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On the Cover
This ICP-MS instrument (inductively coupled plasma mass spectrometer) can measure every metal that exists even at very low levels. This is important for Dr. Barry Rosen who measures lead, arsenic and cadmium, which are hazardous elements found in soil and drinking water.
ARSENIC IS A DANGEROUS carcinogen that can lurk in your next glass of water or the dirt in your garden. Neither industrialized nations nor Third World countries are exempt from the problem, which has proven both difficult and expensive to remedy. Now, however, a Wayne State University professor may have found a solution. Building on the natural arsenic-extracting properties of baker’s yeast and a common type of bacteria, he hopes to make available water filters and soil-purifying green plants that trap the poison for easy disposal.

The secret is in the charged-up versions of yeast and plants, said Barry Rosen, PhD, professor and chair of the WSU Department of Biochemistry and Molecular Biology. All organisms naturally confiscate any arsenic that enters their systems and then eliminate it. Dr. Rosen’s notion was to examine the genetic pathways behind the uptake and release pathways, then maintain or enhance the former while eliminating the latter. By doing so, the yeast and plants would take up arsenic at a steady or accelerated rate, and have no option but to store it.

For remediation of drinking water, a filter impregnated with modified yeast would trap the arsenic. For soil clean-up, plants would accumulate the toxin in their leaves with the help of bacteria genes. The final step is the collection and safe disposal of used filters and leaves.

“The current methods for removing arsenic from drinking water are mainly low-tech, chemical methods, that include acidifying the water and adding a lot of iron to the water. Those methods tend to precipitate out the arsenic in slurries that have to be bottled up somehow and trucked out (to treatment facilities),” Dr. Rosen said. “That’s very expensive, it generates large amounts of sludge, and it also adds things to the water that you have to treat later. With our process, on the other hand, we can eliminate the arsenic all at one time, and it doesn’t change the quality of the water.”
Concern about arsenic has risen in recent years for several reasons. In 2000, the U.S. Environmental Protection Agency recommended lowering the allowable limit for arsenic in drinking water from 50 ppb (parts per billion) to 10, a limit that many American municipalities exceed. “The existing methodologies really can’t handle the cleaning of water at that level, so we need something that is more efficient,” he said.

He pointed out that thousands of Michigan residents, particularly well-water users north of Detroit, have unacceptably high levels of arsenic in their drinking water. “Arsenic is a prevalent element found especially in bedrock, which is where the water tables are. In Michigan, the arsenic comes out of a sandstone formation in the Thumb, and the water just trickles out of there all the way to Oakland County.”

While Americans fretted over their well water, people in developing countries were becoming exposed to high levels of arsenic in their drinking water for the first time. “The World Health Organization and other agencies recommended that they switch to well water instead of pond or river water, because it was often contaminated with pathogenic organisms. But by sinking wells down to bedrock, they ended up with water that is highly polluted with arsenic.”

Soil contamination has also become a concern, primarily as a result of burning arsenic-laden coal, or using pesticides, fungicides and wood preservatives that contain the poison, he said.

The most common method presently used for removing arsenic from soil is even more “low-tech” than the one used for water, he said. “We just dig up all the contaminated soil and truck it off to a toxic-waste site.” In comparing this method and his plant-based option, he remarked, “It’s much easier to get rid of leaves than soil.”

At the foundation of both the soil and water research is a basic understanding of how living things deal with arsenic. “We’ve been working for many years on the mechanisms of arsenic detoxification in organisms all the way from bacteria to humans,” he said. “Using that information, we’ve been able to genetically engineer various organisms to acquire the ability to accumulate large amounts of arsenic.”

Yeast was an especially good candidate for their water-remediation work, because the organism’s genetic make-up is well known, it grows quickly and easily, and it has a very efficient arsenic-removal system. “Yeast normally will excrete a large amount of the arsenic that it takes up, so what we’ve done is ‘knock out’ (delete) the genes that code for those excretion pathways and that results in a strain of yeast that can’t get rid of the arsenic,” he said. “Once we did that, we were able to enhance the uptake systems, and we ended up with yeast that can’t get rid of the arsenic. It stores the arsenic inside of its vacuole, which is its intracellular storage compartment.”

Dr. Rosen’s process is also unusual in that it treats the specific type of arsenic that is often found in well water. “Arsenic comes in either oxidized or reduced forms, and the commercial methods for removal of arsenic usually deal with the oxidized form called arsenate. There haven’t been good methods for treating the reduced form, or arsenite, which is what you would get from deep wells,” he remarked. “Our method is uniquely suited for treating arsenite, so that’s a real advantage.”

He has already filed for a patent.
on the modified yeast, and envisions an arsenic filter that will look like any standard water filter homeowners might use to take out iron or chlorine from their water. He and his research team plan to design the filter prototype, and then work with a manufacturing company to actually produce and market the filter.

In developing countries, where the people typically don’t have private water taps, the filter could be replaced with a packet of yeast, much like those sold at a grocery store for baking bread, he said. “One possibility is to use the yeast directly by simply mixing it into a pitcher of water, letting it settle down, decanting off the water later, and disposing of the yeast.”

For arsenic removal from the soil, Rosen is working with Professor Richard Meagher from the University of Georgia Department of Genetics. “The idea was to genetically engineer organisms to remove arsenic from the soil. That’s where plants come in, because they’re very good at taking minerals out of soil.”

Dr. Rosen recently attended a scientific meeting to talk about the health effects associated with arsenic contamination in India’s ground water. The findings generated by Dr. Rosen and his laboratory team could help filter arsenic from soil and water.

In this case, they have introduced two arsenic-storing genes from the common intestinal bacterium Escherichia coli (E. coli) into a type of mustard plant called Arabidopsis. “We’ve got a way of expressing these genes only in the leaves, so that the arsenic gets taken up through the roots, transported into the leaves and accumulates there in the vacuoles — just as it does in the yeast. Dr. Meagher is working right now on putting the genes in trees rather than Arabidopsis so that we can do the phytoremediation on a much larger scale.”

For both soil and water purification, he said, these methods provide a new option for dealing with arsenic contamination. “Now,” he said, “we hope to take it out of the laboratory and into the field. That’s our goal.”

Dr. Rosen recently attended a scientific meeting to talk about the health effects associated with arsenic contamination in India’s ground water. The findings generated by Dr. Rosen and his laboratory team could help filter arsenic from soil and water.
A PETREL IS A SEA BIRD that spends most of its life at sea, often far from land. One type of sea bird is known as a storm petrel or stormy petrel. There is an old mariners’ belief that the stormy petrels flock closely around ships at sea in rough weather. Thus, over centuries, the appearance of a stormy petrel has come to mean the harbinger of stormy weather. The Oxford English Dictionary offers this definition: a person who delights in strife, or whose appearance on the scene is a harbinger of coming trouble.

TB Hits Detroit

In the early 1900s, thoracic surgery was in its infancy. Surgeons were operating to drain collections of pus from the chest cavity and occasionally repairing a wound of the chest wall or ribs, but that was about the extent of surgery. During the 1920s, tuberculosis was slowly becoming an epidemic, particularly in the crowded, urban areas in this country and around the world. Tuberculosis, also referred to as TB, the white plague and consumption, was ranked among the world’s worst killers.

Antibiotic therapy did not yet exist. Surgery seemed to be one of the best options for treatment, so various surgical procedures were being developed to treat complications of TB of the lung.

At the same time, Dr. Edward (Pat) O’Brien was fighting the TB outbreak in Detroit through his service as chief of surgery at Herman Kiefer Hospital and as a surgeon at Harper Hospital. Dr. O’Brien, a 1909 graduate of the Detroit College of Medicine (now Wayne State University School of Medicine), had his work cut out for him.

Herman Kiefer Hospital began in 1887 as a 10-acre site where contagious disease patients were isolated from the rest of society. There was an old frame building known as the “little old pest house” where smallpox sufferers were placed. The first TB patients sent there by the health department were housed in tents, because it was thought that fresh air was beneficial in the treatment of pulmonary tuberculosis. These tents were eventually replaced by small cottages, then permanent buildings, and in 1928, a seven-story building with a “modern” operating suite and surgical amphitheater. This O.R. was built for the increasing use of thoracic surgery in the treatment of TB. By this time, Dr. O’Brien was also chief of thoracic surgery at the hospital, which had 1400 beds, 800 of which were dedicated to TB patients, making it one of the largest hospitals in the country.

According to James Christopher Stringer, who completed a thoracic surgery residency at Herman Kiefer Hospital in 1938, “Dr. Pat O’Brien was a stickler for fast surgical time. He was an effective teacher, too, but he had a reputation among surgeons for being a champion thoracoplasty speedster. ‘Accuracy first,’ he would bellow as he incised, clipped, clamped and sewed, ‘but be fast.’ The awed residents and interns and other potential chest surgeons wondered if they could ever learn those skills.”
Dr. O’Brien’s penchant for speed was likely fostered by his mentor, Dr. John Carstens who was one of the most rapid operators in the profession in the early 1900s. To Dr. Carstens, “skill, confidence and speed—particularly speed—were the prime essentials.” It was said that he took pride entering the surgical amphitheater smoking a cigar. He would lay it aside, complete the operation before the cigar went out, and leave the Harper Hospital operating room puffing away triumphantly.

During his long professional career, it is estimated that Dr. O’Brien performed more than 30,000 chest operations. By the mid 1940s, he headed one of only 22 accredited thoracic surgery residency training programs in the country, was a clinical professor of surgery at Wayne State, a consulting surgeon for TB hospitals all over Michigan, and subsequently became president of the American Association for Thoracic Surgery and American Academy of Tuberculosis Physicians. He was certainly considered an expert in his field.

