti-cancer agent, for the treatment of leg tumors. As heat was applied in the area of the tumor, the tumor vessels became leakier, increased liposomes were delivered to the targeted location, and the liposome membranes broke apart as they released the drug into the tumor.

Dr. Braun says this therapy has great promise for tumors that are near the skin’s surface and can be heated, but other deeply embedded tumors would probably not respond. The LTSL therapy shows the most promise for tumors of the skin, head, neck, eye, and perhaps the breast and prostate.

Dr. Braun makes liposomes in the lab and uses them to carry drugs to targeted sites and to mark blood flow. As he begins to study drug delivery systems, his research may go in a number of directions, depending on results from his preliminary studies and collaborations. “I am always looking for new ways to get more drugs into the tumor,” Dr. Braun said. “In addition to liposome therapy, I am exploring other treatment options including photodynamic therapy, which uses light and light-sensitive drugs to kill tumors.”

With a National Institutes of Health grant, Dr. Braun is studying the roles of nitric oxide and oxygen in ocular melanoma. By characterizing tumor oxygenation and blood flow in blood vessels and tumors, he is able to understand how drugs can be transported and released more efficiently.

“Dr. Braun used heat-activated liposome therapy to shrink all of the tumors he initially examined.”

Institute for Drug Design Pools Brainpower

“The strategy for drug discovery has changed entirely,” said Dr. Shahriar Mobashery. “Twenty-five years ago, chemists would work on something, then pass it along to the biologists who would evaluate it and send it back. Then the drug metabolism experts would finally see it a year or two later and point out more difficulties, and it was back to the drawing board again. This was not the most efficient way to work.”

To promote multidisciplinary research, Dr. Mobashery has established the Institute for Drug Design at Wayne State University. The institute combines the expertise of more than 30 faculty members from various areas of Wayne State University: the School of Medicine, College of Pharmacy and Allied Health, and College of Science.

“The pharmaceutical industry is healthy enough financially to do much of its own research in-house, but they like getting the unique research angle that an academic scientist can provide,” Dr. Mobashery said. “The pharmaceutical companies have a limited scope in producing pharmaceutical agents that would make them money. University researchers are not held back by corporate decisions. They can work on areas that are scientifically important, even if there isn’t an immediate translational tie. Over time, though, human application may also come from basic science, but industry won’t spend the money on it long-term unless the financial rewards are apparent.”

The Department of Pharmacology, under the leadership of Dr. Bonnie Sloane, is proposing an interdisciplinary training program by the name of D3, which stands for drug discovery, design, and development. WSU is applying for funding for this program that already has support from many pharmaceutical and biotech companies who have agreed to serve as training sites for student and faculty participants. “This program helps universities acknowledge that we must train scientists in a way that meets the needs of the industries we cater to,” Dr. Mobashery explained. “We need researchers to be multidisciplinary, because the pharmaceutical industry certainly is.”
Students go to medical school to learn about restoring the human body. Ironically, the learning process begins by taking it apart.

Gross anatomy is a rite of passage for medical students. On the very first day of class, eager physicians-in-training are handed a scalpel and asked to explore the human body more intimately than they’ve ever done before. It’s ironic that their first experience of compassion and humanity is taught by a cadaver whose name they’ll never know, but whose lessons will be remembered through their entire medical career.
ALTHOUGH dissection feels like a destructive act at first, it is full of purpose and necessity. Approximately 200 people per year donate their bodies to Wayne State University for medical education and research. Barbara Rosso, who has run the Body Bequest Program for the past 11 years, says anatomy is one of the most important courses in the education of a physician and there is a constant need for anatomical material. Bodies donated to WSU are typically stored for two years and are used by medical, dental, physical therapy and nursing students and residents.

“People who donate their bodies to science help health professionals master human anatomy. They teach physicians the intricacies, names, functions and complexities of all the body’s components. After studying countless diagrams, students are able to actually see how systems of the body relate to one another and work together,” Rosso said.

Mark Ireland, PhD, is co-director of the gross anatomy course. He says anxiety is a normal reaction to the dissection experience; and in fact, he believes it fosters humanistic doctors who reflect compassion and empathy for their patients. “The trepidation and anxiety that greets gross anatomy students on day one is eventually replaced with respect for the human body and satisfaction with their ability to understand how it works,” Dr. Ireland said.

“It’s just not the same to learn it in the books,” said student Dan Lis. “Since I was a child, all the biology books were drawn with arteries colored red and veins colored blue. Obviously, that is not realistic, but I half expected to see it that way. It’s incredible to view human structures in their natural state.”

Following the tradition of medical schools across the country, the gross anatomy course begins on the first day of school in early August and lasts until mid-November. During orientation week, students watch an introductory video to help them prepare. They learn about laboratory etiquette, common courtesy and tactile skills to assist their dissections.

The class of approximately 260 students is divided into small groups of 4-5 students per cadaver. Each lab session focuses on a different region of the body and professors circulate to each table to guide students through the discovery process. Day one begins with an incision through the chest and a close look at the axilla, or armpit region. After 33 sessions in the lab, the foot is the final task. Although students say they enjoy it immensely and learn a great deal, they agree it is extremely challenging—mentally, academically and emotionally.

Students are tested through four practical and four written exams. The practical exams are based on basic anatomy learned through the dissections. Students are asked to identify parts of the body and how they relate to one another. The written exams address higher-order learning and ask students what different organs do, how blood is delivered, or how one system affects another.

Former course director, Dr. Jerald Mitchell, retired last year after running gross anatomy for nearly a decade. He often reminded students to appreciate the richness of the experience at hand. “I know that the hectic pace of the course makes it difficult to reflect on your dissection experience, to have time to assess your emotional development and to appreciate the beauty of the organization of the human body. However, take time to get in touch with your thoughts and feelings so as not become just a fact-spouting robot,” he said.

When students are first presented with their cadaver, they know only the person’s age and cause of death. No other information is provided. But, as the weeks progress, students learn a great deal through their own exploration.

Student Dmitriy Nikolavsky from table 56 recalls several key moments during the dissections. For him, the hardest day was removing the leg. “Disconnecting the body felt like a real violation that was difficult to come to terms with,” he said. The messiest day was the pelvis, the most personal day was studying the hand, and the most rewarding day was the heart. His experience echoes that of many students.

In fact, Dr. Mitchell addressed this message to the class of 2004 after they dissected the heart. “The heart dissection lab is always the most rewarding. It is the peak experience; it is the degree of learning going on during the heart lab and this class did not disappoint. Standing ANXIETY IS A NORMAL REACTION TO THE DISSECTION EXPERIENCE; AND IN FACT, IT FOSTERS HUMANISTIC DOCTORS WHO REFLECT COMPASSION AND EMPATHY FOR THEIR PATIENTS.
at the end of the lab, I enjoyed an overview of the extra excitement everyone brought to the dissection. A gamut of reactions was apparent. One student lifts the heart free from the thorax with an expression of triumph; each table evidences a different response. One registers surprise at how the heart suddenly seems smaller once out of the chest, another winces at the sight of its removal, one reflects preoccupation with deep thoughts evoked by the experience. The energy of learning was almost palpable as groups encircled each heart to look intently at the details of its interior. Of course, on reflection, virtually every part of the body is amazing in structure, and important in function. However, perhaps because this hollow muscle, the heart, is so laden with symbolic meanings and rich in emotional connotations, it unfailingly evokes special excitement.

Krishnan Venkatesan said he was able to make clear clinical correlations throughout the dissection. For example, he said he always knew about carpal tunnel syndrome, but it suddenly made perfect sense to him when he personally viewed the anatomy of the arm and wrist. He found himself looking at his own arm, moving it this way and that to see what muscles and tendons were controlling various movements.

“The most amazing thing to me is that most people manage to stay relatively healthy, despite the great multitude of things that can go wrong in the body,” Venkatesan said. In observing several other groups and their prosections, he saw evidence of breast implants, hernias, tumors, a glass eye, surgery scars, a heart bypass, hysterectomy and prostate stones. “It’s remarkable that the body survives so long with so many possibilities for things to go bad. We are really remarkable creatures,” he said.

Each spring, the remains of the bodies are cremated and a memorial service is held to honor those who bequest their bodies. The service is officiated by two pastors and is attended by family members of the deceased and WSU students and faculty. A university burial plot at Oakland Hills Memorial Gardens Cemetery marks the cremated remains of all donors who have served the School of Medicine. The headstone reads: “The dead shall teach the living.”

“I’m glad there’s a memorial service to wrap up the process,” said student Angela Groves. “Although I was eager to learn, I felt a little bad every day, wondering about this man’s family and life. This gives us a chance to thank him for what he did.”

Recalling her gross anatomy experience, Jessica Shill, class of 1991 wrote a letter in the school newspaper called “Dear Friend.” In it, she reflects on the courageous character of those who donate their bodies to advance health and medicine.

“In order to donate your body, not only did you have to be comfortable with the idea that death is final, but to be so giving that in
your last chance to have a say in the world, you put others ahead of yourself. Through your gift, you were telling me that what I needed to do was OK, and that you supported my fellow classmates and me. I was reminded by your courageous and selfless decision, that patients are often much braver than their physicians,” Shill wrote.

Shill’s letter concludes with these thoughts, “I am proud you let me be by your side. Thank you for your bravery, your strong sense of self, and your generosity. In return, I took good care of you, respected you, and learned as much as I could about anatomy and life. I hope I served you right.”

