Dr. Luis Gonçalves improves prenatal diagnosis of fetal heart defects
2 Life-Saving Ultrasound Technique Brings Precision to Detection of Fetal Heart Defects
Experts at WSU and the Perinatology Research Branch bring crystal-clear focus to advanced imaging skills.

8 Over-Exposures
Pregnant mothers risk passing harmful toxins and lifelong deficits to their unborn children.

16 Exploring Atrocities to Bring About Healing
Controversial psychotherapist, Dr. Sander Breiner, tackles taboo subjects to help people through turmoil.

20 Burn Fat Rather Than Store It
Entrepreneurial scientists fight diabetes by going straight to the neurons, genes, tissues and proteins involved.

26 Arriving at “Aha”
Visualization and divergent thinking are keys to nurturing a genius mind, says Dr. Felix Hong.

34 Reshaping Bodies to Rebuild Lives
Bariatric surgery pushes patients from obesity to fitness.

40 WSU’s Most Cited Researcher Keeps Pushing Limits
Dr. Kenneth Honn continues developing novel cancer research and fighting dogma along the way.

44 Reducing the Wait-Time for Cancer Assessment
New radioactive tracers can tell within weeks whether cancer treatments are effective.

48 Ph.D. Student Is Keeping Science Cool
At age 24, Pamela Osenkowski is a stand-out in Wayne State University’s Graduate Program.

50 Graduate School Alum Hits the Ground Running
Grant Blouse, Ph.D., shines as a junior investigator with senior experience.

52 WSU Medical Student Made a Switch and Decided to Stay
Brandy Watson switched majors, accepted a Medical Alumni Scholarship and is in the second year of her four-year degree program.

54 Pioneers for Peace Use Disabilities to Inspire Outcry Against Violence
Victims of violence preach violence prevention through Pioneers for Peace, a program sponsored by the Rehabilitation Institute of Michigan and the WSU School of Medicine.

On the Cover
Experts at WSU and the PRB use a novel procedure to obtain clear views of the fetal heart.
LIFE-SAVING ULTRASOUND TECHNIQUE BRINGS PRECISION TO DETECTION OF FETAL HEART DEFECTS

The imaging advancement reported by Dr. Gonçalves makes TGA, a common congenital heart defect, easier to diagnose prenatally. This significantly improves outcomes.
Nancy and Andrew Sovran’s unborn child will have quite a welcome into the world this summer. Upon delivery, he or she will receive immediate breathing support, prepare for pre-operative procedures, and within a week, he/she will undergo open-heart surgery to correct a congenital defect that his/her mother has known about since 20 weeks gestation. Considering the alternative, this is a fortunate child.

Baby Sovran, who was diagnosed with transposition of the great arteries (TGA) while in the womb, will not be subjected to uncertainty at his/her time of birth. With proper and immediate treatment, he/she will not become breathless after being released from the hospital, will not turn a scary shade of blue due to lack of properly oxygenated blood, and will not be rushed to the emergency room while doctors spend critical time deducing the source of the problem.

This child, unlike 75 percent of others born with TGA, had an expert obstetrician and WSU faculty member who detected the anomaly—a task that is far more difficult than one might think. TGA is a congenital anomaly in which the two arteries that direct blood from the heart to the lungs (pulmonary artery) and to every other organ of the body (aorta) are transposed; that is, they connect to the wrong heart chambers. The disease causes blood to circulate “in parallel” – from the lungs back to the lungs, and from the systemic circulation back to the systemic circulation – preventing blood with poor oxygen content to reach the lungs, where exchange of carbon dioxide by oxygen occurs.

While fetuses are not affected by this problem during intrauterine life because of two small channels that communicate between the two sides of the heart, babies become progressively cyanotic (blue) after delivery and eventually die in the absence of treatment, or if treatment is provided too late.

Experts at the Perinatology Research Branch (PRB) housed at WSU are making the detection of TGA easier and less susceptible to human error. Detecting fatal congenital heart disease in utero allows parents advance notice and to optimize the care of the unborn baby. This includes efficient and life-saving treatment shortly after birth.

The PRB, housed at WSU/Hutzel Hospital, is a branch of the intramural program of the National Institute of Child Health and Human Development. It has made fetal imaging a major priority to assist parents in the prenatal diagnosis of congenital anomalies. Through its research and recruitment of top-notch scientists and clinicians, the PRB is making great strides in improving the quality of medical care for mothers and their unborn children, by specifically studying premature labor and congenital anomalies—the major causes of perinatal morbidity, long-term neurologic handicaps and developmental deficits.