A most interesting story about Dr. O’Brien occurred in 1932, when he was in a car accident near Battle Creek, Mich. His car hit a pole, turned over twice and he broke his back. He was put in a plaster body cast and could only move his hands and arms. Dr. O’Brien insisted on performing chest operations on four women when a suitable substitute surgeon was not able to come in time. How did he possibly manage it? He had himself placed facedown in his body cast on a table raised above the operating table at Herman Kiefer. Then his patients were wheeled in and he conducted the operations, each in less than an hour. Colleagues said it left him exhausted, but elated. “It was what the doctor ordered,” he said. The next day, he refused to be interviewed by reporters and photographers, saying it was just work that needed to be done.

**Along Comes Bethune**

In the autumn of 1924, Norman Bethune and his wife moved to Detroit and according to one account, had $24 to their name. They rented a second-story apartment near the corner of Cass and Selden Streets, a few blocks away from the front door of Harper Hospital and part of Detroit’s ‘red light’ district. Their apartment also served as the office where he saw patients and was in close contact with less fortunate people who had serious medical and financial problems.

On January 16, 1925, Dr. Bethune’s application for the surgical staff at Harper Hospital was recommended for approval and he was soon appointed a voluntary assistant in the department of surgery’s outpatient department. Here, Bethune met Dr. O’Brien and the two were comrades in arms, paying their dues as surgeons in the outpatient indigent clinic. Dr. Bethune began a surgical practice and became a popular lecturer with medical students, particularly when the teaching sessions continued on at one of the local speakeasies.

It has been said that during these two years in Detroit, the Bethunes gained first-hand, personal knowledge of poverty, then affluence, and finally tragedy. He believed money was corrupting the medical system, was troubled by the unattended suffering among the poor, and was becoming regarded as a highly skilled surgeon.

Unfortunately, 22 months after he arrived in Detroit, Dr. Bethune developed bilateral pulmonary tuberculosis with hemoptysis and became so ill that he was confined to a hospital bed, possibly at Herman Kiefer or Harper Hospital. He was admitted to the Trudeau Sanatorium at Saranac Lake, New York, where he remained until 1927. He resumed surgical practice in Detroit, but quickly relapsed and returned to Trudeau.

During this time, he decided to become a chest surgeon. Some say the reason is that he already was a trained surgeon who, in the prime of his life, had been struck down by TB and was now inspired to fight the disease. Many other factors pushed him in that direction as well. For instance, Edward Archibald, the premier thoracic surgeon in Canada at the time, some say the reason is that he already was a trained surgeon who, in the prime of his life, had been struck down by TB and was now inspired to fight the disease. Many other factors pushed him in that direction as well. For instance, Edward Archibald, the premier thoracic surgeon in Canada at the time, had been a TB patient at Trudeau where he subse-
quently met Dr. Bethune. Other physicians, colleagues and friends had similar influences on his decision to become a thoracic surgeon, but one wonders whether Dr. O’Brien in Detroit had already sewn the seeds in Dr. Bethune’s mind before he was diagnosed with TB. It is likely that Dr. Bethune sought Dr. O’Brien’s advice about becoming a thoracic surgeon during two return trips to Detroit in 1927. In my opinion [author; Larry Stephenson], Dr. Bethune, had not only observed thoracic surgery performed ‘O’Brien style,’ but probably assisted him on some cases.

In 1932, Dr. O’Brien became incapacitated as a result of an auto accident and sent for Dr. Bethune, now back in Montreal, to take over his thoracic surgery duties at the various hospitals where he was on staff. After this six-month stint in Detroit, many local surgeons began telling Norman Bethune stories. They liked to talk about him because he was so different from other surgeons. One apocryphal story is that Bethune operated on a patient at the Saginaw County TB Hospital and the patient died on the operating table. Dr. Bethune changed into his street clothes, and as he was leaving the hospital, one of the other physicians said, “Aren’t you going to talk to the patient’s family?” Dr. Bethune replied, “The patient is already dead. What good would that do?” and got in his car and drove off.

Bethune’s Reputation Takes Shape
Dr. Bethune developed a reputation for speed and dexterity. A former intern at the Royal Victoria who assisted Bethune recalls, “At the beginning of the operation he would mention the time of the clock on the wall. At the completion, he again would mention the time. He made the effort to do the operation as rapidly as possible, commensurate with safety, and, of course, the purpose of speed was to reduce the time for anesthesia and the period of shock. There was little criticism of his desire for speed, and his motive was the welfare of the patient.”

During Bethune’s Montreal days, besides speed, he also had a reputation for his inventive capacity. Tradition was his enemy and the status quo was usually challenged. He was described as an energetic and enthusiastic surgeon, but widely known for his impatience. His operating room was anything but tranquil. He threw instruments. When scrub nurses or assistants got in his way, he would give them a hard elbow and shouting matches frequently broke out.

Dr. Arthur Vineberg was a personal friend of Dr. Bethune’s and would become chief of thoracic surgery at McGill University. He commented on an operation where he assisted Dr. Bethune. “He was brilliant, no question about that, and he had technical skills, but the kind of technical skill that kills people, because he always like to go too fast. He did a thoracoplasty for Dr. Archibald in front of a lot of surgeons and he said, ‘Come on, Arthur, we will show them how good we are.’ And out came three ribs. I said, ‘Norman, this guy is going to bleed to death.’ ‘No,’ he said, ‘Sixteen minutes from skin to skin! And the guy died.’

Another surgeon commented, “Norman was what I consider an excellent operator and exhibited sound surgical judgment. His philosophy was that every open case of TB was responsible for at least 10 more. He therefore felt that high-risk procedures were justified and endeavored to convert every open case of TB.”

Involvement in the World’s Social-Political Climate
Back ing a bit, it is interesting to note that Bethune’s education at the University of Toronto Medical School was interrupted in 1914, when he enlisted as a private in the Canadian Expeditionary Forces during World War I. He was wounded in the leg while working as a stretcher-bearer in France. Before the year ended, he returned to medical school and graduated in 1916. The following year, he was stopped on a Toronto street by a young girl who asked him why he wasn’t in France, serving in the trenches. Before he could answer, she pinned a white feather on his jacket, which was a sign of cowardice. Soon, he was back on active duty with the military, but this time in the British Royal Navy as a lieutenant-surgeon on one of the early aircraft carriers. He was hospitalized in 1918 for an inguinal hernia repair and celebrated Armistice Day with fellow patients in the hospital.

He returned to civilian life, going through medical training, internships and surgical fellowships in England. He eventually returned briefly to Canada, but then chose to live in Detroit, because, “It was already the capital of the automotive industry, a sprawling center of America’s mass production industries, a magnet for those seeking opportunity, a new Mecca for those filled with prophecies of the Henry Ford period. America was rich, and a great torrent of its riches washed through Detroit. There, he told himself, he would have to kiss no one’s hand, or bend knee to no British upper class dowager. ‘Detroit,’ he said, ‘is where we shall open our first office.’”

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After practicing in Detroit, developing TB himself, and working in New York’s Ray Brook laboratory for a time, he joined Dr. Edward Archibald, surgeon-in-chief at the Royal Victoria Hospital. He trained there in thoracic surgery, but it wasn’t long before Dr. Archibald became fed up with Dr. Bethune’s behavior. He once commented about Dr. Bethune, “I never really liked him; our outlook on life was too dissimilar.” He found Bethune “… definitely abnormal, but not ‘mental’ and not a genius or leader. … He was an egocentric, his vision was keen but narrow. He wore blinkers. He trod on many toes quite often without knowing it or without caring if he did know it. He had a superiority complex and he was entirely amoral.”

Personal and professional differences resulted in Archibald effectively firing Bethune after he returned from Detroit as O’Brien’s ‘pitch hitter’ in 1932. Bethune was quickly appointed to Sacre Coeur Hospital in Cartierville, a 450-bed hospital 20 miles from Montreal, which was managed and staffed by French speaking Catholic nuns. During this time, Dr. Bethune was also becoming quite active in social-political matters in Canada and at the depths of the financial depression, he took a two- or three-month trip to Russia. Shortly thereafter, he joined the Communist Party, although this fact was not generally known for another two years. His views of social-political matters were usually controversial; he was outspoken and rarely known for his tact.

When the Spanish Civil War began in July 1936, Dr. Bethune felt that the time to fight fascism had come, and he left for Spain. He had almost no money and little support, but in three months, was able to organize a Canadian blood transfusion service, which was the first, or one of the first mobile blood bank and transfusion services in the world. Despite the major contributions made by Dr. Bethune’s blood banking service to the war effort, he was ordered to leave Spain eight months later for a number of reasons, including insubordination, heavy drinking and depression.

Upon his return, hundreds of banner-waving supporters met him at the train station. He spent several months on a lecture tour in Canada and the United States raising money for Spanish Civil War victims. Shortly thereafter, Japan invaded China, and Dr. Bethune met up with Mao Tse-Tung’s 8th Route Army in Yenan. After a one-time lengthy meeting with Mao Tse-Tung, Dr. Bethune joined Mao’s Red Army Medical Corps.

For the next 18 months, Dr. Bethune not only did much to improve the Chinese medical corps organization and training, but also performed a large number of operations himself, often with shells flying over his head, close to the front lines. On one occasion, Dr. Bethune and his group worked for 69 hours straight and performed 115 procedures. His infection rate was unusually low, considering that antibiotics were generally not available and he frequently operated in the open, peasant homes, temples, etc. By the summer of
1939, Dr. Bethune was effectively in charge of Mao’s Red Army Medical Corps and had over 20 hospital units reporting to him.

In late October 1939, he cut his finger on a bone fragment while operating on a wounded Chinese soldier with a septic fracture. Within a week, Dr. Bethune developed fever and on November 12, 1939, died of overwhelming sepsis. In that battle-torn area, the Chinese were unable to find a Canadian flag so they draped Bethune’s coffin with an American flag.