AN ANNUAL MEMORIAL IS HELD TO HONOR THOSE WHO VOLUNTARILY BEQUEST THEIR BODIES TO THE WSU SCHOOL OF MEDICINE. A UNIVERSITY BURIAL PLOT AT OAKLAND HILLS MEMORIAL GARDENS CEMETERY MARKS THE CREMATED REMAINS OF ALL DONORS WHO HAVE SERVED THE SCHOOL OF MEDICINE. THE HEADSTONE READS: “THE DEAD SHALL TEACH THE LIVING.”

FOR MORE INFORMATION ON THE BODY BEQUEST PROGRAM, PLEASE CALL (313) 577-1188.
Some might say that 93 years is a long time to live. For Lawrence Pratt, MD, ’34, it has not been nearly long enough to accomplish all his goals. Born Dec. 20, 1907, in Paris, Ill., Dr. Pratt has accomplished more than most people could in several lifetimes — and he is far from finished.

Dr. Pratt left his tiny, southern-Illinois hometown for Detroit and Wayne State University in 1926. He earned a bachelor’s degree from WSU in 1930 before going on to medical school. (He returned to WSU for a master’s degree in education in 1960.) In 1935, he joined the staff of Grace Hospital as a thoracic surgeon.

While many young physicians of the era heeded the call of World War II, few share war stories of as much historical significance as Dr. Lawrence Pratt.

“I was part of a mobile surgical team in the 3rd Army and we were the only ones who could perform open-chest surgery,” Dr. Pratt said. “Gen. Patton — or whoever made those kinds of decisions for him — shuttled us wherever there was work to do. I’d take care of the backlog of work in one place and then move on.”

In June 1944, Dr. Pratt’s special skills took him to the beaches of Normandy for the Allied Forces’ D-Day invasion. Later that year, his team would be called upon again to take their place in military history at the Battle of the Bulge.

“I had been in Germany, near the Italian border, when I was told we were needed in Belgium,” Dr. Pratt said, recalling his experiences of late-December 1944. “When we arrived, they surrounded my team with the 4th Armored Division and put us on the road to Bastogne.”
Unbeknownst to Dr. Pratt and his team until their arrival, the quaint town of Bastogne, Belgium, just west of the Luxemburg border in the middle of the Ardennes Forest, was under siege by German forces.

“We were on the road for two days trying to get through (the German lines),” Dr. Pratt said. “Finally on our third try, we got through.

As a trained thoracic surgeon, Dr. Pratt was part of a World War II mobile surgical team, providing superior care to fellow soldiers.

“When we finally got into Bastogne, I told my team to get some rest and I would report our arrival. I was taken to the command center and when I got there, the officers’ insignias were so covered in mud, I couldn’t tell who or what any of them were.

“‘It’s nice to have a fresh team here,’ one of the officers told me. When I started laughing, he asked me what was so funny. I recounted our journey for him and told him we might be new, but I wasn’t sure about fresh. I was told afterward that the man I had been speaking to was Gen. MacAuliffe.”

World War II history buffs will remember Gen. A.C. MacAuliffe as the man who led the 101st Airborne during its gallant defense of Bastogne and who, when asked by the Germans to surrender, reportedly offered perhaps the most famous one-word answer in military history: “Nuts.”

Dr. Lawrence Pratt and colleague.
After the war, Dr. Pratt returned to Detroit and his successful medical practice. While most men who served their country during World War II would have been content to live out their years in gainful employ, Dr. Pratt answered the call to serve again in 1963. This time, however, he needed a little encouragement to meet destiny.

“I was living in Grosse Pointe and I had everything: a good practice, a beautiful house, a family. Then, out of the clear-blue sky, I got a call from Washington. ‘We need to talk to about a problem,’ the man on the phone said.”

The man on the phone wanted Dr. Pratt to join the U.S. State Department as a foreign-service officer. More importantly, the man wanted Dr. Pratt to go to Vietnam to do something that had not been done successfully in four tries: start a medical school in Saigon.

“I’m at the top of everything and they want me to go to Vietnam and do this, so I talk to my wife. She tells me, ‘We have everything we can attain materially. Why not let this happen?’”

With that bit of encouragement Dr. Pratt and his wife, a successful dermatologist, departed for Saigon. As with everything else in his life, Dr. Pratt was determined to succeed where others could have – or already had – failed. Dr. Pratt’s relationship with Vietnam would have a lasting impact both on the people of that country and on the doctor himself.

The medical school Dr. Pratt struggled to found and oversee from 1963 to the end of the American presence in Vietnam in 1975 is still operating – producing much-needed physicians for that impoverished country. The successful efforts of Dr. Pratt and his colleagues are chronicled in the book, *Saigon Medical School: An Experiment in International Medical Education* (American Medical Association, 1988).

While the success of the Saigon medical school remains a point of great pride for Dr. Pratt, at the time he was very concerned about the fate that awaited his former students under Communist rule. When more than 500 refugee physicians came to America shortly after the departure of American forces in 1975, Dr. Pratt went to work on their behalf.

“After we got them here, they couldn’t speak English and they weren’t trained in American medicine, so they obviously couldn’t get licensed.

“In the mid-1970s, Vietnam was a dirty word in Washington. Nobody wanted anything to do with it. I went all over before I finally found a man in the Department of Health, Education and Welfare who would help.”

The help Dr. Pratt got was enough financial and political support to establish centers throughout the country that would offer two-month, intensive training programs to refugee physicians.

“Of our original 507 refugees, 497 of them passed the licensing exam on the first try,” Dr. Pratt proudly said. “Most of them went into underserved areas of the United States to practice.”

After he had successfully established the means by which his Vietnamese former students could have the chance to practice in America, Dr. Pratt decided it was time for he and his second wife Susie to relax in the relative peace of San Diego. It was a plan that lasted almost a whole month.

“About two weeks after I got there, I get a call from Orange County. They needed help with the clinic they had set up to treat Vietnamese refugees who were arriving in southern California.

“After I got that up and running, they had something else for me to do, then something else. I ended up working for them for nearly 10 years.”

When his stint in southern California was finally up, Dr. Pratt could not bring himself to “retire” again. Instead, he set his sights on trying to solve the problems of a different continent.

In the mid-1980s, Dr. Pratt established Seven Seas Development Corp. to serve as a catalyst for community development in West Africa. While he has been toiling on this project for nearly two decades, Dr. Pratt is just now seeing the possibility of his plans come to fruition.

“I’ve been funding this project myself for 20 years. Now, I think I may have located some financial partners to assist me.”

Dr. Pratt’s eventual plans for Seven Seas call for money and personnel to help establish a model of community development for the region.

“We want to help people there get clean water, build houses, raise crops and, most importantly, provide their children with an education from an early age. The final part is what I think can make all the difference: education is the key to a better life.”

While his dreams for a better and more livable region for the people of West Africa may be a long way off, Dr. Pratt’s experiences have taught him one thing, if nothing else: patience.

“There’s a lot of work yet to be done, but I’m only 93. I plan to be at this for a long time.”
SEEKING Healthy Sperm
AN INTERNATIONAL RESEARCH TEAM based at Wayne State University is developing a simple, non-invasive screening test that will not only determine whether a man is infertile, but will reveal the cause of that individual’s infertility. On a broader scale, the work may answer the widely publicized question of whether the general male population in the United States and other western nations is actually experiencing a decline in fertility, and if so, identify probable culprits as well as solutions.

For couples who are having difficulty starting a family, the news means that men may soon be able to skip the extensive battery of tests, including a testicular biopsy, that is currently part of the infertility screening. Instead, they may only need to provide a sperm sample. In addition, the research team believes the test may provide enough specific information so that medical professionals can better direct treatments, or can identify which couples will never conceive. The latter diagnosis will allow couples to forgo the lengthy, expensive, and ultimately futile infertility therapy, and begin considering other options, such as sperm donors.

This promising new test will likely have a broad reach, remarked one of the team members. “Infertility involves about one out of every six couples who are trying to conceive, so it is actually a huge clinical problem that many couples face,” said Michael Diamond, MD, the Kamran S. Moghissi Professor and associate chairman of the WSU obstetrics and gynecology department. He added that most infertile men actually produce sperm, but for some reason, those sperm are unable to fertilize an egg. “If this new technique does all of the things we’re hoping and expecting it to do, it could change the way male-factor infertility is diagnosed around the country and around the world.”

Beyond that, he added, “It has all sorts of potential when you start looking at what effects pharmaceutical drugs have on sperm, sperm function and other sperm characteristics. It can also possibly establish the effects of environmental toxins, alcohol, caffeine, smoking or illicit drugs on sperm. So this work may have extensive impacts.”
More Than Just DNA

The test grew from a finding made simultaneously in two labs an ocean apart. Stephen Krawetz at Wayne State and David Miller at the University of Leeds in the U.K. separately verified that male sperm conferred something other than DNA during fertilization. These male reproductive cells also carried mRNA, or the genetic message with the blueprint for making the sperm. Upon learning of his research, Krawetz contacted Miller, and the two started working together. Miller soon decided to spend time in Krawetz’s lab, and is currently at Wayne State pursuing their investigation.

“We thought that if we could analyze that message in the mRNA, and compare an infertile man with men who are normally fertile — those who have fathered children — and see differences, then we would be getting closer to narrowing down what the cause of that man’s infertility is,” said Miller, PhD, associate professor in the department of obstetrics and gynecology at Leeds. “In other words, we feel that the mRNA message is crucial to understanding what’s gone wrong.”