In April of this year, a research team formed by members of the PRB and WSU faculty members reported in the Journal of Ultrasound in Medicine a novel procedure to obtain clear views of the fetal heart, as well as other related heart structures that are traditionally difficult to image with ultrasound. Lead author Luis Gonçalves, M.D., an expert in fetal imaging and assistant professor of obstetrics and gynecology at WSU, said because diagnosis of congenital heart anomalies is heavily dependent on operator skills, TGA is detected prenatally only about 25 percent of the time. This is very unfortunate since there is evidence that if TGA is routinely and accurately diagnosed, unnecessary deaths can be prevented in approximately 15 percent of the cases and another 10 percent can be spared of potential long-term consequences related to poor oxygenation after birth.

The imaging technique developed by Dr. Gonçalves is reproducible and easy to learn and provides a mean for interrogating digital data acquired using three-dimensional (3-D) and 4-D ultrasonography in a novel, but standardized way, to obtain conclusive pictures of the fetal heart and its circulatory branches that could rule out or diagnose commonly missed defects without guesswork.

Picture-perfect diagnosis
Earlier this year, Dr. Gonçalves and Dr. Romero, chief of the PRB, examined a patient referred by Dr. Marjorie Treadwell who had detected a 20-week fetus (Baby Sovran) with a congenital anomaly of the heart. This prompted enrollment of the patient in one of the Perinatology Research Branch’s research protocols and a 4-D ultrasound was...
performed. Using the newly reported techniques, the abnormal connections of the aorta and pulmonary arteries to the ventricular chambers were clearly demonstrated. In normal fetuses, the arteries crisscross in front of the heart, whereas in TGA, the two vessels leave the ventricles in parallel.

The crossing of arteries is easy to visualize using the new 4-D ultrasound approach, even for an untrained observer. TGA has been difficult to diagnose with two-dimensional ultrasound because experience and expertise is required to image the outflow tracts in such a small structure, particularly with the fetus moving in the mothers’ womb at the time of scanning. Some of these difficulties can be overcome with the new technique.

The approach reported by Dr. Gonçalves requires that the fetus remains still for 7.5 to 15 seconds (the time it takes for the ultrasound machine to acquire the four-dimensional volume). After that, the steps required to visualize the outflow tracts have been standardized and tested to assure they can be reproduced by other examiners as well.

While Baby Sovran will experience the immediate benefit of accurate prenatal diagnosis, the Perinatology Research Branch hopes that the opportunity provided by examining his/her heart will be extended to many other babies in the world as the difficulties involved in prenatal diagnosis of TGA are solved.

“This process can be automated in any physician office or clinic, if the sonographer or obstetrician is familiar with the procedure,” Dr. Gonçalves said. “It’s an opportunity to streamline echocardiography and make this a universal standard for routine fetal heart examinations.”

The difficulty and importance of visual evidence

“Heart conditions like this are especially difficult to see for a number of reasons. First, a fetal heart at 20-weeks gestation is the size of a nickel. So finding a defect would be akin to finding something the size of Jefferson’s nose within a three-dimensional, working, beating, complex organ—also through layers
Wayne Medicine / 2004

At 20 weeks gestation, the fetal heart is the size of a nickel, so finding a defect would be akin to finding something the size of Jefferson’s nose within a three-dimensional, working, beating, complex organ.

Four-Dimensional Ultrasound of the Fetal Heart

These four-dimensional images show a marked difference between a normal heart and one with TGA, even to the untrained observer.

By changing reference points, angles and planes of view, Dr. Gonçalves has developed a reproducible approach to consistently obtain images of the outflow tracts using four-dimensional volumes.

Color Doppler allows clear visualization of the heart’s outflow tracts.

of noise that are obscured by a fetus moving inside the uterus. Second, the fetal heart is a very complex structure and discerning normal versus abnormal anatomy requires knowledge, expertise and experience,” Dr. Gonçalves said.

“In addition, there are an infinite number of ways to view the information provided by the ultrasound equipment. A 4-D machine stores not just a plane of information, but a whole cube. How you slice that information is up to you, and each practitioner does it a little differently, based on his or her experience. Entire radiology courses are taught on various ways to image a fetal heart, but defects still go undetected all the time, indicating that this is a complicated and subjective process.”

Dr. Gonçalves is particularly interested in TGA because he has been touched by two patients with very different experiences: one who was devastated by it and one who overcame it, thanks to prenatal detection. While practicing in Brazil in 1996, Dr. Gonçalves missed the diagnosis of TGA during a routine ultrasound examination and the baby died after birth. He was devastated, because he felt he had the necessary skills and equipment to diagnose it. Later, he made an early TGA diagnosis on the daughter of a personal friend. The girl underwent corrective surgery, and now lives a perfectly normal life.

“Every time I look at this little girl, who is now about six years old, I remember that she provided me with a good reason to stay in this field. Now, with the opportunity to dedicate time to research, my deep desire is that we can make a meaningful contribution to prenatal diagnosis of this disease and help save not one, but many lives.”

Dr. Roberto Romero, chief of the PRB, indicated that fetal imaging is the most important technological advance in obstetrics in the last three decades and has made it possible for the fetus to become a patient.