Dr. Leo Eloesser, a prominent thoracic surgeon from San Francisco who also served as a volunteer doctor in the Spanish Civil War, wrote an In Memoriam about Norman Bethune that appeared in the April 1940 issue of The Journal of Thoracic Surgery. Excerpts follow: “None of our members (American Association for Thoracic Surgery) has had more stirring actions, and few, perhaps more useful ones, crowded into the years of his life than Norman Bethune, the stormy petrel, as Dr. Archibald aptly characterized him.” Eloesser, whose political views were similar to Bethune’s, goes on to say, “What better end could any man have than this fellow member of ours, who spent his life and met his death in the service of his ideals—humanity and freedom.”

The Bethune Legend Lives On

There have been numerous articles written about Norman Bethune, as well as at least 10 books and several film documentaries. Stories about Bethune’s family, involvement with the art world and activities with social medical reform in Canada have been told over and over again. A hospital, medical school, museum, mausoleum and even several Chinese and Canadian postage stamps commemorate his name.

After Dr. Bethune’s death, Mao Tse-Tung wrote an essay, “In Memory of Norman Bethune,” which later became either highly recommended or required reading for all Chinese adults, many of whom committed it to memory. Different versions of it would be taught to school children. The Chinese leadership chose Dr. Bethune as a symbol of selflessness, dedication and responsibility. Meanwhile, until the early 1960s, Bethune was officially ignored by the Canadian government and considered somewhat of an embarrassment, but all that has changed.

The late Dr. Alexander Walt, former chair of surgery at WSU and former president of the American College of Surgeons, wrote an article about Dr. Bethune called, “The World’s Best-Known Surgeon,” which was published in Surgery in 1983. According to Irene Walt, Alec Walt’s widow, he was fascinated by Dr. Bethune and during two trips to China in the late 1970s and 1980s, they would travel a hundred miles out of their way just to meet and talk with a person who had known Dr. Bethune.

Although 20 years after his death, Bethune’s popularity soared in the 1960s when he became the subject of a book called “The Scalpel, the Sword,” written by Canadian Communist Party members Ted Allen and Sidney Gordon. The book sold millions and in 1964, the National Film Board of Canada produced a documentary, “Bethune,” that portrayed him as a hero. The United States government, unhappy with the heroic portrayal of a Communist, requested that the Canadian government stop selling the documentary in the U.S., but Dr. Bethune was on his way to becoming a hero.

There are numerous statues of Bethune in China and two in Canada. One is located near McGill University
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in Montreal where he trained as a thoracic surgeon and served on the faculty. The other is in his hometown of Gravenhurst, where the house he was born in is open to the public and now managed by Parks Canada, the national park service.

Donald Sutherland, who played Dr. Bethune in a 1990 movie, wrote an editorial in the Jan.-Feb. 2003 issue of the *Journal of Cardiac Surgery*. He said:

“Bethune felt a personal responsibility to act… That was the underlying reason for his decision to train in thoracic surgery. Tuberculosis by his definition was a social disease, spread by poverty. Surgery was the only cure for the disease; social action was the only way to eliminate its existence.

“His memory is dear to my heart; the memory of his spirit constantly stamps its feet in my soul to remind me of the necessity for the selflessness that he so perfectly represented. My affection for him is undying.”

**What Happened to Bethune’s Teacher**

Dr. Bethune’s Detroit friend, colleague, and temporary mentor, Dr. O’Brien, remained active on the staffs of Herman Kiefer and Harper Hospitals until early 1959. He died on October 19, 1959 at Harper after a long illness. His successor, Dr. William Tuttle, memorialized Dr. O’Brien in the September 1960 issue of *The Journal of Thoracic and Cardiovascular Surgery* as excerpted:

“He was Irish and a good politician and he used it to the advancement of care for tuberculosis sick. Almost single-handed, he built institutions for the care of this disease, not only in Detroit, but in the entire state. He labored tirelessly, until at an early date, Michigan had the most adequate hospital treatment and control system in this field.

“He was a man of strong opinions. He could be kind. He could be most unkind. He was a restless soul. He did the right thing as he saw it. He was a stormy petrel on a windswept sea, but when the evening came, there was peace at last.”

**SERVICE AND POLITICAL ACTIVISM INSPIRE WSU MEDICAL STUDENTS**

BY AMY DICRESCE

IN EARLY 1970, A WAYNE STATE MEDICAL STUDENT named Robert Frank joined together with some altruistic classmates to form the Norman Bethune Collective. The group of 20 or so students had progressive ideas about national health care coverage and social responsibility, lived in a commune, and made a commitment to serve under-treated and under-insured people.

“We all read ‘The Scalpel, the Sword,’ which told the life story of Dr. Bethune and we loved that his motto was ‘Serve the people.’ We knew that Dr. Bethune practiced in Detroit—in this same neighborhood where we were going to school—and he likely contracted TB while in the Cass Corridor,” said Robert Frank, MD, who is now an internist and associate dean for academic and student programs at his alma mater. “We were impressed that he put his money where his mouth was—working in battlegrounds, disreputable parts of town, and foreign countries—because he followed his ideals.”

The Norman Bethune Collective matured into a group of WSU School of Medicine graduates, all of whom agreed to apply to Detroit General Hospital for residency during their graduation years, 1972-1975. “We thought that we could make an impact if we all supported each other and went into this together,” Dr. Frank said. “I would say we had some real success. People who raised their eyebrows at us 30 years ago have since told me that maybe our ideas weren’t so crazy, after all.”

First and foremost, the Bethune group followed the internationalist philosophy of their namesake. At the time, there were few American residents at Detroit General; most were foreign medical school graduates. Dr. Frank recalled, “We moved in and immediately became friends with our colleagues who were mostly from India, Pakistan and Turkey. These were more than professional work relationships that helped us learn different skills. These were lasting friendships. We went out together, our spouses became friends, and we played alternating football and soccer games on weekends, just to make it fair for international sporting interests. My wife even wore a sari at our wedding, after having received it as a gift from our friends.” This example of respectful diversity was talked
about around the hospital and people began to take note as the group tried to bridge relationships among different classes and races.

Politics inspired Norman Bethune and they affected his cohorts in Detroit. Dr. Frank and his group found themselves on the picket lines in 1974, when they supported the striking LPNs (licensed practical nurses) at Detroit General. When Mayor Coleman Young saw a television news clip of young white doctors picketing with mostly older black nurses, he called the president of the hospital, and the strike was settled in less than a week.

A few years later, when Detroit was trying to close Detroit General as a city-run hospital, loyalists of the Norman Bethune Collective protested at a city council meeting and got arrested after refusing to leave. “Our position was: there must be a safety net for uninsured people, and the city has to be the safety net,” Dr. Frank said. “Detroit General eventually became a public/private enterprise which has endured, but it’s always threatened. While we failed at ‘saving’ Detroit General, we were successful at ensuring that those served by outpatient clinics made the move to the University Health Center. We considered that a victory.”

When their residencies were over, the 20 residents from the group spread out around Michigan and the United States, but they took the Bethune message with them. Most went into academic medicine, one became a prison doctor, a few devoted their careers to occupational and environmental medicine, and four or five stayed in Detroit.

Dr. Frank recalled that Dr. Vainutis Vaitkevicius was an early supporter of the group who recognized the good work they were doing. “I had the privilege to work with this remarkable group of young physicians, first as a faculty adviser, and later as acting chief of medicine at Detroit General/Detroit Receiving Hospital, where we tackled a number of their projects: rejuvenation of Receiving’s medical residency, Jeffries Housing Health project, and Save Detroit General, to name a few. Drs. Robert Frank, Lawrence Leichman, Stephen Leonard and Stewart Robertson stick in my mind as the activists of the time,” Dr. Vaitkevicius said.

“I think we all had this consciousness that doctors aren’t the only people involved in health care. We saw that it takes teams of people inside and outside of hospitals to do it well,” Dr. Frank said. “As we’ve gone on in our careers, I think we’ve preached similar messages: to stay true to the well-being of patients, to deal with the pressure of economic survival, but never at the expense of good care, and to be socially responsible.”

Although statues of him may never be built and his writings may not be scrutinized by foreign governments, Dr. Robert Frank has embodied the spirit of selflessness that Dr. Norman Bethune preached. He is an active member of Physicians for Social Responsibility, an advocate for often forgotten patient groups like the elderly and the indigent, and he was twice nominated for the Humanism in Medicine Award from the Association of American Medical Colleges. As a clinician, Dr. Frank operates a medical clinic at St. Patrick’s Senior Center, where he challenges “healthy elderly” people to live full lives.

As an associate dean at the WSU School of Medicine, he continually advances the curriculum to include progressive subjects like doctor-patient communication, end-of-life care, geriatric medicine, environmental health exposures, and cultural competence.

“It is a privilege to have Bob Frank serve as associate dean for academic and student programs. His commitment to student education, while remaining true to his social beliefs, brings an important and appropriate balance to medical student education,” said Dr. John Crissman, dean of the WSU School of Medicine. “Social responsibility is an intrinsic component of the education of a physician and we are proud that this mission is an integral part of the Wayne State University School of Medicine.”

As a WSU medical student in the 1970s, Dr. Frank helped establish the Bethune Collective, a group of colleagues devoted to socially responsible health care. He continues to see patients in the Cass Corridor and has twice been nominated for the AAMC’s Humanism in Medicine Award.
“More is better” seems to be a natural assumption, particularly when you’re talking about cancer treatment. We know radiation kills cancer cells, so we may feel inclined to blast lots of radiation to ensure maximum effect on the scary disease.

Well, slow down, says Michael Joiner, PhD, a new Wayne State University professor who joined the Barbara Ann Karmanos Cancer Institute in 2001. An overzealous use of radiation actually weakens its response, according to years of research by Dr. Joiner and his colleagues from the Gray Cancer Institute in England.