The collaboration didn’t end there. “At the same time, I met David Dix of the Environmental Protection Agency,” said Krawetz, PhD, of the WSU obstetrics and gynecology department, and the university’s Center for Molecular Medicine and Genetics (CMMG) and Institute for Scientific Computing. “We put together this research triangle between Wayne State, the EPA and the University of Leeds, and through that, I was invited to be one of the founding members of the EPA Microarray Consortium (http://www.epa.gov/nheerl/epamac). This partnership enabled us to produce arrays that were capable of examining expression of testes-specific genes, which allowed this research to advance more quickly than relying on commercially available arrays,” Dr. Krawetz said.

Microarrays have become a crucial component of the project because of their capabilities as high-tech indicators that can quickly search out specific genes present in genetic material, and detect whether they are affecting fertility.

Microarrays and mRNA

With their verification of mRNA in sperm and the addition of microarrays to their research, the team’s work began in earnest. “The first question we posed when the group got together was: Could we use this technology to rapidly identify what mRNAs are present in human sperm?” Dr. Krawetz recalled. They could, and they did.

“We isolated some 20,000 mRNAs from a pool of normal individuals just to get an idea of what the normal human population has,” he said. They then developed microarrays containing tiny sites that trap specific mRNA. When sperm is added, color changes at each trap site indicate whether the sperm includes each bit of mRNA. Almost immediately, the researchers can scan the sperm to tell which mRNA, and which associated genes, are present. They already have a basic profile of a fertile male, and are refining it now.

Next, they will begin to study infertile men. Using the same technology, they will add infertile sperm to the microarrays to compare it against the fertile-male profile. They will then document the points of difference, run those discrepancies through an algorithm they are developing with help from the WSU computer science department, and deduce the causes of male-factor infertility.

“We would ‘spot,’ or add, onto the microarray all the genes that we find are associated with male factor infertility,” Dr. Miller described. “Then it would be a machine, basically, that would read off and give the clinician some idea of a) what the underlying causes are, and b) what options the patient has for treatment or management of his infertility.”

Dr. Krawetz added, “On the basis of this work, we believe we will be able to devise a preclinical screen for men or couples who are seeking infertility counseling. We should be able to detect a certain percentage of the population who are infertile based on their patterns of mRNA.”

Environmental Health

This work may also have ramifications for male reproductive health in general, the research team asserts. “We feel this is going to be quite important in the next few years in not just unraveling what causes a man’s infertility, but also in helping us to understand whether there really are reductions in sperm counts occurring in men in the West. If that’s the case, we might get some handle on what’s causing that too,” Miller said, explaining that the normal-male profile will again provide the basis for the comparison.

“Over the last 10 years, there has been an increasing amount of concern about the potential effects of environmental exposures on human reproductive health,” reported team member David Dix, PhD, a research biologist and microarray specialist at the EPA. He cited the recent media coverage of endocrine-disrupting chemicals and their possible connection to male fertility as one example.

With the new normal-male profile and microarrays, Dr. Dix said, “We now have a window into the male reproductive system in which we can monitor overall reproductive health with precision. In fact, we can get tens of thousands of different questions answered from a single experiment — not only predicting for us whether this individual
will be fertile or not, but giving us a detailed description of the gene-environment interaction for that individual.” In the latter case, microarrays would target genetic differences between the normal-male model and men who have been exposed to suspected toxins. “You can create a whole series of tools, or perhaps one very large microarray tool, that would allow you to monitor the potential effects of environmental chemicals on male reproductive health,” Dr. Dix said.

The microarray test would give a man a quick determination of whether his sperm had been adversely affected by a toxin. “That approach would take into account not only how most people respond and the exposure limits that have been set on how most people seem to respond, but how each individual responds,” he said, pointing out that different men have different genetic susceptibilities.

It would be particularly beneficial to men who are at high risk of environmental-toxin exposure through the workplace, Dr. Krawetz added. A company, for instance, could use the microarray test to monitor its male employees for overall exposure-induced changes in fertility, while an employee who was trying to start a family might request a test to ensure he was fertile. If a problem did arise, the employee could curtail his exposure, and simply wait the average 60-90 days for his body to replace the old sperm with new, unexposed sperm. Dr. Krawetz noted, “This is the future of testing and patient care.”

**Patents and Potential**

In addition, their research may be a boon to animal husbandry, he continued. “Beef production is a good example. Cattle have a long gestation time, so if you could ensure that every pregnancy outcome was successful, you could increase your beef production, and the profit margin would then go up considerably.”

Dr. Miller added, “It can be applied to any animal of economic value to help improve the breeding stock. We know that most other animals that have been studied have mRNA in their sperm, too, so it wouldn’t be difficult to extend this to examine the spermatozoa of those animals.”

Buoyed by their success and the great potential of this work, the researchers have jointly filed provisional-patent applications on the technology, and anticipate full patents by the end of 2002.

Mostly, however, they look forward to the research yet to come.

“This shows that international collaboration is essential to furthering successful science,” Dr. Miller remarked. “It also shows that there is room still for communication beyond the bounds of the United States and vice versa, and it is going to be for the common good.”

Added Dr. Diamond, “We’ve heard so much about the Human Genome Project. At least on the OB/GYN side, this will be one of the original approaches that actually takes some of that information about all of the genes that have been identified and brings it to the practice of medicine. This is the type of thing that can come from these sorts of investments in the future.”

Dr. Krawetz is creating genetic profiles for fertile and infertile men.
WAYNE STATE DOCTORS PREVIEW 4-D ULTRASOUND TECHNOLOGY

PARENTS-TO-BE NOW HAVE AN alternative to the hard-to-inter- pret ultrasound pictures of their growing fetus. In contrast to tra- ditional two-dimensional ultra- sound, new 3- and 4-dimensional (4-D) imaging techniques allow physicians to create a real-time, life-like picture of the fetus, which can be rotated and viewed from many different angles, aiding in the detection of congenital anomalies of the face, skull, spine, heart, abdomen and extremities.

For the past year, Wayne State University physicians at Hutzel Hospital have been previewing the latest 4-D ultrasound equip- ment to evaluate its advantages over 3-D imaging. They are cur- rently reviewing data to compare resolution and other factors. Potential advantages of the Medison 730 machine are greater sensitivity to tissue differentiation and real-time capabilities.

Numerous studies from across the country have shown the value of 3-D ultrasound imaging over the traditional two-dimensional method in detecting fetal abnor- malities and estimating fetal weight and growth. The major advantage is this: 3-D imaging relays multiplanar information and assesses volume, while tradi-
tional ultrasound can only represent flat images. The advantage of 4-D imaging is the added element of time. Surface renderings constructed in 3-D require frames to be frozen and reconstructed. With 4-D there is little time delay.

“In most cases, a standard 2-D image provides enough diagnostic information about the baby. But higher resolution ultrasound is extremely useful for a fetus with a cleft lip or other surface abnormality, for example. The technology allows us to pinpoint subtle features and understand the extent of the problem before we counsel parents and other specialists about treatment,” said Dr. Marjorie Treadwell, associate professor of obstetrics and gynecology at WSU, and director of obstetric ultrasound at Hutzel Hospital.

Although the 3- and 4-D procedures are similar to traditional ultrasound, the high-tech machines cost more than the standard machines found in most obstetrician offices. This added expense may limit general use of the new machines. “For now, the primary clinical application of 3- and 4-D imaging in obstetrics is further evaluation of fetal anomalies,” said Dr. Treadwell. “Studies already show success in screening for congenital anomalies. Other uses are still being developed and evaluated, including use in tumor evaluation, cardiac evaluation and diagnosis of fibroids.”

WSU’s Perinatology Research Branch Improves Health for Women and Children

SINCE THE EARLY 1990S, THE WAYNE STATE University School of Medicine and Hutzel Hospital have been home to the Perinatology Research Branch (PRB), an intramural branch of the National Institute of Child Health and Human Development of the National Institutes of Health (NIH). Based on the resources and expertise provided by the PRB, researchers and clinicians at WSU and Hutzel Hospital are able to offer a superior level of obstetrical care for women in the Detroit community, while contributing to national research programs that improve the health of women and children across the country.

The PRB at WSU is one of the few NIH branches located outside of the Washington, D.C. area, and this is the only arrangement of its kind between the NIH and an academic medical center.

The existence of an NIH branch on a university campus constitutes a unique advantage to the university and the Detroit Medical Center. Thanks to the advantages made available by the presence of the PRB, Hutzel Hospital has continuously achieved higher levels of favorable outcomes than the majority of hospitals, despite its disproportionately high number of high-risk pregnancies.

According to Dr. John Malone, chair of obstetrics and gynecology, it is crucial to the people of Michigan that WSU retain the PRB. “Although the center is dedicated to research, the byproduct of this endeavor is improved patient care through the latest research and technology available,” he said. “The PRB guarantees world-class care that would likely be unavailable otherwise for underserved, high-risk populations.”
BETWEEN WORKING to start up a major transplant center, leading transplant teams in such groundbreaking procedures as the world’s first living-donor, mother-to-infant nerve transplant, actively participating in the research behind the nation’s first hand transplant, and conducting research, Dr. Scott Gruber is always busy. For example, when Wayne Medicine finally caught up to him for an interview for this article, he was just winding up a very long day in which he performed back-to-back kidney transplants.
GRUBER, MD, PhD, HAD GRAND PLANS when he joined Wayne State and the Detroit Medical Center (DMC) last July. With positions as WSU professor of surgery, as well as director of the pancreas transplant program at Harper Hospital, he wanted to create one of the nation’s foremost organ transplant centers. He is already well on the way.