The difference between prenatal and postnatal diagnosis of TGA is significant. Congenital heart disease is the leading cause of infant mortality related to birth defects in the United States. Heart anomalies occur at least twice as often as any other birth defect, including CNS, chromosomal and
Thanks to her experience with high-risk pregnancies and advanced imaging, Dr. Treadwell was able to make the TGA diagnosis on Baby Sovran, but she knew that Dr. Gonçalves had the budding technology to back it up with visual reinforcement.

**Cataloging images for future reference**

A major goal of the PRB team is to develop non-invasive fetal imaging techniques such as 3-D and 4-D ultrasound to assess fetal size, anatomy and the early diagnosis of birth defects.

Over the past several years, the PRB has been creating a valuable resource—a digital library of anomalies that can be stored, analyzed and interrogated to improve the understanding of disease and prenatal diagnosis.

The capabilities of advanced ultrasound equipment and techniques are significant. “I can spend 10 minutes doing a 4-D scan with a patient, then take it back to my office, spend some time on the computer and look at the same information from a hundred different perspectives. It is possible to verify information offline. The value of advanced imaging is immeasurable and its potential is only just beginning to be tapped,” Dr. Gonçalves said.

Nancy Sovran expects to deliver her already-diagnosed baby via c-section sometime in June 2004. She is already under the supervision of Richard Humes, M.D., professor of pediatrics at WSU, director of echocardiography and pediatric cardiologist at Children’s Hospital of Michigan, and Henry Walters, M.D., associate professor of surgery at WSU and pediatric cardiac surgeon at Children’s. They will perform open-heart surgery within a week or so to switch the arteries and they fully expect the child to live a life free of complications thereafter.

“We are just heartened to know that this is a problem with a one-time fix. After a couple weeks in the hospital, our baby can expect to live a totally normal life,” said Andrew Sovran, the baby’s father. “They tell us the prognosis is really good, since the problem was detected in utero. That’s really the key. We’re lucky.”

respiratory defects. Of these heart anomalies, TGA is among the most common found in newborns, with an incidence of 20-30 per 100,000 live births.

Research shows that prenatal detection significantly improves morbidity rates on all measures: mechanical ventilation, metabolic acidosis and hospitalization. If left untreated, the mortality rate for transposition is approximately 30 percent in the first week, 50 percent in the first month, and 90 percent by the end of the first year. Thanks to improved diagnostic, medical and surgical techniques, the overall survival rate is better than 90 percent if corrective surgery is performed quickly, with an early (preferably prenatal) diagnosis.
The Perinatology Research Branch (PRB) is housed at Wayne State University and represents a 10-year $125 million contract with the National Institute of Child Health and Human Development of the National Institutes of Health (Department of Health and Human Services). This multidisciplinary research program has been developed to address complications of pregnancy that result in an excess of premature labor and congenital anomalies—the major causes of perinatal morbidity, long-term neurologic handicaps and developmental deficits.

Dr. Roberto Romero, chief of the PRB, is establishing a research agenda that promises to change the way obstetrics is practiced in years to come. The branch uses state-of-the-art technology such as genomics, proteomics, genetics, imaging and pathology to improve the understanding of the mechanisms of disease in obstetrics with the goal of developing new diagnostic methods and treatments to prevent adverse pregnancy outcomes.

Although a core group of scientists and facilities are already in place at the PRB and WSU, Dr. Romero continues to attract researchers from the U.S. and all over the world to join the branch. Major renovations have been completed at the C.S. Mott Center for Human Growth and Development, where the primary PRB laboratories will be housed.

The Mott Center is in the midst of a $15 million building renovation, one-third of which will be devoted to the PRB. The third floor of the building has modern wet labs designed for easy collaborations among PRB scientists and 10-12 major principal investigators will house their research here. In addition, Hutzel Women’s Hospital is making space available near patient care areas for convenient interaction among physicians and patients.

“This research is critically important to the children of today and the adults of the future,” said Dr. Romero. He believes the Detroit-based PRB will continue to bring prestige, expertise and much needed assistance to the area.
Pregnant mothers risk passing harmful toxins and lifelong deficits to their unborn children.

BY AMY DIGRESCE

Pregnant Mothers Risk Passing Harmful Toxins and Lifelong Deficits to Their Unborn Children
The health of a mother and child are inextricably linked in the womb, but science shows that a mother’s responsibility for the health of her baby is more serious and quantifiable than ever before. Modern mothers-to-be have heard and, for the most part, paid attention to doctors’ warnings about dangerous prenatal exposures. There is already a societal stigma against pregnant women drinking, smoking and using drugs, and most mothers understand that their behaviors could directly result in a child with fetal alcohol syndrome or a serious drug exposure.