“Radiation oncologists are always trying to strike a balance between injury to normal tissue and the effect on the cancer,” Dr. Joiner said. “So, through the years, we have standardized dosage charts in an effort to preserve healthy cells and eradicate cancerous ones. But here’s what we’ve discovered: In 80 percent of our laboratory studies, cancer cells responded more sensitively to radiation if it was given in small dose packets.”

Conventional radiation is typically delivered in dose packets of 2 gray or Gy, the symbol for the international unit of radiation dose. So, a person with prostate cancer might be treated with 2 Gy of radiation, 5 days a week for 6-7 weeks for a total of 60-70 Gy. Dr. Joiner has shown in experimental models that a quarter of the traditional packet size works twice as well.

But, how can the impact of 0.5 Gy be greater
Dr. Joiner uses this X-ray unit to bathe cells in powerful radiation, so he can study the subtleties of various doses and administration protocols.
than 2 Gy? Dr. Joiner believes it has something to do with a cell’s repair mechanisms and that there is a threshold for detecting damage. In other words, a cancer cell subjected to 2 Gy of radiation enacts aggressive damage repair measures to save itself, thereby giving it increased radioresistance (IRR). But at 0.5 Gy, the damage to the cell’s DNA might be low enough that repair responses are not activated, making the cell hyper-radiosensitive (HRS).

“In this phenomenon, cells die from excessive sensitivity to small single doses of ionizing radiation, but remain more resistant (per unit dose) to larger single doses,” Dr. Joiner said. “If we give small doses, the cell might not make an attempt to repair itself. Nature has a wonderful way of eliminating damaged cells, so if we give the cells minor damage through radiation, perhaps the body could efficiently eliminate the cancer cells itself.”

Data from Dr. Joiner’s team shows that IRR/HRS is widespread. It has been tested in many types of cancer cells: colorectal, bladder, skin, kidney, prostate, cervical, lung, neuroblastoma, melanoma and glioma. Although these results haven’t yet been clinically applied, Dr. Joiner has evidence to entertain high hopes. “At low doses, cells can be in excess of 20 times more sensitive than at traditional doses. Imagine how much more effective radiotherapy might be with simple, new dosing protocols,” he said.

Of course, he understands the logistical and financial implications of administering smaller doses of radiation more frequently. It would require more patient compliance and treatment sessions, more nursing hours, more physician hours, and more machines—but once those relationships are sorted out, Dr. Joiner thinks optimal treatments should be adopted, even if they are a little less convenient to schedule. “I’m not afraid to push these things forward, despite what everyone might say about cost and convenience. Which way saves more lives—the old way or the new way? We’ll see what happens and proceed accordingly.”

**Treatment Strategies, Old and New**

It’s very difficult to predict how specific cancer types will respond to specific treatment details. There are thousands of molecular pathways and response mechanisms that are not well explained. In addition to his work with fractionated radiation, Dr. Joiner is looking at basic factors like cell proliferation, hypoxia and intrinsic radiosensitivity to help understand the biological characteristics of individual cancers in order to tailor the most beneficial treatments.

“With every new finding about reactive oxygen species, cell-death mechanisms and radioresistant triggers, scientists begin to follow new pathways backward, to disease onset and cause. We are all trying to get to the top of the pyramid to find the ultimate cancer trigger—the great antennae for all cell damage,” he said. Such information generally...
Furthering the research program in radiation oncology at Wayne State University and the Barbara Ann Karmanos Cancer Institute is the newly recruited team of research biologists from the Gray Cancer Institute in England. Together they are furthering the understanding of radiotherapy and developing advanced cancer treatments.

Michael Joiner, PhD
Brian Marples, PhD
Simon Scott, PhD
George Wilson, PhD

Washington to direct beams of X-rays to individual cells or parts of cells with amazing new technology.

“Radiotherapy doesn’t get as much attention as drug therapy these days, in part, because pharmaceutical companies don’t really profit. But make no mistake, radiation treatment is not old news. There is much research to be done in tailoring its usefulness and efficiency.” Dr. Joiner added that nearly 90 percent of cancer cures involve the use of radiation therapy.

An exciting new prospect for cancer elimination is gene therapy. Dr. Joiner’s group is using “suicide” gene therapy, in which a tumor is injected with a DNA vector that can be switched on by radiation to activate the death of malignant cells. The injected gene vector essentially contains a “promoter” that makes radiation work in a more effective, more targeted way. The synthetic promoter is switched on during normal radiation treatments and has only a local effect in the tumor. This could be particularly beneficial for gliomas, which tend to be resistant to conventional treatments.

The lab is focusing on controlling the expression of such genes with radiation, which allows both temporal and spatial control of suicide vector activation combined with proven benefits of conventional radiotherapy. They are also developing chimeric gene promoters that can be switched on by radiation or hypoxia. They are working with researchers at Beaumont Hospital and, in fact, Joiner’s team found that hypoxia and radiation used together may work better than either alone. As Dr. Joiner said, “This strategy allows the tumor-specific hypoxic microenvironment to activate the suicide therapy in those areas of the tumor where radiation is less effective.”

Dr. Joiner says the entire team has felt very welcome at WSU and Karmanos, because they have been able to fill an obvious void in the radiation oncology research program. “This is a very busy and successful clinical enterprise, but there weren’t many longstanding research projects involving radiotherapy when we arrived. We are here to learn, and teach, and contribute in every way we can and to make the best cancer center in Michigan even better.”

Drs. Simon Scott and Olga Greco do DNA separations to understand the power of radiation and hypoxia in eradicating cancer cells.

Drs. George Wilson and Brian Marples use expertise in flow cytometry to measure radiosensitivity in cells.

Radiation Biologists Recruited from United Kingdom

Furthering the research program in radiation oncology at Wayne State University and the Barbara Ann Karmanos Cancer Institute is the newly recruited team of research biologists from the Gray Cancer Institute in England. Together they are furthering the understanding of radiotherapy and developing advanced cancer treatments.
INSTITUTE
TO
ADDRESS
HEALTH
OF

URBAN
POPULATION

New institute to
determine and
manage underlying
genetic, social and
environmental
predictors of disease
People living in large urban areas, especially those that are medically underserved, are subject to an unnecessary burden of chronic disease. This not only limits their own lives, but also limits the economic well-being of the entire area.

Consider this: African-Americans are at a much higher than normal risk for dying from breast cancer, colon cancer, prostate cancer, hypertension, stroke and coronary heart disease. Similarly, Arab Americans may be less likely to seek and receive appropriate testing and screening for high cholesterol, uterine cancer and breast cancer, compared to other individuals in the state of Michigan.

The causes for such disparities are complex and include genetic, environmental and social factors. They are just now coming under intense investigation, but are far from being controlled. The Wayne State University School of Medicine is leading the establishment of the Institutes for Population Studies, Health Assessment, Administration, Services and Economics (INPHAASE) to identify predictive risk factors in particular communities and populations and to learn how to manage risk and improve the health and economic conditions of urban areas such as metropolitan Detroit.

“The identification of unique populations with statistically significant exposure response patterns and identifiable biomarkers will lead to quantum leaps in the predictive assessment of occupational or environmental disease,” said Gloria Heppner, PhD, who is responsible for the development of INPHAASE. “To ignore the risk factors associated with urban subpopulations is to ignore treatment options and hope for healthier lifestyles.”

The new organization essentially umbrellas many productive areas that already exist at Wayne State University. Its purpose is to coordinate the efforts of many research programs relevant to urban health, environmental health, chronic disease and health economics. INPHAASE reaches across the entire university and brings together the Institute of Environmental Health Sciences, the Center for Chemical Toxicology, the Karmanos Cancer Institute’s Cancer Population Studies, the College of Business Administration’s Information Systems, and the Center for Healthcare Effectiveness Research, among many others. The aim of the new population-based program is to improve the prevention and detection of chronic
diseases, reduce health care costs and implement tailored community-based interventions among identifiable ethnic, gender or social groups.

With large numbers of African-American, Arabic, and other diverse populations, metropolitan Detroit offers a unique site to investigate and develop effective chronic disease control measures for at-risk individuals. According to Dr. Heppner, accurate prediction of at-risk populations ultimately leads to focused, cost-effective prevention. “This is critical to the long-term economic health of our region since the majority of health care costs, estimated to approach two trillion dollars nationally, are borne by corporate sponsored health care and government programs.”

Although not all genetic problems are curable as yet, certain susceptibilities, like environmental toxic exposures, are preventable, if researchers understand more about them. Entire populations could be protected from harmful exposures through efficient preventive programs. The traditional model of environmental health research has argued for precaution: pregnant women limit their fish intake to avoid mercury contamination, public smoking areas limit second-hand smoke exposures, and children with asthma remain indoors on ozone action days.

Newer models of environmental health argue for prediction and prevention of disease. For instance, researchers have identified two genes that may predict how a person reacts to organophosphate pesticides. People with these genetic markers can’t break down pesticides. With that knowledge, they could avoid chemical exposures that would be toxic for them, but inconsequential for others. Similarly, particular subpopulations may have a predisposition to lead poisoning because of a genetic defect that controls lead metabolism or how the bones store the substance.

Dr. John Crissman, dean of the WSU School of Medicine, said development of the INPHAASE is a number one priority. He has committed $5 million to this venture over the next five years and is exploring a suitable building site to house a facility that will bring population scientists, clinicians and resources under one roof.

“Most current research programs that address the adverse health consequences of urban life lack significant focus on relevant minority populations and on assessment of disease risk using genetic and protein level biomarkers as subclinical predictors of at-risk populations,” Dr. Crissman said. “Through institute collaborations, experts will conduct applied and basic research with the common goal of reducing and managing disease development through identification of early genetic predictors of environmental and occupational exposures.”