In the four months since he arrived in Detroit, Dr. Gruber had pulled together the makings of a stellar surgical transplant team, boosted the number of kidney transplants from an average of about two per month to two per week, and taken steps toward setting up an ambitious transplant center to serve the needs of Michigan residents.

“This is the vision for the future of transplantation at the DMC,” Dr. Gruber said. “Our first goal is to greatly expand the number of kidney transplants being done at Harper. Fortunately, the institution decided to invest heavily in transplantation, and that challenge to rebuild and rejuvenate the transplant program is what brought me to Detroit. Now, compared to a program that did 25 kidneys a year, we’ve already done 12 in the last six weeks.” He envisions the center averaging 60-70 kidney transplants annually.

He also began recruiting members to the transplant team. One of the first was transplant surgeon Miguel West. “He’s a fabulous guy,” Dr. Gruber declared. “He was just voted one of the top 100 African-American doctors in the country. He’s an expert laparoscopic surgeon, who was chief of kidney and pancreas transplantation at Howard University in D.C. I was fortunate enough to be able to recruit him here because he wanted to do more transplants.” Dr. Gruber has also signed on a second transplant nephrologist, a pathologist, third and fourth coordinators, and a full-time transplant social worker, and is looking for yet another transplant surgeon and a clinical transplant pharmacist. He is assisting in the recruitment of a new director of the HLA Laboratory and a fourth pediatric nephrologist for Children’s Hospital.

Beyond personnel, his vision includes a fully renovated transplant floor at Harper that will feature a new “step-down” area. “In the past, newly transplanted patients would always go directly to the ICU, which was a really expensive and unnecessary waste of resources.” He explained that the new step-down area has a 1:3 nurse-to-patient ratio around the clock, and will permit the transplant
team to cater more fully to the patients’ needs. “These are just a few examples of the million little details that make a transplant program work: everything from new drug assays, to making sure patients get their chest X-rays before surgery, to pharmacy issues.”

The results are already paying off. “A few weeks ago, we did Harper’s first laparoscopic live-donor nephrectomy and living-donor kidney transplant. In this procedure, the kidney is removed from the living donor through a small incision with the use of the laparoscope,” he explained, noting that Dr. West performed the donor surgery and he the recipient surgery. “The donor has less pain, gets home faster and returns to work a lot quicker, so more people are willing to be living donors.” He and his transplant team have already begun publicizing the laparoscopic donor procedure as a new option at the DMC.

He also hopes to begin offering pancreas transplants, a service that he believes Michigan sorely needs. “More than half of the donor pancreases that are procured in our state are sent out of state to be transplanted elsewhere. And an additional good number of suitable pancreases are not even being procured — the most common reason being that no surgeon is available to procure them.” He added, “In fact, while all over the country the number of pancreas transplants has doubled between 1993 and 2000, in our state, it has halved.”

Dr. Gruber, whose specialty is pancreas transplants, is ready to fill the void. “We already have approval for a pancreas transplant program from the United Network for Organ Sharing, but we still require the “certificate of need” (CON) from the state, and Michigan is the most restrictive state in the country in terms of CON requirements for pancreas transplants.” He has already made three trips to Lansing in pursuit of the certificate and the group at DMC has followed up with letters to congressmen. “We’re fighting for this big-time, because there is an urgent need for another pancreas transplant program in the state.” He noted that of the three facilities in Michigan that are currently authorized to perform pancreas transplants, one has shut down for the last three years, another only does two to three per year, and the busiest does only 12 a year. As a result, many pancreas transplant candidates — usually people who have long-standing, insulin-dependent diabetes — now travel from Michigan to Minnesota or other nearby states for transplants, he said.

He also looks forward to continuing his work with nerve and hand transplants. He remarked, “These transplants are exciting, they’re cutting edge, but they’re clearly experimental.” In one case, he led the team that transplanted nerves from a woman into her 8-month-old son. The November 2000 surgery treated obstetric brachial plexus palsy, a childbirth-caused condition that left the child with no use of his left arm. The surgery marked both the youngest patient ever to undergo a nerve transplant, and the first time that a living donor had been involved in a nerve transplant. Dr. Gruber was also a member of the Louisville hand transplant team that performed the January 1999 removal and attachment of the hand and forearm from a cadaver to a 37-year-old patient.

Such procedures are called composite transplants, because of the variety of tissues involved, Dr. Gruber said. “The transplant consists of a variety of different tissues – skin, muscle, bone, nerve,
cartilage, tendon, bone marrow – each of which has a different tendency for rejection. It’s not like a kidney, which is one solid organ, one tissue.” Other medical teams around the world have since followed the lead and conducted their own successful unilateral and bilateral hand transplants.

Besides adding composite tissue transplants to the options at the DMC, he anticipates devoting more time to his research interests once the clinical demands of his new position stabilize. “For instance, I was involved in some basic research that demonstrated the feasibility of proceeding with the hand transplant,” he remarked. “I had always been interested in local drug therapy of organ transplants, that is, giving the drug directly to the transplanted organ as opposed to giving it systemically. The idea is to prevent rejection, but decrease systemic side effects.” He and his research group conducted a series of studies to evaluate the pharmacokinetic advantage of intra-arterial infusion of immunosuppressive agents into the limb.

For now, however, Dr. Gruber is concentrating on increasing the variety and number of organ transplants available at the DMC, and initiating a full-fledged transplant institute where researchers and clinicians can work together and share ideas. “Transplants are a very unifying thing because they span so many different areas,” he said, pointing to the connection between hand and nerve transplants and the Rehabilitation Center; between a proposed islet-cell transplant program, whole-organ pancreas transplants, and the treatment of young diabetes patients at Children’s Hospital; and between advanced technology research and new surgical techniques, such as laparoscopy.

His vision for an institute is taking shape. “I think that the opportunity is great. So far, everything that I’ve been promised seems either to have come true or to be coming true. Considering that I’ve only been here since July 1, things are already moving at supersonic speed.”

The transplant team recently performed Harper Hospital’s first laparoscopic live-donor nephrectomy and living-donor kidney transplant.
IF ASKED TO LIST AMERICA’S GREATEST PUBLIC-HEALTH concerns, few of us would be likely to include work-related illness and injury near the top of the list. While some of the individual cases may sound relatively minor, some can be very serious, even life-threatening. Besides, one look at the statistics may prompt us to reconsider. According to the National Institute for Occupational Safety and Health (NIOSH), an average of 9,000 U.S. workers sustain disabling injuries on the job each day. Another 16 workers die each day from an injury sustained at work while 137 more die from work-related diseases.

The economic burden of work-related health risks is also high. Data from a NIOSH-funded study reveal that the direct and indirect costs of occupational injuries and illnesses in the United States approach $171 billion annually.

As might be expected, an employer as large and diverse as the city of Detroit experiences its fair share of worker illness and injury. With nearly 18,000 full-time employees, Detroit is one of the largest employers in southeast Michigan and one of the largest local-government entities in the country. Between its police force, fire fighters and other municipal employees, the city has between 800 and 1,200 ongoing workers’ compensation cases at any given time.
Until recently, administration of Detroit’s workers’ compensation program was a logistical nightmare. The city had no real way to track or investigate claims, making it nearly impossible to determine their legitimacy or to identify epidemiological trends that could be used to reduce risk factors. All this changed when James Blessman came along.

James Blessman, MD, MPH, assistant professor in the WSU Department of Family Medicine and director of its Division of Occupational and Environmental Medicine (OEM), has served as medical director for Detroit city employees for the past five years. In addition to providing a safer work environment for city employees, Dr. Blessman estimates that he and his colleagues have saved the city more than $15 million.

As a kid growing up on Detroit’s southeast side, James Blessman had no burning desire to be a physician. He was more interested in the growing world of computers than he was in any of that boring biology stuff. Despite his lack of interest in the more traditional science fields, young James was an exceptional student who longed to tackle new academic challenges of any kind. When presented with the opportunity to attend prestigious Cass Technical High School – even if it was through the school’s chemical-biological curriculum – he jumped at the chance.

Despite any early apprehensions he may have had, James Blessman has developed a fairly deep interest in biological science in the years since. After graduating with honors from Cass Tech, his interest was piqued enough to go on for an undergraduate degree in zoology from the University of Michigan, a medical degree from Michigan State University and a master of public health degree from the University of Washington.

It is ironic that, in his current role with the city of Detroit, Dr. Blessman relies just as much on his longstanding interest in computers as he does his background in medicine. One of his first accomplishments as medical director was to create a database that allowed the city to track its more than 45,000 workers’ compensation claims.

“It allowed them to do all kinds of things they couldn’t do before,” Dr. Blessman said. “Now, they could track each incident, generate reports for themselves and for department heads and see where the recurring problems were.”

While his role does not include actually seeing injured workers in a clinical setting, Dr. Blessman’s ability to analyze the data he was able to generate has drastically improved the city of Detroit’s ability to characterize health risks, which is the first step toward prevention.

“His organization of the data has helped us get a clearer picture of each individual case and of all our cases as a whole,” said Angela Moss, the city’s risk manager and Dr. Blessman’s supervisor. “In all, his involvement has made this a much safer place to work.”

According to Dr. Blessman, his desire to understand why people become ill is a big part of what sparked his interest in occupational and environmental medicine in the first place and the city of Detroit later.

“When illness clusters in certain working groups, you have a greater chance of recognizing the cause; and if you can remove the cause, you can stop the illness,” Dr. Blessman said of his interest in the field.

“Then, when the opportunity presented itself to get this contract with the city, I had the feeling I could really make a difference.”