What’s new in the field of perinatology and passive fetal exposures is indisputable evidence of long-lasting consequences for the affected child who will live with his or her deficits well into adolescence and adulthood. Also surprising is that even seemingly insignificant exposure levels are associated with measurable impairments. All this makes a fetus even more dependent on his or her mother for a healthy start.

Wayne State University researchers are conducting innovative studies and issuing warnings about exposures that can harm children. Sandra Jacobson, Ph.D., professor in the Department of Psychiatry and Behavioral Neurosciences, is an expert in infant and child development and behavioral teratology. She says more knowledge can help mothers give their babies more opportunities.

She and her husband, Joseph Jacobson, Ph.D., chair of psychology, came to Wayne State in 1978 after completing graduate work in infant and child development. “Several decades ago, we weren’t sure if a mother’s use of alcohol or drugs or exposure to environmental contaminants would adversely affect her baby. People used to think the placenta would protect the fetus from most substances. We’ve learned now that many substances and chemicals pass freely to the placenta, and the fetus lacks filtering and detoxification abilities,” Dr. Jacobson said.

With major funding from the National Institute of Environmental Health Sciences and the National Institute on Alcohol Abuse and Alcoholism, the Jacobsons have focused their studies on quantifying and understanding the effects of in utero exposures to alcohol, cocaine, PCBs and other substances. The effects range from severe (such as those seen in fetal alcohol syndrome) to subtle (such as slower processing skills), but as Dr. Jacobson said, “These exposures all result in diminished potential in the child.”

An occasional drink won’t hurt, will it?

In the late ’70s and early ’80s, Dr. Jacobson undertook a collaboration with Robert Sokol, M.D., distinguished professor of obstetrics and gynecology and director of Wayne State University’s C.S. Mott Center for Human Growth and Development. This collaboration was aimed at determining the lowest levels at which detrimental effects of alcohol could be detected in children. They used reliable measures developed by Dr. Sokol and his colleagues for assessing degrees of alcohol exposure during pregnancy and utilized the highly sensitive Fagan Test of Infant Intelligence to assess a child’s visual recognition memory and speed of information processing. Through these measures, they were eventually able to determine that an average of just one drink per day during pregnancy was related to slower reaction time and processing speed in the children. However, they found that all but one woman in their large, longitudinal Detroit study did not drink everyday and concentrated their drinking on 1-2 days per week, thereby exposing the fetus to five or more drinks per occasion, which proved to be the level of exposure that is harmful to the infant.

Dr. Sokol established and directed the Fetal Alcohol Research Center, funded by the National Institute on Alcohol Abuse and Alcoholism and located at Wayne State University/Hutzel Hospital, from 1986 to 1997. Because there is no known safe level of alcohol consumption during pregnancy, Dr. Sokol cautions women alcohol is simply not safe.

“We still don’t know the threshold of tolerance, so we can’t say with any certainty that amount X is acceptable but amount Y is not. But, if I were pregnant, I wouldn’t drink,” Dr. Sokol said.

“There’s no doubt that drinking hurts pregnancy,” said Dr. Jacobson. “This information has important implications for many women—both casual and heavy drinkers. We need to be cautious, yet informative when we report the results of these studies.”

Alcohol moves freely across cell membranes, so alcohol in a mother’s system passes easily to the baby’s. Teams of WSU researchers have shown in multiple studies that even light drinking has long-term consequences.

Alcohol-related birth defects cover a continuum from fetal alcohol syndrome that includes nervous system abnormalities, mental retardation, growth retardation and underdevelopment of the middle part of the face—to less severe abnormalities of the heart, kidneys, respiratory organs, limbs, joints, muscles, not to mention problems with speech, language, hearing, motor skills and IQ.
Virginia Delaney-Black, M.D., professor of pediatrics, conducted a study showing that women who drank the equivalent of one cocktail a week during pregnancy were three times more likely to have a child diagnosed with behavioral problems such as aggression, delinquent behavior and attention problems.

"Adverse effects of prenatal alcohol exposure on childhood behavior are seen at lower levels of exposure than previously reported," Dr. Delaney-Black said. She is currently developing novel instruments and tools to help early education teachers assess problem behavior in children prenatally exposed to drugs and alcohol.

“What’s interesting in our Detroit research is that even though most of the drinking women are not alcoholic and many consume alcohol at only moderate levels, we can still detect adverse effects of alcohol on their children many years after birth,” Dr. Jacobson points out. Current studies are underway to further examine the long-term physiological and neurological damage incurred and the patterns of drinking that are most harmful.

Dr. Jacobson notes that although at lower levels we are not seeing fetal alcohol syndrome with its concomitant major mental impairment, moderate to heavy drinking can have a clear impact. Perhaps of even more concern are the long-term outcomes. Some investigators have reported that at age 14, children born to low-level drinkers are still shorter and weigh less than average.