THE AIM OF INPHAASE IS TO IMPROVE THE PREVENTION AND DETECTION OF CHRONIC DISEASES, REDUCE HEALTH CARE COSTS AND IMPLEMENT TAILORED COMMUNITY-BASED INTERVENTIONS AMONG IDENTIFIABLE ETHNIC, GENDER OR SOCIAL GROUPS.
Inphaase Leadership

The following list shows the lead participants in key research areas of Wayne State University’s Institutes for Population Studies, Health Assessment, Administration, Services and Economics (INPHAASE). Additional faculty will be recruited in the next several years.

Special Assistant for Development of INPHAASE
Gloria Heppner, PhD
Professor of internal medicine, oncology
Wayne State University School of Medicine,
Barbara Ann Karmanos Cancer Institute

Health Services Research
R. Michael Massanari, MD
Professor and director, Center for Healthcare Effectiveness Research
Wayne State University School of Medicine

Population Studies
Ann Schwartz, PhD, MPH
Associate professor of internal medicine, oncology
Wayne State University School of Medicine,
Barbara Ann Karmanos Cancer Institute

Health Risk Assessment
Raymond Novak, PhD
Director, Environmental Health Sciences Center in Molecular and Cellular Toxicology with Human Applications
Director, Institute for Environmental Health Sciences
Professor of pharmacology
Wayne State University

Health Management and Informatics Research
Joseph Tan, PhD
Professor and chair of information systems and manufacturing
Wayne State University School of Business Administration
Detroit needs to do a better job in alleviating the major health problems that plague African Americans: namely, obesity, cardiovascular disease and cancer. Detroit has the third largest population of African Americans among all cities in the United States, but has the highest percentage of any major U.S. city. Furthermore, the most recent census data measured the index of dissimilarity between whites and African Americans, and showed the Detroit metropolitan area to be the most segregated in the nation. Obviously, the health of African Americans is a critical concern for the region, the state of Michigan, and the entire country.

John Flack, MD, MPH, is hoping for a National Institutes of Health grant to establish the Wayne State University Center for African-American Urban Health. In a nutshell, his $6.5 million proposal seeks to uncover new ways to redress health disparities by identifying preventive strategies and therapeutic approaches to chronic diseases that plague this population.

“African Americans comprise one of the largest minority groups in the United States, and they suffer excessively from a wide range of obesity and lifestyle-related health conditions,” Dr. Flack said. “We hope to alleviate the disproportionate burden of disease.”

The NIH expects to award approximately $15 million to seven or eight centers to study population health and health disparities. If the NIH funding is granted to WSU, Dr. Flack will act as the principal investigator and enlist the commitment of 34 investigators from five core areas of expertise. Together, they will work on four specific projects that focus on precursors and factors mediating chronic conditions in African Americans. These projects are:

• Obesity, Nitric Oxide, Oxidative Stress and Salt Sensitivity
• Weight Loss in Breast Cancer Survivors
• A Dyadic Intervention for Cardiac Rehabilitation Patients, and
• Promotion of Health Behavior in African American Women.

“These projects have been carefully chosen for inclusion in the research portfolio of the center because of their thematic linkage to one another,” Dr. Flack said. “They are all related to obesity, diet and other lifestyle factors that impact cardiovascular disease and cancer. Furthermore, by building on WSU’s current strength in genomics, population studies, and cancer epidemiology, for example, the investigators can test a broader range of hypotheses than would be possible with stand-alone projects.”
This center for health research and treatment is a prime example of what Dr. Gloria Heppner envisions for Wayne State University’s Institutes for Population Studies, Health Assessment, Administration, Services, and Economics (see prior story). "Population-based research endeavors like this help us understand relationships among variables that affect health. These studies consider environmental, psychosocial, biological and genetic factors to see how they interact to affect the health of a particular group with commonalities," Dr. Heppner said.

Already, WSU has a terrific model to follow regarding population medicine. The Barbara Ann Karmanos Cancer Institute operates a Population Studies Program under the leadership of Ann Schwartz, PhD, Rick Severson, PhD, and Omer Kucuk, MD. Their work is facilitated by access to the federally-supported Surveillance, Epidemiology and End Results (SEER) cancer registry that gathers information on all newly diagnosed cancers in defined populations and geographic areas. This large database and pool of expert researchers allows multidisciplinary approaches to the research, treatment and prevention of disease.

Dr. Flack, who has published extensively on African Americans’ salt sensitivity and predisposition to hypertension, understands the unique health needs of the population to which he refers and belongs. As a professor of internal medicine and community medicine, he sees the immediate link between a person’s individualized health concerns and those they are automatically subjected to by virtue of their geographic location, gender, age, race or ethnicity.

"We need to evaluate health on both personal and population bases in order to get the whole picture," Dr. Flack said.

Dr. John Flack hopes to alleviate the disproportionate burden of disease for African Americans.
Dr. Ashraf Mohamed discusses treatment options with this patient who suffers from facial, back and stomach pain. He is the only neurologist in Michigan who did fellowships in pain and anesthesia. He has dual appointments in WSU’s neurology and anesthesiology departments.
AGONIZING, THROBBING, EXCRUCIATING, JABBING — everyone has used words like these to describe pain. Whether it is a migraine, a toothache or a back spasm, we temporarily endure the pain, all the while looking forward to the time when it’s gone and life can finally go back to normal.

For people with chronic pain, however, life is anything but normal. They must not only deal with the pain itself, but with the knowledge that it may never go away. Many of these patients turn to the School of Medicine’s University Pain Clinic (UPC) for help. With a multidisciplinary team of pain specialists, the UPC offers patients a full range of services, plus an unusually sympathetic and determined staff of professionals. At the top of the list is the clinic’s medical director, who began his career in anesthesiology after facing chronic pain himself several years ago. “I had gone to the hospital to have a bone tumor removed and ended up with some nerve damage,” said John Kurtz, MD, who had just been accepted into medical school at the time of the injury. The diagnosis was reflex sympathetic dystrophy, which is also known as chronic regional pain syndrome.

He recalled, “I felt what this pain is like, and I saw how it messes with your sleep, affects the way you think and makes you a little crazy. I couldn’t think straight for a couple of months because of the pain.” Fortunately, his anesthesiologist was well-versed in treatment options, and, after trying a range of powerful pain medications without success, he administered a nerve block that eventually led to a cure. “I was really, really lucky, because you just don’t see many people who are cured from this type of pain.”

The experience changed his life, Dr. Kurtz said. “When the anesthesiologist came in, did this nerve block, and it worked, well, that’s why I decided to go into anesthesiology.”

A multidisciplinary team
Although most people don’t know it, anesthesiologists do more than assist in the operating room. “Interestingly enough, about 80 percent of the specialty of pain management in this country is performed by anesthesiologists,” Dr. Kurtz said. Their expertise extends to specialized nerve blocks, like the one that cured Kurtz, intrathecal pumps that deliver pain medications directly into the spinal fluid, and a variety of other treatments.

The University Pain Clinic staff includes several different anesthesiologists who have extra training in pain management. In addition, it has a psychologist specialized in chronic pain, a PhD pharmacologist, a neurologist, a full-time nurse to help manage the patients with intrathecal pumps and a complete office support staff. “By having people from different specialties working together under one umbrella organization, we can optimize a patient’s pain relief,” Dr. Kurtz said.

Clinic staff also have the opportunity to work with a cadre of specialists within the Detroit Medical Center (DMC). In particular, the University Pain Clinic confers with, refers patients to and accepts referrals from the Rehabilitation Institute, as well as a number of neurosurgeons who focus on pain treatment. One such neurosurgeon is Jeffrey Brown, MD. New to the DMC, he is among the select few neurosurgeons in the country performing a promising procedure called motor cortex stimulation to treat facial pain (see related article).

Usually, patients come to the University Pain Clinic when their pain has lasted more than six months, and they have run out of other options. “For example, there is a subset of cancer patients maybe 10 to 20 percent who some time during the course of their disease, experience pain that cannot be controlled adequately even with high doses of narcotics.” Other common pain-clinic candidates are patients with back injuries, herniated disks or deformities of the spinal column.
The challenge of chronic pain

“Whenever we have a new patient, we do a full history and physical, we go over what modalities the patient has had 1) to diagnose and 2) to treat their pain,” Dr. Kurtz explained. “The first key thing is to try to get a diagnosis, which gives us a better chance of treating the underlying cause.” While that’s the goal, it is not always possible. He explained, “A surprising number of patients – approaching 50 percent never receive a true diagnosis other than something generic, like ‘back pain.’”

As the next step, the staff takes a fresh look at the patient to decide how clinic services can help. “In some cases, we may determine that a patient only requires a nerve block every few months,” he said. At its simplest, a nerve block may be a shot of cortisone to alleviate the inflammation of tennis elbow. In other cases, a patient may need to return to the clinic every few weeks as the staff deduces which medication has the most benefit and the mildest side effects. Treatment options also include physical therapy, acupuncture or an intrathecal pump, which is a hockey-puck-sized device implanted beneath the skin. The pump delivers a constant flow of pain-relieving drugs through a thin catheter to a targeted area of the spinal column. Dr. Kurtz, who underwent a separate fellowship to learn to administer the pumps, has found them particularly useful in relieving cancer pain.

All said and done, Kurtz estimates that 80—90 percent of clinic patients receive at least some pain relief. However, he acknowledged, “There have been very few patients that I have ever cured of chronic pain. It just doesn’t happen. So, part of the patient-physician relationship is getting the patient to accept that life is going to be different: It’s going to involve this pain, but that doesn’t mean that your life has to revolve around the pain.” That realization is where the clinic’s psychologist comes in.