Academically, Dr. Blessman is interested in understanding the factors associated with delayed recovery, musculoskeletal illnesses such as low back pain or carpal tunnel syndrome, and physical fitness as a preventive measure.

Maryjean Schenk, MD, MPH, MS, who, as chair of the WSU Department of Family Medicine, works closely with Dr. Blessman on a daily basis, sees him as the perfect person for his role with the city of Detroit.

“The database he created for them is important because it generates data that causes you to ask questions that you wouldn’t be able to ask otherwise,” Dr. Schenk said. “James has the intellect not only to ask the questions, but to find the answers.”

A five-year contract that ended in 2001 originally brought James Blessman to his role as medical director. He has been informed that the city of Detroit intends to continue the relationship and has renewed its contract with the Detroit Medical Center, keeping him in his position.

“He has made a huge difference here,” said Angela Moss, the city’s risk manager. “It’s a win-win situation having him here. We have everything to gain and nothing to lose.”

Not bad work for a kid who didn’t even want to be a doctor.
In January 1998, the American College of Occupational and Environmental Medicine (ACOEM), the nation’s largest medical society dedicated to promoting environmental and occupational health issues, defined a list of professional competencies for its 6,000 member physicians. The purpose of this list, according to the organization, was “to clarify the identity of the field of occupational and environmental medicine (OEM) in the face of a rapidly changing medical model and to enhance the understanding of what an OEM physician does and what an OEM physician has to offer society.”

Among the first in the world to develop such competencies for their own graduate medical students, faculty members in the Wayne State University Department of Family Medicine played an important role in the development of the ACOEM guidelines.

According to Richard Gallagher, PhD, professor of family medicine, the most important aspect of this learner-centered approach to training is the “learning contract” that is developed between the student and teacher.

“It’s a great communication tool,” said Dr. Gallagher who played a key role in the development of the program. The learning contract is a written agreement negotiated between the resident, program director and off-site placement faculty that summarizes the specific competencies that are to be mastered at a given training site. “It allows everyone from the student to the preceptor to the residency director to know exactly what is expected of the resident. It also clarifies the teacher’s responsibility to arrange the learning environment so as to insure that the designated competencies can be mastered.”

While the concept of listing resident skills was developed at the University of Massachusetts, WSU faculty took the idea a step further when they broke these skills down into 114 well-defined, behaviorally categorized competencies.

Under the direction of Dr. James Blessman, director of the OEM residency program as well as head of the division, there have been changes to the residency program to better operationalize the teaching of occupational medicine competencies in the clinical setting.

According to Maryjean Schenk, MD, chair of the Department of Family Medicine, the program is having a positive impact on OEM residents and the reputation of her department’s educational program.

“When residents leave here, I know they know how to perform,” Dr. Schenk said. “More importantly, the industry knows it, too. Government organizations and corporations, big and small, are hiring our graduates to run their programs.”

WSU Breaks New Ground in Training Occupational and Environmental Medicine Specialists
AFTER 17 YEARS OF WORK, a Wayne State University professor believes he has found avenues that will greatly enhance treatment for some of the most dangerous cancers, including colon cancer. He has already received two patents and anticipates a third that together will offer new protein-therapy and gene-therapy options, introduce a prognostic marker for cancer progression, and yield information about cancer and how it spreads.

Adhip Majumdar, PhD, who holds a joint professorship in the WSU internal medicine department and at the Barbara Ann Karmanos Cancer Institute as well as a research scientist position at the Detroit VA Medical Center, began his research in 1983 at the Martinez VA Medical Center, an affiliated teaching hospital of the University of California at Davis, where he held associate professorship in biochemistry. He moved to Detroit in 1986 — not for financial reasons, he quickly added, but because the San Francisco Bay-area facility was built on a fault. With the prospect of major earthquakes behind him, he settled into his work at Wayne State. “The primary focus of my research has been on aging and the increased incidence of gastrointestinal (GI) cancer, such as stomach and colon cancer,” he described. Colorectal cancer is the second most predominant type of cancer in the United States with 100,000 new cases each year. While looking for differences between GI and other tissues, he focused on cell proliferation. The proliferative potential of most tissues slows with age, but in the GI tract, it increases. “That, we thought, probably predisposes the GI tract to carcinogenic processes with aging,” he said, noting that cancer is uncontrolled cell growth. “So we began looking into the regulation of cell proliferation in the GI tract, particularly in the stomach and the colon, which are the areas where most cancers develop with aging.”

He paid special attention to a receptor with demonstrated connections to cell proliferation and to cancer. “The epidermal growth factor (EGF) receptor is actually involved in numerous malignancies,” he explained. “Expression of this growth factor receptor increases heavily with cancer, and is actually a poor prognosis of many cancers: pancreatic cancer, breast cancer, and also gastric and colon cancer.”

Dr. Majumdar surmised that blocking the EGF receptor might be a key to halting the spread of the often-deadly GI cancers.

The discovery that turned speculation into a working hypothesis came in the form of a small protein that not only became more prevalent as tissue aged, but that had a striking similarity to the EGF receptor. At first, Dr. Majumdar and his research group only knew that the apparently age-related protein was not particularly large. “We wanted to know what sort of protein this was, so we decided to go for cloning,” he recalled. Cloning allows a researcher to target only those gene(s) and the specific DNA (called cDNA) responsible for making the protein. “So, about four or five years ago, we made antibodies against that particular protein and used the antibodies to screen the cDNA library (a database of genes and associated cDNA), and we saw a lot of clones. We started analyzing these clones for nucleotide sequences, and suddenly we saw that one of the clones was homologous with epidermal growth factor receptor.”
Since the EGF receptor, at 170 kilodaltons, is about three times the size of the membrane protein we were analyzing, the protein wasn’t a perfect fit for the entire receptor. The protein clone did, however, approximate one area of the receptor. “The EGF receptor has three domains: an extracellular domain, which is outside the cell; a transmembrane domain that crosses from the outside to the inside of the cell; and an intracellular domain. Our sequence matched very nicely with about 80 or 90 percent homology to the extracellular domain.” With a little more work, they obtained the full clone of the protein, pinpointed it to 1,958 base pairs that expressed a 55-56 kilodalton protein, and named it ERRP, or epidermal growth factor receptor-related protein.

To test its function, Dr. Majumdar’s group inserted ERRP’s cDNA into cancer cells and watched the cell-growth rates. “We looked at colon cancer, prostate cancer and breast cancer cell lines, and found that when we overexpressed ERRP, it markedly inhibited their growth,” he said. “Remember that epidermal growth factor receptor concentration actually increases with aging as well as with the cancer, but when we overexpressed ERRP, the cell proliferation decreased. It also reduced activity of the EGF-receptor. Other experiments further confirmed this finding. When we saw that, we thought, ‘oh, this is fantastic’! We were able to conclude that ERRP is a negative regulator of EGF receptor.”

They followed up the work by analyzing several kinds of cancerous tissue. “We looked at prostate, colon, pancreatic, bladder and other cancers. Very interestingly, we found that expression of ERRP is actually extremely low in the cancerous portion of the tissue, but it is very high in the normal tissue. At the same time, EGF receptor activity is just the opposite: high in the cancerous portion and low in the non-cancerous portion.”

With the link between cancer, EGF receptor activity and the newly identified ERRP, Dr. Majumdar began considering possible clinical applications. “Imagine what would happen if you could put back ERRP or the gene for ERRP into the tumor,” he remarked. “That would probably cut EGF receptor activity and possibly stop the cancer from spreading, and that’s what we’re trying to prove now.”

He now has convincing evidence that this works in animal models. He has successfully shown regressed tumors and colon cancer cells in nude mice studies.

In the meantime, Dr. Majumdar has already received two patents for his work and is awaiting a third. “One patent is for ERRP as a protein therapy. Because it is an extracellular protein, we believe we can inject ERRP directly into the tumor or into the muscles, just like you use insulin as a therapy, and it will go directly to the tumor to inhibit cell growth,” he said. A second patent covers ERRP cDNA, which has potential as a gene therapy to essentially “turn on” the body’s own production of ERRP and mount a defense against cancer. A third patent is on the ERRP antibody, which can be used as a prognostic marker. Already, he and his research group are generating large quantities of the protein in the lab—a prerequisite for the animal studies, pharmaceutical work and human clinical trials that he hopes will follow. Several companies have already expressed interest.

“We believe that we can use this particular protein, ERRP, against cancer in all epithelial cells. That is, it can be used to treat pancreatic, colon, breast, prostate and many other cancers, because the EGF receptor is present in all these types of cancers.” If EGF receptor is one of the common denominators in the cancers, he concluded, then ERRP may be an ideal intervention. He estimated that with a little luck and sufficient research funding, the protein therapy might make it to the hospital bedside, hopefully, within the next few years.
THE WORLD IS A VERY BUSY place, and physicians feel the grueling pressures of an especially busy lifestyle. Between the demands of patient care, nights on-call, and the need to stay on top of medical advances, they have not a minute to waste.

With that in mind, educators, administrators and faculty members at the Wayne State University School of Medicine are looking for ways to save time through technology. Distance learning tools are providing medical professionals with a convenient, interactive outlet for continuing training and education.

“Distance education means people in any location can have equal access to the latest information, courses and learning programs,” said David Pieper, PhD, assistant dean for continuing medical education (CME). Dr. Pieper has been asked to step up Wayne State’s electronic CME offerings by distance education technology whenever it is most appropriate and useful.