“These are not disabled children. Most are in regular classrooms doing regular school work, but they process information more slowly because of their exposures, which makes them slower learners. The effects may be subtle, but they are long-standing and make it more difficult for them to function well in school,” Dr. Jacobson said.

Older mothers beware

Although the physiological details are still unclear, an “under/over 30” phenomenon most certainly applies to mothers who drink while pregnant. A woman over age 30 who drinks moderately to heavily is 2 to 5 times more likely to have a child who is functionally impaired than a mother under 30 years old.

According to study authors Drs. Joseph Jacobson, Sandra Jacobson and Robert Sokol, age-related increases in maternal body fat-to-water ratio and a faster rate of alcohol metabolism in chronic drinking women may account for the greater vulnerability of offspring of older mothers. These age-related body changes lead to higher peak blood alcohol concentrations and expose the fetus to heavier doses of alcohol for a longer time.

Maternal age is an important moderator of vulnerability not only to fetal alcohol syndrome (FAS), but also of the alcohol-related deficits in physical growth, mental development and information processing speed associated with prenatal alcohol exposure in non-FAS infants, the researchers said.

These data mean that older mothers should be specifically targeted and educated about the harmful effects of alcohol during pregnancy. “A drinking mother who has given birth to one or more healthy, well-functioning babies during her early twenties may be understandably skeptical of warnings about the importance of reducing her alcohol intake during pregnancy. It is, therefore, important that she be informed that the risk of adverse effects on her offspring increases substantially as she grows older,” Dr. Sokol said.

The same research group also found that binge drinking is particularly harmful in older mothers. An over-30 mother who drinks five or more drinks on one occasion once a week does more damage than if she drank one drink per day on five consecutive days. Functional cognitive impairments were seen in children born to binge-drinkers, whereas more subtle impairments were reported in children born to regular or daily drinkers.

“Binge drinking means a fetus gets a more concentrated exposure which poses a greater threat. The pattern of drinking is as important as the quantity of alcohol. These effects of concentrated drinking have also been demonstrated in animal research,” Dr. Jacobson said.

A mother’s aging body does less to protect her fetus from toxic insult and, in fact, makes threshold levels even lower. The measures of pregnancy drinking that have the greatest impact on development are bingeing and average number of drinks per occasion, Dr. Jacobson said. Furthermore, the risk of FAS increases markedly with increased maternal age, and alcohol studies have shown that each successive child born to an alcohol-using mother was virtually always more severely impaired than the previous one.

Increased maternal age requires a woman to be more cautious and stringent in refraining from alcohol if she is to protect her baby from harm.

Unless you know your waterways, consumption of sport fish may be harmful to the fetus

Pregnant women are often warned not to eat sushi or raw fish, but cooked fish was generally thought to...
be a fine dietary choice. Problems in the waters, however, can be transferred through fish—even if it’s cooked.

Drs. Sandra Jacobson and Joseph Jacobson screened more than 8,000 women in four western Michigan hospitals in order to recruit their cohort of 313 fish-consuming women and their infants. They found that those who ate considerable quantities of Lake Michigan fish during their pregnancy were unknowingly passing along PCB contaminants (polychlorinated biphenyls). By contrast to prenatal alcohol exposure, the Jacobsons have determined that PCBs had no effect on the infants’ processing speed, but did adversely affect their recognition memory, which is likely to lead to poorer learning in childhood. They subsequently found that short-term memory deficits continued to be evident through preschool age and later childhood. PCBs have been banned in the United States since the 1970s, but lake waters are still contaminated, although less so than in the past.

The Jacobsons found a dose-dependent relationship between mothers’ reports of Lake Michigan fish consumption and concentrations of PCBs in the umbilical cord blood. The researchers are conducting similar studies in Greenland and in an Inuit population in northern Quebec. Residents of these regions have some of the highest PCB exposures in the world because their traditional diets are based on fish and fat from Arctic sea mammals, which has been contaminated with these environmental toxins.

“One very interesting finding is that prenatal exposures are potentially far more harmful than postnatal exposures,” explained Dr. Jacobson. “Although breastfeeding mothers transfer relatively high quantities of PCBs to their infants through their breastmilk, we have found virtually no evidence of harm from PCBs transferred to the infant via lactation.” The prenatal exposures are apparently most toxic because they occur during critical periods of brain development and the relative concentration is higher since the fetus is so much smaller.

Dr. Jacobson says not all exposures cause severe problems, but there are clear indications of “diminished potential” and that is troubling.
Drugs use leaves permanent scars on the non-drug user

For a child born to a drug-using mother, detoxification is only the beginning. He or she can also expect growth deficits, poor language skills, increased problem behaviors and lower achievement in school, according to studies by WSU research teams including Drs. Sandra and Joseph Jacobson, Virginia Delaney-Black, Robert Sokol, Joel Ager, Beena Sood and Chandice Covington (now at UCLA).