Mind games

“The longer a pain problem goes on, the greater the impact it has on a person’s life,” said UPC clinical psychologist John Dooley, PhD, who has been specializing in chronic pain since 1980. “Chronic pain wears a person down, it creates all sorts of lifestyle disruptions, like work problems or financial difficulties, and that then generates secondary psychological side effects, such as depression, anxiety and unhelpful coping responses. My job is to help people learn to accept the presence of the pain and start to make more active coping efforts to live their lives around the pain problem.”

Acute pain and chronic pain are totally different problems, Dr. Dooley said. “With acute pain, the pain is a symptom. It’s a sign of an underlying disorder. You put your life on hold, and a physician diagnoses and then treats that underlying disorder.” Usually with a few days of rest, the patient recovers.

“With chronic pain, to a certain extent, the pain itself becomes the disease,” he described. “Here, excessive inactivity causes muscle-fiber shortening, deconditioning, and therefore greater pain when you do move. That further extends and complicates lifestyle disruptions, which can then lead to depression. So the coping approach, the whole conceptualization medically and psychologically has to change when you switch from acute to chronic pain.”

Frequently, Dr. Dooley finds that patients with chronic pain will either dwell on the pain almost exclusively, or will alternate between extremes. In the latter, a patient shifts between inactivity and overactivity. “When a person pushes too hard, that patient is punished with increased pain. Inactivity winds up being reinforced, because it reduces or alleviates their pain,” he said. In other words, pain can have behavioral components that encourage a patient to begin a downward spiral.

Beyond helping patients learn to cope positively with chronic pain on a day-to-day basis, Dr. Dooley provides psychological assessments that can affect the success of medical treatments. “The current focus of pain management is increasingly emphasizing medical interventions, like intrathecal pumps, spinal cord stimulators, lumbar fusions and other elective surgeries. A lot of evidence shows that psychological factors can

“THE LONGER A PAIN PROBLEM GOES ON, THE GREATER THE IMPACT IT HAS ON A PERSON’S LIFE.”
Psychologist Dr. Dooley talks about coping with chronic pain.

significantly affect the long-term outcomes of these procedures.” Through psychological assessments, Dr. Dooley can help determine whether a particular patient makes a good candidate for a specific treatment. For instance, a patient’s psychological profile may indicate compliance problems that would make him or her unsuited for treatments that continue over a long period of time. Another patient may have unreasonable expectations about a medical treatment, making recovery unlikely for any therapy that falls short of total pain relief. “I look for anything that could interfere with the patient’s ability to respond appropriately and could potentially affect the treatment,” Dr. Dooley said.

A history of care
Together, the psychological therapy and medical treatments have made a good combination at the University Pain Clinic, which opened for business in May 2002. Its roots, however, date back to the early 1980s when the anesthesiology department started up an office to provide inpatient pain treatment. While the office provided needed services, it didn’t offer the follow-up care so many patients required, according to Dr. Samir Fuleihan, vice-chief of anesthesiology. What they really needed was a pain clinic with its own assigned and complete staff. “We had a large patient population who required these services, and also a large number of physicians who wanted to refer their patients with chronic pain somewhere in central Detroit,” Dr. Fuleihan said.

The anesthesiology department stepped up to the challenge, and under the leadership of Drs. Fuleihan and Pramod Kerkar, assistant professor of anesthesiology, set the wheels in motion for what became the University Pain Clinic. The clinic hit the ground running, and began taking patients as soon as it hung its shingle last spring.

“We haven’t been able to help everyone, but we have helped most people,” Dr. Kurtz said. “In particular, we have helped them realize that chronic pain is about change: It’s about changing your life and changing your behavior. It’s not always about changing the pain.”
WITH THE HELP OF TECHNOLOGICAL ADVANCES, doctors are now using time-tested equipment and surgical procedures to offer hope to patients who previously had little. An advanced technique, called motor cortex stimulation, has proven helpful for many patients coping with facial pain, according to Jeffrey Brown, MD, who specializes in facial pain and performs the surgery. The surgery is also currently being studied for its effectiveness in treating stroke patients.

Dr. Brown, a professor of neurological surgery, and chief of pain and functional neurosurgery, who had become well-known as a facial-pain expert, began seeing more and more patients who were at the end of the rope. Some had the stabs of pain, but some had intermittent electric sensations, and some had both. “The reason I was seeing them was because their problems were unsolvable,” he said, noting that the patients had found medications to either be unsuccessful or have too many side effects, and other surgical procedures to be too risky. “These patients were going around the country, and sometimes even around the world, looking for anybody to help them.”

In response, he has become a proponent of motor cortex stimulation. It works like this: Through tiny openings in the skull, the surgeon threads a needle of electrodes. Using computer technology called neuronavigation, along with MRI, the surgeon chooses a precise target just over the motor cortex, the portion of the brain that controls movement. The electrodes never actually penetrate the brain, but instead rest barely beneath the skull and above the thin membrane (the dura mater) that covers the brain. A controlled electrical pulse is transmitted to the motor cortex region of the brain.

“It is as if the brain is an engine that is missing a spark plug,” Dr. Brown said. “By stimulating the motor cortex, it is as if a new plug has been inserted. The engine that is the brain runs more smoothly and the pain is relieved.”

The ability to target a very specific area of the brain was the breakthrough that opened motor cortex stimulation use for facial pain, Dr. Brown said. The new, neuronavigation technology pinpoints the location of different areas in the brain, much like an air-traffic-
control system is able to find a jet in three-dimensional space. With this technology, the surgeon can take a pointer armed with infrared light-emitting diodes (LEDs) and a sensor array, move it anywhere over the skull, and simply follow along on the computer screen to find out what part of the brain lies beneath. He explained, “Now, without seeing the brain, we can place the electrode array over what we know anatomically to be the area of the brain that corresponds to the face or the hand or the leg.”

Dr. Brown calls the procedure a success when he can turn on the electrical current and at least half of the patient’s pain disappears. “When it works, patients find it most remarkable. They will just break out in tears and say, ‘I don’t understand this; this is amazing.’ There’s no concept to explain how you can turn on an electrical switch, and pain can get better or sometimes even go away.” If initial results are positive, he connects the electrode wires to an implanted “pulse-generator,” a programmable, pacemaker-type device that drives the electrode.

“IT IS AS IF THE BRAIN IS AN ENGINE THAT IS MISSING A SPARK PLUG. BY STIMULATING THE MOTOR CORTEX, IT IS AS IF A NEW PLUG HAS BEEN INSERTED. THE BRAIN RUNS MORE SMOOTHLY AND THE PAIN IS RELIEVED.”

April Mingus spent five years in excruciating pain before she met Dr. Jeff Brown. Now, she has an implanted neurostimulator, which has been dubbed a “pacemaker for pain,” and she has returned to a normal life.
Dr. Brown uses motor cortex stimulation to relieve patients of seemingly unsolvable pain.

"THERE'S NO CONCEPT TO EXPLAIN HOW YOU CAN TURN ON AN ELECTRICAL SWITCH, AND PAIN CAN GET BETTER OR SOMETIMES EVEN GO AWAY."

Studies following facial-pain patients for two years after the surgery report that 75 percent have more than half of their pain alleviated, Dr. Brown said, cautioning that not all people with facial pain are good candidates for the surgery. He will continue to follow the patients to determine the surgery’s long-term effectiveness. He is also watching similar surgeries to treat other types of pain. “The success rate appears to be a little less (to treat pain) in other parts of the body, but it’s being used in the hand and sometimes even in the arm for indications such as stroke and shingles.”

Currently, Dr. Brown is also leading a multi-center study of motor cortex stimulation for another use. “This study is based on observations of patients who were treated with the cortical stimulation for pain after stroke. Even though some of the patients didn’t get good pain relief, they still insisted on keeping the stimulator because it gave them improved use of their hand.” Since the initial observations, animal studies have had similar results: increased motor function upon stimulation of the motor cortex.

Dr. Brown has first-hand knowledge of potential benefits. “I had a patient from Colorado who had suffered a stroke. He couldn’t move one side of his face, and he had had pins-and-needles pain in his face for six years. At the time I saw him, he was taking massive doses of oxycontin, and the highest doses of opioids I’ve ever seen in my life. Nobody knew what to do with him,” he remembered. “I did the motor cortex surgery, and he woke up from the surgery with a full smile on his face.”

Some people have mistakenly called motor cortex stimulation “experimental,” Dr. Brown said, but the only new part of the procedure is the computer advancements. “The surgical procedure is more than a dozen years old. It uses equipment that has been around for 25 years, but in a different way. The technology has simply made it more accessible.”

He also stressed that the procedure isn’t a guarantee. Because it involves the brain, he noted, it also has at least some element of risk, although considerably less than surgeries that actually penetrate brain tissue. “This procedure is a lot for a patient to go through, but these patients have been through a lot before they get to this point,” he said. “The reason they’re willing to do this is because they are facing such terrible, life-affecting problems. They had no hope. Now they do."
At a moment’s notice, Dr. Sean Blackwell can access important electronic medical records for his high-risk pregnant patients.
CREATING A PAPER TRAIL IS RARELY EASY. For the medical profession, it’s a nightmare. Patients move from primary physician to specialist and back, from lab to lab for various tests, and even from doctor’s office to hospital — and they expect their medical records to follow them through the maze. A new computer program, created at the WSU School of Medicine, is helping to make that expectation a reality for one of the most difficult-to-follow groups of patients: pregnant women.

The developers are Sean Blackwell, MD, assistant professor in the Division of Maternal-Fetal Medicine, WSU Department of Obstetrics and Gynecology, and Ryan Blackwell, a senior database administrator in the department’s informatics unit. The two are brothers. Together, the men are developing an advanced computer system that takes electronic medical records well into the 21st century. Targeted specifically for tracking expectant women, especially those with problem pregnancies, the system is called the Women, Infant and Neonatal Database, or WIND. It allows authorized clinicians and researchers to use the Internet as the vehicle for tapping into patient information, risk factors, the results of lab tests, sonograms and any other procedure information relevant to the care of the mother and child.