Students, residents and veteran physicians are praising WSU’s current online alternatives that eliminate the need for them to drive to one particular location for medical lectures or programs. Other departments at the School of Medicine are following their lead and providing distance-learning opportunities for segmented audiences at multiple locations.

Two WSU faculty members in particular have established award-winning programs in distance education for two distinct audiences. Dr. Tsveti Markova has brought family medicine residents online for weekly seminars. Dr. Marilyn Wayland has brought Internet-based patient care training to elderly people and their caregivers and she teaches violence prevention to young women, all through the powers of videoconferencing.

**Web Conferencing Joins Family Medicine Residents, Despite Location**

“Geographic distance plays a much less significant role in our learning programs,” said Tsveti Markova, MD, residency director and assistant professor in family medicine. “We have used web conferencing to eliminate the commute and increase the ability of our physicians to communicate, interact and share ideas with one another. Nevermind that they are not in the same room, or even at the same hospital or facility. They are connected and in touch.”

In July 2001, Dr. Markova introduced web conferencing to deliver the didactic curriculum component of residency training in family medicine. With this method, a lecturer is in one location, and the learners or residents are in multiple locations, watching and listening to the lecture on their computers. The presentations are based on PowerPoint slides that are transmitted over the Internet and stored on a server, so residents can refer back to them later.

Conferences are an important component of residency training and account for a significant portion of residents’ formal education, so it was important for Dr. Markova to make sure that the distance-learning tactic was meeting the needs of everyone involved.

Her research studies have shown consistently that the distance-learning classrooms report similar results related to satisfaction and educational outcomes as traditional classrooms. “Distance was not a factor in the reported and tested learning benefits,” she said. “Whether the residents were face-to-face with the lecturer or at another location entirely,
there was no difference in the learning of educational material.” The added benefit of distance learning is a 25 percent increase in conference attendance, since residents now have some flexibility regarding the time and location of the lectures.

When Dr. Markova joined the WSU family practice residency program, she saw a need for a different innovative educational approach. “I have always been able to adapt to the times. I saw an opportunity for the residents to have more efficient access to the lectures with decreased commute time, so I educated myself about the subject of distance learning. From all available options, I was looking for a cost-effective, easy to use method, using widely-available equipment. Data conferencing was the best option for our conditions. The residents and faculty embraced the idea and adjusted quickly to the new method,” she said.

She developed this program as part of her National Institute of Program Director Development fellowship, sponsored by the American Academy of Family Physicians. She became interested in technology for educational purposes, and made this program her personal project. She had no budget to get started, but with a laptop computer, an LSD projector, an Internet connection and a phone line, and she had all she needed.

Her colleagues around the country are taking notice of her work and she is providing some of the first documentation about distance learning for graduate medical education. “The business schools have been doing this for a long time, but the uniqueness of the medical conferences made it challenging for medical schools to get onboard quicker,” she said.

Dr. Markova feels that it is important to share her knowledge and experience on the subject, and has a publication in press about the use of data conferencing in the residency program. In addition, there are plans to invite other attendees to get connected. Community preceptors, other residency programs and some community hospitals have expressed an interest in receiving the opportunity to participate. Plans for such partnerships are in the works.

Community Education Provided Via Distance Learning

Marilyn Wayland, PhD, has made a career out of training and teaching people through innovative tools and programs. She established the Learning Without Limitations Laboratory to provide rehabilitation training for people who may have compromised use of their arms, legs or motor skills. As she became more interested in technology-assisted learning, she was able to overcome even more limitations such as distance, inconvenient class locations, and restrictive schedules of homebound patients, busy faculty members and members of the community.

As assistant professor of physical medicine and rehabilitation and director of research and education at the Rehabilitation Institute of Michigan, Dr. Wayland is accustomed to providing services for people with disabilities. “Technology and distance-based learning allows us to eliminate many hindrances to medical education and training for the people who need and desire it,”
Dr. Wayland said. “Mobility and travel can be difficult for many of our audiences, but interactive, computer-based programs can ease that burden.”

Her pet project, Caregiver College, is a free eight-week community education program to improve the quality of life for elderly people with chronic illness by improving the knowledge and skills of their caregivers. “We want to make care in the home setting safer and easier for everyone involved,” she said.

Because there were large numbers of people who wanted to participate in the program and they lived all over metropolitan Detroit, Dr. Wayland set up videoconference classrooms at various locations such as churches, hospitals, nursing homes and senior centers. Educational programs are simulcast from a single instructor to multiple audiences in Michigan including Detroit, Novi, Southfield, Oak Park and West Bloomfield. Recently, other states have asked to be linked and are now participating in the Caregiver College program as well.

“The videoconferences are totally interactive,” she said. “The instructor and students can see and hear each other. Slides, overheads and videotapes are used for multi-media presentations, and classes are kept small, so they maintain an informal atmosphere conducive to discussion.”

In 1998, Caregiver College was honored by the State of Michigan with an Innovations in Elderly Care Award. Nearly 1,000 community members have completed the eight-session training series and have expressed great satisfaction with the program. Based on this success, Dr. Wayland has also added two more caregiver series: one for parents of children with disabilities and one for caregivers of people with traumatic brain injuries. In partnership with WeMedia Inc., a disability website, throughout the 2000 academic year, Dr. Wayland conducted a pilot study videostreaming the courses on the Web.

As the parent of a child with a significant disability, Dr. Wayland takes special interest in ensuring health and safety for children. She has established two innovative distance-learning programs for middle-school and high-school students. The first, Power of One, is a domestic violence prevention program for young women. A videoconferenced educational program is shared with teens throughout Michigan who learn about domestic violence, date rape and safe, healthy relationships. Over 400 students participated in the 2001-2002 school year.

“Part of our mission is to prevent disabilities from occurring in the first place—and the primary prevention of domestic abuse is through educational programs such as Power of One,” Dr. Wayland said.
The WSU School of Medicine has many distance-learning opportunities available for medical students, residents and veteran physicians.

“As Detroit’s only medical school, we provide the major medical content and training for the metropolitan area and the entire state,” Dr. David Pieper said. “In fact, 60 percent of southeast Michigan’s practicing physicians completed all or part of their training at WSU.”

A sampling of the computer-based educational opportunities available to medical professionals are listed below.

**UNDERGRADUATE MEDICAL EDUCATION**
- **Self-Instruction:** A large portion of School of Medicine lectures are available online or on videotape, audiotape, or CD. These options are advantageous for students who want further detail on particular subjects, or for those who learn at a faster or slower pace than the lecturer. In addition, lectures presented in digital formats may include diagrams or animations that can clarify difficult concepts or biological processes.

**GRADUATE MEDICAL EDUCATION**
- **Morning Report Reviews:** This website provides a virtual format of the patient cases presented at Morning Report sessions at the Detroit Medical Center. Four to six cases are featured each month to enhance residents’ clinical knowledge, skills and attitudes. For more information, visit www.mdmorningreport.com.
- **OHEP GME Courses:** The WSU School of Medicine partners with the OHEP Center for Medical Education to provide training for surgery, OB/GYN and internal medicine residents in community hospitals including St. John, Providence, Henry Ford and St. Joseph Mercy. Topics vary each month. For more information, visit: www.ohep.org.

**CONTINUING MEDICAL EDUCATION**
- **Ground Rounds Videoconferencing:** Several programs regularly provide live and stored webcasts of Grand Rounds presentations. Participating departments include the Center for Healthcare Effectiveness Research, family medicine, obstetrics and gynecology, and physical medicine and rehabilitation. For more information, visit: www.cme.med.wayne.edu/.
- **Journal-Based CME:** Physicians who are unable to attend live conferences can earn continuing medical education credits through journal-based evaluation and testing. WSU offers CME credits in each issue of *Journal of Clinical Outcomes Management* and *Advance for Physician Assistants*.

The program has been supported by the Blue Cross Blue Shield of Michigan Foundation and is a collaboration with Wayne County Prosecutor’s Office, Detroit Police Department Domestic Violence Unit, and LACASA, a domestic abuse community-based program.

Power of One built on the success of the Pioneers for Peace National Videoconference series, a national program that featured former Rehabilitation Institute patients who suffered permanent disabilities because of interpersonal violence. “The image of a young person coping with serious injuries provides a serious wake-up call to kids about long-term consequences of risky behaviors,” Dr. Wayland said. “The more people we can broadcast that message to, the more disabilities we hope to avoid.” Schools in California, Missouri and Pennsylvania participated in this program.

In addition, like Dr. Markova, Dr. Wayland has made the didactic curriculum of the rehabilitation residency program completely distance-learning based. Since 1999, residents have had the luxury of videoconferencing which has proven to be cost-effective, efficient, well-accepted by residents, and educational outcomes have been outstanding.

“Dr. Wayland has been a leader in technology-based education,” said Dr. David Pieper. “She has instituted interactive, quality programs that others at the School of Medicine are using as models. Her dedication and expertise are really unmatched. She is getting the educational programs everywhere they need to be.”

“Technology and distance-based learning allows us to eliminate many hinderances to medical education and training”
WHEN DR. SYLVIE NAAR-KING sits back in her office chair and begins telling the stories of people who have inspired her groundbreaking work to reduce risk behaviors in HIV-infected youth, the effect is at once chilling, heartbreaking and encouraging.

There’s the naïve young teen who contracted HIV from an older man during his first sexual experience. That tragedy began a downward spiral of self-imposed separation from his family, “survival sex,” or trading sex for having a place to sleep, and the use of drugs and alcohol.

There’s the young woman who came from a broken home and had four children by age 21. She contracted HIV from one of her partners and passed the virus along to one son. Her children ended up in foster care as she unsuccessfully battled depression. She was getting therapy, but it didn’t help.