In 1996, WSU colleagues were the first to find substantial evidence of cognitive deficits related to heavy cocaine exposure. Previous studies confirmed that in utero exposure produced smaller infants, shortened gestation and intrauterine growth deficits, but for the first time, neurobehavioral deficits could be seen in infancy. Since then, researchers have been evaluating these children to see if early signs could reflect the types of impairment they could expect to experience as they grow older.

“These early problems raise serious concerns about the risks faced by drug-exposed children in adolescence,” Dr. Delaney-Black said. With funding from the National Institute on Drug Abuse, she and her team are evaluating 500 13- and 14 year-old adolescents who were previously tested at ages 6-7 and found to have substantial deficits. Preliminary data shows a propensity for exposed boys to have hyperactivity, poor conduct and poor behavioral control. Exposed girls tend to have overall deficits in achievement and central processing.

Researchers asked teachers to report on the behaviors of their students, blinded to whether or not the children had been exposed prenatally to alcohol or cocaine. Their response showed serious problem behaviors in the exposed group. The delinquent behaviors were clinically significant.

Data collection continues as Dr. Delaney-Black tries to pin down what these children are exposed to after birth. That is, if a child continues to live in an environment of drug-use, it is complicated to figure out what behaviors are based on prenatal exposures and what behaviors are based on violent neighborhoods, unstable parenting, or other social risk factors that have a major influence on children. With $1.1 million from the U.S. Department of Education, Dr. Delaney-Black is also studying the effects of community violence on childhood learning.

“The very significant effects of postnatal risk factors on child outcome is both distressing, and, at the same time, cause for optimism. There seems to be potential for amelioration of child outcome through intensive family interventions,” she said.

Searching for a trace

Adults are environmentally exposed to toxins like lead, mercury, cadmium, pesticides and PCBs all the time, but researchers are trying to measure and evaluate toxic exposures in utero to determine if mere traces of filtered toxins have detrimental effects on childhood development.

Enrique Ostrea, M.D., professor of pediatrics, has developed and patented meconium testing as a standard toxicologic test for newborns. By looking at babies’ first stool samples, researchers can detect exactly what a fetus has been exposed to. With more than $3 million from the National Institute of Child Health and Human Development and the U.S. Environmental Protection Agency, Dr. Ostrea is tailoring his methods and trying to understand
The parents of four grown children, Sandra and Joseph Jacobson study childhood development and the effects of potentially dangerous prenatal and postnatal toxic exposures.
What a mother consumes during pregnancy often affects her children later in life.

whether prenatal exposures, even at low levels, may cause permanent deficiencies in the brain.

“We are looking at seemingly harmless ambient exposures that could turn out to be toxic during critical periods of development,” Dr. Ostrea said. “Even slight disturbances in neuronal proliferation and growth or hormone levels could alter child development and contribute to the rising rates of developmental disabilities and neurodevelopmental diseases that have been dominating in the past decade.”

He and his colleagues are going a step beyond the guidelines that have been set for adults regarding safe thresholds of tolerance for substances. They are looking at prenatal exposure levels and combining them with factors of duration, genetic susceptibility, confounding chemicals and age.

“A fetus is fully reliant on its mother for all nutrients and filtering of toxins, with passive acceptance,” he said. “It’s scary, but if we know what we’re dealing with and mothers know what to avoid, we can prevent a lot of problems by simply altering our environment and controlling our exposures.”

Avoiding threats of exposure
Sandra and Joseph Jacobson’s major contribution to the field is their application of the most sensitive tools available to measure prenatal exposures, to detect the most subtle deficits and to predict outcomes. They very carefully consider potential confounding factors like mother’s IQ, life stresses, depression, pre- and postnatal smoking and drug use and other socio-environmental factors, and still they find evidence that what a mother consumes during pregnancy often affects her children later in life.

These sensitive new tools are helping toxicology researchers around the world explore many new avenues in depth. They are concentrating on timing of exposures, pattern and dosage of exposures and genetic vulnerabilities to see how these factors determine whether adverse outcomes occur or are more severe in certain individuals. In addition, they are beginning to explore some polymorphisms or other factors that may be protective.

“This is very exciting because there may be the potential to identify socio-environmental variables that may modify the effects of prenatal exposures. These factors could suggest the basis for future interventions that could help ameliorate developmental problems associated with these unintended exposures,” Dr. Jacobson said. “Or perhaps we can find some protective effects like some of those we’ve seen for breastfeeding. For example, we have found that the adverse effects of PCBs are generally seen primarily in children of women who did not breastfeed. We need to do intervention research once we have a better grasp of what the underlying core deficits are; human trials are difficult undertakings and must be conducted with extreme caution.

“We can’t undo all of the damage, such as that found in children with FAS, but perhaps we can find ways to enhance development and counteract some of those deficits that come from exposures. Ultimately, the goal is to provide the best start for all our kids.”
**Left:** According to studies by Dr. Delaney-Black, school-aged boys who were prenatally exposed to cocaine have hyperactivity, poor conduct and poor behavioral control. Exposed girls tend to have overall deficits in achievement and central processing.