Paperless Patient Records Advance Care for Pregnant Women

Tailored computer program gets noticed by medical and technology industries

By Leslie Mertz

One Site Fits All
With WIND, a physician can find all needed data through a single Web interface. As an example, Dr. Blackwell turned to his computer and accessed a Web page. “This is a picture of a baby’s heart that has a hole in it,” he said, pointing to the screen. “This page links this picture to her clinical information, the diagnosis, the mother’s age or risk factors, and a variety of other information.” No other available system has this capability, he noted. “What I’m showing you here is straight off of the Internet (through WIND), and this system is being used every single day to take care of patients.”

In addition, he said, WIND allows an authorized researcher to go into the system and, for example, view the pertinent data from all the women whose babies had the same heart condition. “The researcher can bring up all of the pictures and have access
to them, whether the researcher is in this building, across town or anywhere else. The ability to do that from a research standpoint is something that’s unique.”

Before WIND, researchers routinely sent nurses to the various clinics to manually root through patient charts to find those who might be good candidates for a specific research project. At a hospital system that delivers more than 6,000 babies a year, the job was monumental. WIND’s ability to do that electronically is a considerable time-saver, said Ryan Blackwell.

**Simple, Secure, Unified**

With the groundwork laid, they had three major considerations:

1) how to make the system simple for the researchers and clinicians who are inputting or extracting data,

2) how to protect a patient’s confidentiality, and

3) how to incorporate different types of information into one Internet-based system.

**Working From Scratch**

The brothers didn’t start out with the idea of developing a new system. Rather, they hoped to find something already on the market that they could use right from the box or with a few modifications. “There is just nothing out there that meets the bar that was set for us,” Dr. Blackwell said. The “bar” originated with the National Institutes of Health (NIH), which has its intramural Perinatology (pre- and post-birth) Research Branch at Wayne State. Along with the branch, the WSU Department of Obstetrics and Gynecology received a 10-year grant of more than $140 million to focus on women’s health, pregnancy and prenatal diagnosis.

“As part of that grant, we had to meet several requirements, one of which was that we have higher functioning perinatal databases for both clinical care and for research.”

It was a daunting task. As they began, they learned that at least seven out of 10 medical applications fail, primarily because developers misunderstand users’ demands. The WSU team didn’t have that problem.

Dr. Blackwell, who is both a researcher and a clinician who specializes in high-risk pregnancies, provided a clear vision. Ryan Blackwell, on the other hand, is a skilled programmer who was able to use his expertise in computer languages and Web-based technology to bring the vision to life.

The team had one more thing in its favor. Ryan Blackwell remarked, “I’m 100 percent committed to Sean and this application, and (because we’re brothers,) there’s no lack of communication and no lack of directness. There are no political problems between the developers coding the application and the clinicians defining its functions.”

The latter was a particular challenge, Dr. Blackwell said, because they needed to combine basic clinical information, research information, and data coming from a variety of sources, such as fetal magnetic resonance images (MRI); 2-, 3- and 4-dimensional ultrasounds; color Doppler ultrasounds; and numerous medical units. “Linking the different media types is really problematic, but we did it,” he said. The result is an application that combines everything from charts to pictures to text seamlessly.

For a user, WIND is easy to operate. A doctor or nurse entering basic clinical information about a patient simply fills out a straightforward, on-screen form. Since the clinical and research pages are linked, the system eliminates much of the duplication of efforts that currently plagues medical record-keeping. In addition, each page has its own table of contents, forward and back buttons, pull-down menus, calendars and a large help-desk icon. “The help desk is important, because if the doctor or nurse doesn’t know what to do next and gets frustrated, they’ll just shut it down and won’t use it.”
Security was also vital to protect patient-doctor confidentiality, the brothers said. The WIND provides role-based access, data encryption, and other security protocols making its security above that of online banking, Dr. Blackwell said.

The two men have been working on the application for almost three years, and it is already at work in the obstetrical and gynecological units in the perinatal research program. Dr. Blackwell said he needs to see how well WIND operates for three to five years before he would declare it a complete success, but he allowed, “I think what we have done is terrifically promising, and has come up to our expectations.”

Drawing Notice

Others are impressed, too. At the 2002 Application Development Competition, sponsored by tech giants Microsoft, Dell, Intel and VeriSign, the still-incomplete WIND system placed 14th out of 17,000 applications, said Ryan Blackwell. “When we submitted our application, it was only about 5 percent done. I was told they couldn’t place us higher than 14th because they couldn’t fully judge our application.” He is anxiously looking forward to the next competition.

In the meantime, the men are continuing to widen the system’s capabilities to encompass the entire program within obstetrics and all of the associated units in women’s health at Wayne State. The system, now copyrighted, has the potential to expand even further. While they are now solely focused on meeting their internal needs, they have already seen some outside interest from administrators at other research/clinical institutions.

Ryan Blackwell added, “I hesitate to say this, but WIND does impress people, because of where we’re jumping from. This is, from what we can see, just generations ahead of what’s currently being used.”
Dr. Donald Kuhn has one of only three K05 grants in the state, and is the only WSU faculty member to hold such an award.
e is one of the few people at his level in the profession who continues to perform experiments in the laboratory. This has to be a very deliberate choice on his part, as most principal investigators do not have the time. But, one can tell this is where he is in his element,” said Samuel Parks, who is completing his PhD under the tutelage of Dr. Kuhn in Wayne State’s cellular and clinical neurobiology program.

Echoing that sentiment is Timothy Geddes, a member of Dr. Kuhn’s lab. “Although he is the principal investigator and wears the administrator’s hat, he also is a ‘hands-on’ participant in the laboratory. Thus, he serves as an inspiration to members of the lab.”

Recognizing the difficult balance between teaching, publishing and performing research, the National Institute on Drug Abuse (NIDA) has honored Dr. Kuhn with its Senior Scientist Award. This funded award enables Dr. Kuhn to increase his research time in the laboratory and advance his important studies into the neurotoxicity of amphetamines and the biochemical, molecular and behavioral characterization of drugs of abuse.

Donald Kuhn, a Wayne State University professor in psychiatry and behavioral neurosciences and the Center for Molecular Medicine and Genetics, came to Detroit in 1986. He also serves as a member of the Institute for Chemical Toxicology, and balances multiple collaborations and multidisciplinary projects.

“Dr. Kuhn’s troubles are really good ones to have,” jokes Dr. Thomas Uhde, assistant dean for neurosciences at the WSU School of Medicine. “His reputation as a fantastic mentor and a terrific researcher is far-reaching, so he gets pulled in many directions. He handles it with remarkable grace, however, and manages to devote great attention to his collaborators, students, research team and colleagues inside and outside the university.”
His work is beginning to unravel the neurochemical systems in the brain and has application for people who suffer from drug abuse, Parkinson’s disease, depression, obsessive-compulsive disorder and schizophrenia. Already, Dr. Kuhn can be credited with the following research contributions:

- the biochemical and molecular characterization of how reactive oxygen and reactive nitrogen species modify the function of protein targets known to be damaged by neurotoxic amphetamines,
- behavioral characterization of hallucinogenic drugs of abuse using drug discrimination techniques,
- and regulation of the neurochemical function of monamine neurons.

With the NIDA Senior Scientist Award, Dr. Kuhn plans to hire two new scientists in his lab to step-up his work creating a genetic switch, or conditional knock-out mouse model through homologous recombination. Additionally, he is very interested in the use of mass spectrometry in characterizing how drugs of abuse modify key proteins in the brain. Finally, he is applying functional genomics and proteomics to the evaluation of neuronal gene and protein expression patterns of specific drugs.

“His work is always meticulous, intellectually rigorous and meets the highest standards of the field,” Park said of Dr. Kuhn. “He has taught me a lot about how to do science, to think in the right ways, and to understand what will work and what won’t. He balances the theoretical and the practical. He works as hard as anyone I know. First to come in, last to leave.”

Ever the mentor, Dr. Kuhn has often said, “Education is inseparable from research.” He clearly lives that philosophy and shows it, in part, by leading a NIDA-sponsored training program that helps develop the careers of young researchers in biomedical and behavioral neurosciences. The program trains four research fellows each year and helps expand the field of drug abuse and drug addiction.

Dr. Kuhn earned a bachelor’s degree from Presbyterian College in South Carolina in 1972, and a doctorate from the University of South Carolina in 1976. He did postdoctoral fellowships at Princeton University and the National Institutes of Health, before his first faculty appointment at the George Washington University Medical Center in Washington, D.C. He has published more than 100 articles and 35 book chapters, been a reviewer for more than 25 academic journals, teacher for six Wayne State courses over 13 years, and director for five dissertations. His first grant support came from the...
National Heart, Lung and Blood Institute in 1976—the year he earned his PhD—and he has enjoyed generous funding and recognition thereafter.

Although he’s being honored as a seasoned senior investigator, Dr. Kuhn often reflects on his junior years, and sees it as his duty to perpetuate good science and nurture those at the beginning of their own careers.

“My success helps the junior scientists around me. We all work to support one another, and I am grateful to many colleagues who have helped me secure this K05 grant, particularly Drs. Paul Walker, Matt Galloway, Manny Tancer, Tom Uhde and Dan Walz. Our lab has reaped great benefits from these supporters,” Dr. Kuhn said. 

Strides in the Kuhn laboratory are generated through teamwork. Pictured here are: (back row) Tim Geddes, research assistant; Stacey Sakowski, graduate student; Dr. Donald Kuhn; Dr. David Thomas, assistant professor; Dina Verbeem, research assistant; (front row) Mahdieh Sadidi, graduate student; and Xiuli Liu, research assistant.