“Even when we had all these services to offer, even when she had the psychotherapy, she still couldn’t do it,” said Dr. Naar-King, 32, a Wayne State University assistant professor of psychiatry and behavioral neurosciences.

“Traditional psychotherapy may not be the best approach because you have to be so motivated to change to make that work. You have to get to the appointments and show up regularly. You have to be very ready. That’s why we’re trying to help people increase their motivation.”

Dr. Naar-King and her co-principal investigator, Dr. Kathryn Wright, are trying an innovative approach to help young people with HIV avoid sexual risk behaviors and substance abuse while developing good health habits.

The unique four-session intervention is called “Motivational Enhancement Therapy.” It has worked with adult alcoholics in the U.S., but has never been tried with HIV-infected adolescents.

Simply put, motivational enhancement therapy, with its non-judgmental style and relatively intense treatment period, seems to work where traditional psychotherapy fails. It may kickstart participants into engaging other medical and social services, including traditional treatment.

“In a nutshell, it gets people ready to change,” Dr. Naar-King said.

If it works in Detroit, Dr. Naar-King says it has “huge implications” for the rest of the country. It may be the one of the keys to unlocking the dilemma of treating adolescents with HIV and may help curb the spread of the disease.
This metro Detroit program is funded by two federal grants. The first — a three-year, $300,000 grant — is from the National Institute of Drug Abuse, part of the National Institutes of Health. In addition, there’s a two-year, $400,000 grant from the Special Project of National Significance designed to enroll and retain youth in HIV-oriented primary care.

There is an urgency to the task: The Office of National AIDS Policy estimates that half of new HIV infections occur in youth under age 25. African-American women are the fastest growing segment of new HIV infection.

Sexual risk behaviors and substance use appear to be highly prevalent among HIV-positive teens. And young people with HIV can’t seem to manage their disease. They are miserable at keeping doctor’s appointments, taking medication and tending to their general health, said Dr. Naar-King.

Detroit has a high incidence of HIV-infected youth. The Detroit researchers will draw 60 participants from a local pool of about over 400 known HIV-positive youth, ages 13 to 24. Most of them were infected through sexual contact.

“That’s why we’re targeting these three behaviors — health, drug use and sexual risk,” said Dr. Naar-King. “It’s about taking care of yourself. It’s about being able to be assertive, making the right choices and being motivated to change.”

Some of the motivation to attend appointments will come in the form of incentives, from movie passes, to gift certificates for Farmer Jack and Target.

Dr. Naar-King understands that motivation is not just about material things or monetary rewards, but such incentives may urge people to take the first step and come to their first appointment.

As she lays out a new path for the treatment of HIV-infected adolescents, she can’t help but reflect on a family member who suffered from what she calls the "stigma" of the disease.

In 1991, Dr. Naar-King’s brother-in-law Kevin died from AIDS at age 29. Kevin was a hemophiliac who never told his extended family that he had contracted the deadly virus until he was in the final stages of the disease.

Dr. Naar-King was 20 and working on her PhD in psychology at the University of Colorado at Boulder when her brother-in-law died. His death prompted Dr. King and her husband Scott, a microbrewer and a Michigan native, to set down roots in Clawson.

Dr. Naar-King is pregnant with her second child — a son whose middle name will be Kevin. In both a personal and professional way, Kevin’s legacy continues to motivate the young psychologist.

“He shaped our lives in so many ways,” said Dr. Naar-King. “Kevin was the driver for this whole thing.”
In a historically unprecedented move, faculty members at the Wayne State University School of Medicine joined together last fall to formally announce the establishment of the Wayne State University Physician Group, a non-profit organization that has banded together the area’s top doctors in 19 specialties.

As one of the largest practice plans in the metro Detroit area – representing more than 750 doctors – the WSU Physician Group will enhance faculty’s efforts to provide patients with easy access to advanced, comprehensive care. To learn more about what the group is and what its goals are, Wayne Medicine spoke with Dr. Stephen DeSilva, president of the WSU Physician Group, and Dr. Bruce Deschere, president of University Physician Services Inc., the physician group’s management services organization.

Q. What is the Wayne State University Physician Group?

Dr. DeSilva: The Wayne State University Physician Group is a practice plan that represents all full-time faculty members at the WSU School of Medicine. A lot of people who aren’t in an academic medical center environment sometimes think that medical school professors are people who sit in ivory towers and teach all day. While we are dedicated to our teaching mission, which makes us unique, we do treat patients.

Q: What makes a faculty physician different from other doctors?

Dr. DeSilva: Our mission here is three-pronged: to care for our patients, to conduct research that will lead to advances in medicine and to teach students who will be tomorrow’s doctors. Each piece of the mission that our practice is founded on enhances the others. Many of our doctors are pioneers in their fields and are working to solve the health problems that affect our community every day. That research and the interaction with students help to keep them sharp and to provide the best patient care possible.

Q: Why was the WSU Physician Group formed?

Dr. DeSilva: This has been one of Dean [John] Crissman’s top priorities since he was appointed dean of the medical school in 1999. He understood that our unique mission needed a unique business plan. Forming a unified practice plan was a natural step in our evolution. We all know the health-care industry in recent years has seen some rocky times, to say the least. Dr. Crissman recognized that we needed not only to protect our mission and our physician practices, but also that we needed to be a role model for how business should be conducted in our field.

Q. So how does University Physician Services, the management services organization for the WSU Physician Group, fit into this picture?

Dr. Deschere: Wayne State University Physicians see about 1 million patients annually and collect about $200 million in fees each year. We’re a large group, and the magnitude of our business is great. We saw an opportunity to cut down on wasteful duplication of effort, so University Physician Services was established as a for-profit management services organization to handle these issues and streamline business operations in a number of ways.

The Wayne State University Physician Group was launched in 2001 to join WSU doctors in a comprehensive practice plan.
Q. Can you tell us specifically what services UPS provides for the WSU Physician Group?

Dr. Deschere: We do a number of things and we’re hoping to expand our role as the Physician Group evolves. First and foremost, though, we have focused on contracting with health-insurance companies. These companies are now realizing that they have to negotiate with our entire group of 750 doctors, rather than a smattering here and there in each of the individual practice groups. We’re already starting to see the “750-pound gorilla effect,” as Dr. Crissman would say. We’ve leveraged our position just through the sheer size of our group and the diversity of our specialties, and people are recognizing that. At the same time, we can deliver a complete network of physicians to insurers coming into southeast Michigan.

Q. Is contracting the only focus at this point?

Dr. Deschere: No, not at all. We’re working to get all of our physicians on one billing system. This helps us, because we can keep better track of who’s getting paid appropriately, but it also helps our patients. We want them to get one, easy-to-read bill. We’re also working on streamlining compliance with regulatory mandates, which is becoming increasingly important, given the new HIPPA legislation. Encouraging referrals among our own doctors, which is probably our largest untapped source of referrals and new patients, is also a top priority.
Q. Are there plans to market the Wayne State University Physician Group?

Dr. DeSilva: Absolutely, and that effort is already underway. While our ultimate goal will be to bring in more patients through a large-scale marketing effort, we recognize that we first have to lay the foundation with a solid brand awareness campaign. We kicked that off in July 2001, with an hour-long weekly radio program on WJR, “The Medical Hour,” that highlighted our doctors’ strengths. We’re following up with an internal campaign to ensure everyone is on board and understands what we are. This is really a key step for us, particularly because our operation is so large and diverse. During this phase, you’ll start to see more of the WSU Physician Group brand in the places where we work. Eventually, we will expand this into a more aggressive effort to build the brand outside of the university as well, but that will be something dictated by the strategic plan.

Q. What is the strategic plan and where are you in implementing it?

Dr. DeSilva: Obviously, every business needs a strong plan to ensure it succeeds. Currently, we are hosting retreats every couple months or so that include about 70 physicians and members of our support staff. Participants are broken into workgroups to evaluate several aspects of the plan, including competitive strategy, business operations and relationships with the Detroit Medical Center. These groups are working hard, and completion of the plan is imminent. We’re excited about moving forward more aggressively once it is in place.

Q. How does the DMC fit into this equation?

Dr. DeSilva: The Detroit Medical Center is our primary partner for providing facilities for clinical practice. They have always fulfilled this role, and we will continue to work with them. However, the WSU Physician Group represents the faculty doctors who work at the DMC. We will continue to work on behalf of our physicians to ensure that their interests are protected, whether it’s in relation to the DMC or in relation to some health-insurance company. Our bottom line is to ensure that our faculty physicians have what they need to practice good medicine, to research good medicine and to teach good medicine. That can only nurture first-rate patient care.

For more information about our services, please call 1-877-WSU-DOCS.
WHAT DOES IT MEAN TO BE A WAYNE STATE UNIVERSITY FACULTY PHYSICIAN?

Your doctor is a member of the Wayne State University School of Medicine Physician Group.

This means that your doctor is a full-time faculty member engaged in the training of medical students and other physicians. As such, your doctor is knowledgeable about the latest medical treatments and technology. In fact, many WSU School of Medicine Faculty Physicians are among the foremost experts in their medical specialty or subspecialty. Your doctor may also be engaged in medical research to help bring new and effective applications to all physicians.

What does this mean to you? At times, one or more students may be with your doctor at the time of your appointment. Your doctor may ask you for permission to have a student observe, or to interview and examine you. At all times, you may feel free to either accept or refuse. By accepting, not only are you helping your doctor to keep his or her oath to help future physicians, you are also helping to ensure that the most caring, competent doctors are available to treat our future generations.