**Below:** Dr. Sokol established and directed the Fetal Alcohol Research Center at WSU. Because there is no known safe level of alcohol consumption during pregnancy, Dr. Sokol cautions women alcohol is simply not safe.

**Above:** Dr. Ostrea is trying to understand whether toxic prenatal exposures, even at low levels, may cause permanent deficiencies in the brain.

**Below:** Much can be learned from the Fagan Test, which measures a child’s visual recognition memory and cognitive processing speed as he or she looks at two images on a video screen.
Controversial psychotherapist tackles taboo subjects to help people through turmoil

BY ANITA LIENERT

When Sander J. Breiner, M.D., was a 20-year-old Army private in 1945, his father Alfred became the chief interpreter at the Nurnberg trials, where former World War II Nazi leaders were indicted and tried as war criminals by the International Military Tribunal.

Dr. Breiner, a decorated soldier who had landed at Normandy a couple of weeks after D-Day, eventually reunited with his father at the trials in Germany. He asked his father, a civilian general, if he could see some of the material the Allies had gathered about the concentration camps and the Holocaust. His father refused to show him even a single photograph.

“The things I’m reading and studying and translating and the pictures are so terrible, that it’s too much for a young person like you to see,” he said.

“But, Dad,” his son responded. “I’ve been in combat. I’ve seen a lot of things.”

“Nothing you’ve seen in combat even touches what I have been seeing,” his father said.

That long-ago moment — the action of a protective, loving Jewish father — was one of the rare instances where Dr. Breiner managed, against his will, to avoid the toughest of subjects.

In the ensuing decades, the Wayne State University assistant professor of psychiatry and behavioral neurosciences has made a career out of tackling difficult and taboo subjects, including the aforementioned Holocaust, child abuse, sexual abuse, homosexuality and the genital mutilation of women in the Third World.

“I WAS NEVER CONCERNED ABOUT POLITICAL CORRECTNESS. I’M CONCERNED ABOUT MY OWN INTEGRITY. MY FUNCTION IS TO HELP PEOPLE BECOME FREER TO BE THEMSELVES.”
EXPLORING ATROCITIES TO BRING ABOUT HEALING
A highly sought after media spokesperson, often cited therapist, and controversial philosopher, Dr. Breiner makes no apologies for his positions. In fact, he prefaces his comments, saying that he is only controversial “to the people who disagree with me.”

The first hint of his controversial approach to dealing with both psychohistory and psychoanalysis comes in the waiting room of his office, in a bucolic setting just across the street from the Franklin Cider Mill.

Hanging on the wall is a framed copy of the last paragraph of his 1990 book “Slaughter of the Innocents: Child Abuse Through the Ages and Today.”

The book examined five ancient cultures, most notably the way the average person responded to women, children and slaves. The excerpt on the office wall takes direct aim at what Dr. Breiner, the father of three, calls the “denigration of females” in places like the Arab world: “When all is said and done, the most important person in our universe is the mother who can pass along her love, nurturing, serenity and stability to her daughters, who will continue the cycle and pass along these characteristics to her children. The perfection for motherhood begins in infancy. Without this foundation in the first two or three years of life, the little girl will become impaired in her functioning as a mother. This means that the most important person in the world is a newborn female child. What a horrible tragedy that she has been the object, throughout history, of society’s prejudice and abuse. Without that love from mother, we flounder; without it, there is pain, violence, death – even war. The only hope our civilization has lies in changing our response toward women. They should not be treated as equal to men; they deserve better.”

A smiling patient emerges from Dr. Breiner’s office and the 78-year-old physician appears in the doorway, a tall man dressed in a gray suit and tie with a carefully groomed beard and a rather formal demeanor.

Inside, textbooks and pop-psychology tomes such as the 1960s bestseller “I’m Ok, You’re Ok,” line one wall. A couch with a pillow and a rust-colored afghan dominates the room and abstract artwork hangs on the wall.

During the next 90 minutes, Dr. Breiner, an American citizen who was born in Fiume, Italy, will hold forth on a number of topics. “I’m an individualist who is very fond of humanity and who wants it to constantly improve,” he responds, when asked to describe himself. “You saw the quote from my book. That book is the best thing I ever wrote. That last paragraph is the most direct expression of my feelings. The only way you’ll change the world is when you change the way you treat newborn girls and women. They are the basis of all civilization. You can pretend all you want to that it is men, but it’s women. You can pretend God is a man, but he isn’t. Treating female children as the most important in the world is controversial.”