“EDUCATION IS INSEPARABLE FROM RESEARCH.”
PROTEIN DYNAMICS

Seen Up Close With New NMR Equipment

By Amy DiCresce
The new NMR machine has been delivered to Wayne State University’s Eugene Applebaum College of Pharmacy and Health Sciences. Assembly and calibrations are now underway under the supervision of the NMR team led by: Shahriar Mobashery (Institute for Drug Design), Tim Stemmler (assistant professor of biochemistry and molecular biology), Pat Woster (pharmaceutical sciences facilities director), and George Corcoran (chair of pharmaceutical sciences).

Structural biology makes good intuitive sense. If you can see how a molecule is constructed, you can better understand how it works. This basic law of construction and engineering has been the push of biologists and biochemists for half a century. But structure begs the question of functionality, which leads scientists to their next frontier—dynamics.
“The speed of advancement in the area of structural biology is astounding. Thanks to recent innovations in theory and instrumentation, we can quickly determine the solution structure of very large biomolecules,” said Timothy Stemmler, PhD, assistant professor of biochemistry and molecular biology who was recruited to Wayne State in 2000. “An enzyme’s function is dictated to a large degree by its structure, so having a comprehensive picture of how all atoms are arranged makes it much easier to characterize their reaction mechanisms. However, it is becoming increasingly clear that enzymes do not behave as static molecules during catalysis, and in fact, it is their dynamic properties that, in part, allow them to function. To completely understand what a protein is doing, you need to have working descriptions of the dynamic properties of its atoms.”

But these inner workings of proteins can only be seen with technologically advanced instrumentation. Of course, higher resolution requires higher-end equipment. The Wayne State University School of Medicine recognized this important need and is currently making the final calibrations on a 600 MHz high-field NMR (nuclear magnetic resonance) spectrometer in a core facility accessible to all WSU researchers. The purchase was made possible with a National Institutes of Health Shared Instrumentation Grant and support from the WSU School of Medicine. Until recently, no such instrumentation existed at WSU for characterizing large proteins. This instrument will be used for the high throughput characterization of biomolecules in solution. The additional purchase of a cryoprobe will increase the sensitivity of the spectrometer, allowing scientists to look at very low protein concentrations.

Dr. Stemmler’s research would basically be halted without the use of an NMR spectrometer. Until now, he had to request access to instruments at the National High Field Magnet Laboratory in Tallahassee, Fla., to get spectrometer time to characterize the solution structure and dynamics of his protein samples. Now, he can walk over to the NMR core facility in the Eugene Applebaum College of Pharmacy and Health Sciences on the WSU medical school campus.

“NMR spectroscopy is a key tool in research endeavors related to structural biology. These important areas include cancer cell proliferation, cellular metal toxicity and bacterial resistance to antibiotics, among others,” said Shahriar Mobashery, director of the WSU Institute for Drug Design and principal investigator on the shared instrumentation grant. “The availability of this instrument will further stimulate multidisciplinary research and enhance the capabilities we already enjoy in X-ray structure determination.”

“NMR spectroscopy is really the premiere methodology for characterizing the dynamic properties of proteins, and new automated spectral analysis computer programs are allowing us to work through a large amount of data very quickly,” Dr. Stemmler said. “It’s funny that computer scientists have become so intimately woven into basic biochemistry, but combined sciences are absolutely essential in addressing research dilemmas. The School of Medicine’s new NMR spectrometer is a great instrument with scientific and clinical relevance for all of us.”
Primary NMR users will include these faculty members and research projects:

Shahriar Mobashery - to determine how proteins bind to antibiotics and catalytically make them inactive

Timothy Stemmler - to look at metal response proteins involved in neurodegenerative disorders

Rafael Fridman - to determine the molecular mechanisms involved in tumor cell invasion and metastasis and eventually inhibit the activity of matrix metalloproteinases in malignant processes

Avraham Raz - to further study cellular interaction and motility related to cancer metastasis in order to develop antimetastatic drugs and antibodies against metastatic-related genes for tumor diagnosis

Barry Rosen - to understand transport systems that produce drug resistance mechanisms to arsenicals, antimonials and other soft metals
Baby Ethan Holbert and his parents utilized the expertise of the Wayne State University Perinatology Research Branch (PRB) when they learned that Ethan had major problems with his digestive system and would require surgery immediately upon birth. Through the PRB, faculty members are learning more about diagnosing and treating complications associated with premature births and congenital anomalies, like this one.
HEALTHY MOTHER, HEALTHY FETUS, HEALTHY LIFE

WSU WINS MULTI-MILLION DOLLAR AWARD FOR THE PERINATOLOGY RESEARCH BRANCH

BY JENNIFER DAY

“Congenital anomaly” is a sterile medical term at the root of a terrifying experience for Laura and Daniel Holbert. Laura Holbert, an elementary school principal, was four months pregnant when she and her husband, Daniel, received devastating news: Her unborn son’s intestines had slipped through a hole in his stomach and were resting outside his body.

“It was truly a very devastating day but we tried to keep it in the back of our minds that it could’ve been a lot worse,” said Laura Holbert, of St. Clair Shores.

What followed were five nerve-wracking months of doctors’ appointments, medical testing and counseling. On Aug. 25, Ethan Holbert was born and immediately whisked from his mother’s bedside to Children’s Hospital of Michigan, where he underwent surgery to repair his digestive system. Two weeks later, he was healthy and at home with his mother in St. Clair Shores.

In the grand scheme of things, Ethan was lucky. According to the March of Dimes, each year in the United States 150,000 babies are born with a birth defect, and one in five dies. To improve the odds, the National Institutes of Health recently announced that its Perinatology Research Branch will work with Wayne State University’s School of Medicine to study infant health and mortality. The two partners recently signed a 10-year, multimillion-dollar contract that will have profound social and economic impact on Detroit and its surrounding communities.

“This contract underscores both the importance of our work in the area of maternal-fetal medicine, as well as the strength of our program,” said Dr. John Crissman, dean of the School of Medicine. “Our faculty is uniquely qualified to contribute to the success of national research programs that will ultimately improve the health of women and infants across the country.”
The PRB was created to address the causes of high infant mortality in the United States, with a particular emphasis on premature birth and congenital anomalies. It will establish a multidisciplinary program combining the expertise of clinical and basic science to improve the understanding, diagnosis, treatment and prevention of disorders responsible for infant mortality. Although the center is dedicated to clinical research, the ultimate goal is to ameliorate pregnancy outcomes, especially for underserved, high-risk populations.

The branch’s impact has already been felt in Michigan. Although this new contract signifies a long-term commitment to the city of Detroit, as well as increased funding, the PRB actually has been housed at Wayne State University for about a decade on a temporary basis. The branch’s work in the 1990s helped women to have healthier births, while saving the state of Michigan’s Medicaid program money. It’s estimated that the state saved as much as $4.5 million annually because of the better outcomes Hutzel Women’s Hospital was able to achieve with the help of the PRB, even though it handled a disproportionately high number of high-risk pregnancies.

But the work is not done. Dr. Roberto Romero, chief of the PRB since 1992 and a prominent intellectual leader in the field of obstetrics, has developed a research program that could result in better health for Detroiter — and eventually all Americans — for years to come.

According to Dr. Romero, there is now compelling data that prenatal life is the most important determinant of adult health and disease. Problems developing as early as the fetal stage of life can predispose people to coronary artery disease, stroke, hypertension, diabetes, obesity and renal failure.

“Conditions we are very concerned with in adult life now appear to have their origins in fetal life,” Dr. Romero said. “Not only will we be able to address the immediate problems of the perinatal period, but ... by improving the health care of the child at birth, we improve the outlook for our adult life.”

Dr. Romero outlined advances in technology and understanding that have become stepping stones in the work toward improving fetal health. For example, 4D ultrasound, which allows physicians to see into the womb in real-time, aids in the diagnosis of congenital anomalies like Ethan Holbert’s. In some cases, diagnosis of one physical abnormality can indicate an increased risk for other health problems. Furthermore, this technology allows families and physicians to plan for treatment that will be required once the baby is born.

Advanced forms of diagnosis also allow physicians to better plan surgical interventions while the child is still in utero. In conjunction with the PRB, WSU School of Medicine was one of the first to successfully perform a procedure that saved an unborn child from dying before birth because it was connected to a twin without a heart. Had the surgery not been possible, the healthy child’s heart would have failed under the strain of providing blood circulation for two bodies.

In addition, physicians now know that common microorganisms present in a mother’s body can migrate into the womb, causing infection and systematic inflammation that may lead to long-term complications, such as cerebral palsy. The PRB is currently working on a study to determine whether treating intra-amniotic inflammation during pregnancy will prevent premature birth and lead to healthier children.

Part of the PRB’s efforts will be conducted through partnerships with private corporations. In February, the School of Medicine and the PRB announced they will be working with Genaissance Pharmaceuticals Inc. on studies involving the role of certain genes in unhealthy pregnancies. This is expected to be the first of many such ventures.

“You have just begun what this is going to become, the research you’re going to see,” said U.S. Rep. Carolyn Cheeks Kilpatrick, D-Detroit, who followed the evolution of this contract from the application stage to its award. She noted that funding from private corporations interested in the PRB’s work, along with the influx of federal monies, will be a major boost for the city’s economy.

Perhaps one of the biggest benefits the PRB affords, however, is the ability to recruit and retain some of the leading physician-scientists in the field of obstetrics and gynecology, said Dr. John Malone Jr., chair of OB/GYN at WSU School of Medicine.

And part of what makes these specialists outstanding is not only what they know, but also how much they care, according to the Holberts, whose son, Ethan, continues to thrive.

“It could’ve been a lot worse for us to go through without the way they handled it,” Laura Holbert said. “When we left there, I thought we could never do their job and have to tell parents the things they tell them. They made us feel confident right away that, as upset as we were, that things were going to be OK.”