A Wayne State University Physician has access to the most advanced educational resources and the latest research and technology that only an academic affiliation can provide. Thank you for joining in this important partnership.
IN EIGHTH GRADE, Blaine White read about the development of anesthesia in Thorwall’s *Century of a Surgeon*— and he thought about becoming a doctor. A few years later, he read about the first microscopic organisms in Paul de Kruif’s *Microbe Hunters* and then it was decided. “Medicine is a terrific story. It tells of human compassion and human discovery, both,” he said. “As a kid, I just loved the science part. Imagine, back in the day, testing 900 compounds trying to find something to kill syphilis. Later, as an adult, I worked in the emergency room at Detroit Receiving Hospital—a tough place. You have to take anything the world can throw at you. Such is the life of a physician and scientist.”

This past year, Blaine White, MD, was elected to membership in the Institute of Medicine of the National Academy of Sciences. A professor of emergency medicine and physiology at Wayne State and a 20-year veteran of Detroit’s emergency rooms, Dr. White is one of only about 600 people in the entire country to be invited to join the prestigious group.
Created in 1863 by Abraham Lincoln, the National Academy of Sciences was established to gather scholars who would “advise the federal government on scientific and technical matters.” That tradition continues today, making Dr. White’s membership both an honor and an obligation. On one hand, it is an honor to be held in such high esteem by one’s colleagues. On the other hand, all members are expected to work on research studies and projects that shape health policy.

Dr. White has already contributed a great deal to the body of scientific knowledge. In 1999, he participated on an Institute of Medicine committee that issued a report about methods and protocols for resuscitating wounded military soldiers in the field, until they could be transported for professional medical attention. The report, called *Fluid Resuscitation: State of the Science for Treating Combat Casualties and Civilian Injuries*, offered guidelines for field medics who must rescue and resuscitate fellow soldiers in difficult terrain with limited medical gear and unruly conditions. The information contained in this report is also relevant to civilian populations because it addresses technology and medical needs in the first line of emergency trauma care.

Throughout his career, Dr. White has been at the forefront of basic science research related to post-ischemic reperfusion injuries in the brain. His work is critically important in emergency medicine, since only 3 percent of the 70,000 patients who are resuscitated from cardiac arrest each year regain full cognitive capabilities.

His well-funded research team, that currently includes four other faculty members, has provided a better understanding of many processes and mechanisms associated with neurological injury including: oxygen radical formation, identification and tissue mapping of lipid peroxidation, identification and tissue mapping of protein modifications causing loss of protein synthesis in injured neurons, and recovery of protein synthesis induced by growth factors such as insulin.

“Blaine has the distinction of being the longest NIH [National Institutes of Health] funded researcher in emergency medicine,” said Dr. Judith Tintinalli, former WSU colleague and current professor and chair of emergency medicine at the University of North Carolina at Chapel Hill. “His research into the basic mechanisms of cell death is creative and innovative. Blaine has never been...”
afraid of thinking, asking questions, and of challenging existing dogma. These are attributes of every great researcher.”

Drs. White and Tintinalli are two of the founding members of WSU’s Department of Emergency Medicine. They shared an office at the old Detroit General Hospital with Ron Krome and Brooks Bock in the early 1970s. “Blaine and I did a few very early ‘studies’ together. The word studies deserves to be in quotes because back then, we did things by the seat of our pants, having no knowledge of study methodology,” Dr. Tintinalli said. After some experience, they began making important discoveries and eventually, were the first to demonstrate that hyperglycemia was responsible for hypersmolarity during resuscitation, not hypernatremia, as had been assumed.

Although he graduated from Wayne State University in 1972 with a medical degree, Blaine White could have easily been a PhD, because he was so fascinated with science. “The NIH says we need more physician scientists, and I agree. What they bring to hardball molecular science is that in-the-gut understanding that there is a real disease out there, with real patients. There’s no substitute for that,” he says.

Taking great pride in his role as professor and mentor, Dr. White says he is committed to “growing excellence at Wayne State.” He has cultivated and nurtured many research assistants who have earned their doctoral degrees, completed training, earned faculty positions and secured their own grant funding. Two of his graduate students, Jonathan Sullivan and Donald Degracia, are now assistant professors in emergency medicine at WSU.

“We ought to be more focused on faculty development than faculty recruitment,” said Dr. White. “We have many young researchers who are committed to this place and we need to assist them in developing their own lines of investigation.”

In his own lab, Dr. White has allowed many team members to serve as principal investigators on work he started himself. “There are plenty of variables and scientific questions to be answered in our work with neurologic injury. Each member of the lab has a significant role to play in enhancing our understanding of the process. My researchers are all committed to internal pride and an unrelenting expectation of excellence.”

Although they have made great inroads in molecular mechanisms of brain death, reperfusion and cardiac arrest, Dr. White admits that scientists in this field have a long way to go before they can improve cognitive abilities following resuscitation. “We still need a quantum step to get to the first level of effectiveness,” he said. “What we seek is a multi-drug strategy that has a measurable clinical outcome. It’s very difficult, because in reperfusion, nothing works alone. Many chemical processes are at work and often at odds during ischemia. This isn’t the sort of problem that will be solved with a single miracle drug. We can begin by trying to get existing drugs to work together, but these interventions are very difficult.”

Does that mean Dr. White will stop looking for clinical solutions? “No way. I did more than 20 years of inner city emergency medicine. What we do is important because the patients are important; the people are important. We will keep doing everything we can to improve outcomes.”

“BLAINE HAS NEVER BEEN AFRAID OF THINKING, ASKING QUESTIONS, AND OF CHALLENGING EXISTING DOGMA. THESE ARE ATTRIBUTES OF EVERY GREAT RESEARCHER.”
AS A BOY growing up in Baltimore, Harvey Pass watched his father practice an old-fashioned brand of community medicine. Dr. Isidore Earl Pass, a Maryland general practitioner, delivered babies, made house calls and seemed like the type of genial doctor portrayed by Norman Rockwell on the cover of the *Saturday Evening Post.*

Today, his son, now a physician and the man who literally wrote the reference book on lung cancer, is launching a 21st century brand of community research from the parking lot of the Harper Hospital Professional Building. The vehicle for this effort is a modified white Ford E-350 utilivan with the words “Mobile Early Detection of Cancer of the Lung“ plastered on both sides. Inside is a sparkling white mini doctor’s office, with an area designed to take sputum samples from smokers and a deep-freeze in which to store them.

The rolling lab – the first of its kind in the U.S. – will head out onto Michigan roads in early 2002, with an ambitious clinical research goal: To triple the number of people diagnosed early with lung cancer and shift the survival curve upwards within the next 10-15 years.

Lung cancer is the leading cause of cancer deaths in both men and women, according to the American Lung Association. The disease will cause an estimated 157,400 deaths in 2001, accounting for 28 percent of all cancer deaths.

“You have to be able to get to people,” said Dr. Pass, a self-described workaholic who is a professor of surgery and oncology at the Wayne State University School of Medicine. “You can’t expect people to come to you. We’ve got to get out into the community and fight the belief that lung cancer is universally fatal.”

This innovative lung-cancer community screening effort is funded by a two-year, $1.4-million grant from the National Institutes of Health and the National Cancer Institute, along with a $63,000 donation from the Veterans of Foreign Wars. Dr. Pass made the pitch for the donation to Michigan VFW commandants in Lansing in December 2000.

“I said we want to do lung-cancer screening for veterans,” he said. “We’ll have a van and do it for nothing. They loved it.”

Initially, the van will travel to 40-50 VFW posts throughout both peninsulas of Michigan, studying 2,500-3,000 patients. The study will focus on a high-risk population – people who are current and former smokers, 40 or older with approximately a pack-a-day habit. Eventually, Dr. Pass and his team, which includes oncologist Dr. Omer Kucuk, the head of chemotherapy prevention for the Barbara Ann Karmanos Cancer Institute, hope to extend the community outreach research effort to factories, community centers and local health fairs.
If patients are found to have abnormal sputum, they will be offered a free LIFE bronchoscope. LIFE stands for laser-induced fluorescence endoscopy, a procedure that can detect changes in the lining of the lung.

Those patients with suspicious changes will become part of a six-month trial of a chemotherapy prevention drug called zileuton, which is currently used to treat asthma and may turn off pre-cancerous cells.

Because there are two ways to screen for lung cancer — through sputum testing and CAT scans — there is a second, complementary aspect to this study. Volunteer patients who pay $250 — hundreds less than the cost of a typical CAT scan — will receive a low-dose, 15-second CAT scan at Rose Imaging, a community imaging center in Farmington Hills. If nodules are detected, they can take the results to their physician for further treatment.

On an afternoon in early December, Dr. Pass — fresh from the operating room where he’s just removed a cancerous tumor from a patient — leaps into the van and passionately begins to explain why he is so committed to community-wide lung-cancer screening.

“This is the worst cancer,” said Dr. Pass, a 51-year-old Ann Arbor resident and father of twins who was a long-time senior investigator at the NIH. “The five-year survival rate is atrocious — around 14 percent. ‘People who do the best have tumors that are detected earlier, but only 20 percent of those tumors are detected at Stage One.

“The purpose of this research in lung cancer screening is to find these tumors before they are actually cancer. It’s all about validating whether lung-cancer screening can save lives. That is unknown. We’re hoping to show if we do the screening, we will detect early lung cancers and save more lives.”

For more information, call 1-800-KARMANOS.