Dr. Breiner spends a significant part of the time explaining his work as a member of the scientific advisory committee to the National Association for the Research and Therapy of Homosexuals. The nonprofit, educational organization based in Encino, Calif., says it is dedicated to the research and therapy of homosexuality. Dr. Breiner, who earned his M.D. in 1953 from the Chicago Medical School, explains his commitment to what some may see as the unorthodox idea of homosexual therapy. “I’m not a proponent of homosexual therapy,” he said. “I’m a proponent of anybody who wants to have therapy to get it. A symptom of discomfort should be approached and the person should be allowed to explore it.

“If a person is uncomfortable being a homosexual and says ‘I wish I weren’t,’ it should be looked at. I’m in favor of that. I strongly support it. Many people in the community who are homosexuals say if you approach homosexuality as if it’s a problem, you are being hostile and negative to homosexuals. Nonsense.
“I was never concerned about political correctness. I’m concerned about my own integrity. My function is to help people become freer to be themselves.”

Dr. Breiner recently disputed the idea of “internalized homophobia” at a national seminar in Salt Lake City in November. He repeated the presentation in March at Wayne State University during grand rounds in the department of psychiatry.

“Some writers who are gay have come up with the idea of ‘internalized homophobia’ to describe anybody who wants to help homosexuals through things such as psychotherapy,” he explained. “I indicated there is no such thing. Homophobia — like any phobia — has to have phobic criteria. It doesn’t meet the criteria. These people are using the concept for political purposes to attach to those who want to be helpful. They don’t realize that homosexuality is a normal part of development. But for gays, it becomes a point of fixation. It’s like a fever. It becomes a symptom.”

Dr. Breiner becomes a fascinating sounding board in an era in which pop star Michael Jackson dominates the headlines with charges of child sexual abuse. To this psychiatrist, the subject of pedophilia becomes “a lecture of its own.” “Pedophilia covers a multitude of things from something which is rather minor and trivial to something which is destructive,” he said. “It’s like calling every fever a terrible thing or every ache arthritis.

“What is significant is if the individual who is using a child for sexual activity is a caregiver, then the caregiver has some significant psychological problem. Therefore, the sexual activity may not be so significant for the child, but the caregiver is a disturbed individual. So a great deal is focused on the sexual activity, rather than the emotional climate around the child.”

As a sidenote, he adds: “I’m also not against pornography. But I am against sadistic pornography. The idea that sex is dirty or forbidden is anathema. ...I’m not against it, if it’s not injurious to women and children,” Dr. Breiner says, offering his longstanding litmus test.

It comes as little surprise that the man who takes on such weighty subjects as child abuse and homosexual therapy will tackle the origin of civilization in his next book. Or that he’s recently completed a chapter on the psychohistory of anti-Semitism in an upcoming book.

“The biggest challenge is getting people to appreciate that only through understanding mankind and its development will you save mankind from destroying itself,” he said. “Anything which is anti-understanding of human development is injurious to mankind.”

“TREATING FEMALE CHILDREN AS THE MOST IMPORTANT IN THE WORLD IS CONTROVERSIAL”... BUT ONLY “TO THE PEOPLE WHO DISAGREE WITH ME.”
Entrepreneurial scientists fight diabetes by going straight to the neurons, genes, tissues and proteins involved.
Michigan is fat. That may sound a bit blunt, but it’s true (see sidebar). A higher percentage of people in Michigan, and especially metropolitan Detroit, are obese than in nearly every other geographic area in the nation. As a result, Michigan also is at or near the top of the list for the incidence of type 2 diabetes, which is common among overweight individuals.

A unique center at Wayne State formed in 2001 to try to stem the tide. Called the Center for Integrative Metabolic and Endocrine Research or CIMER, it is a collection of researchers with one aim: to find new drug targets for obesity and diabetes.

“We’re a group of scientists with industry and academic experience,” said James Granneman, Ph.D., professor of psychiatry and behavioral neurosciences. He and the center’s other two researchers worked in drug development at a pharmaceutical company. “That experience gives the center a very important focus on translational research: finding out things in the basic-science world that we can use almost immediately to help out in drug discovery. That’s the niche we try to fill.” In addition to Dr. Granneman, CIMER includes Todd Leff, Ph.D., and Robert G. MacKenzie, Ph.D., who are both associate professors of pathology. Plans are to add a fourth researcher to the center soon.

Although CIMER has only been in existence for two years, its research projects are well under way. Already, the three researchers are beginning to understand the link between obesity and type 2 diabetes, an illness that can lead to a slow erosion of bodily functions and result in heart failure, stroke, blindness and other organ failures. Dr. Granneman noted that type 2 diabetes was traditionally called “adult-onset” diabetes, because the typical patient was 55 years old or older. With the acceleration in obesity and the type 2 diabetes in adolescents, however, “adult onset” is no longer an accurate descriptor and has been abandoned by much of the medical community.

Dr. MacKenzie’s research centers on nerve cells in the brain that control body weight and appetite. When the activity of these so-called “obesity neurons” changes in a particular way, they trigger obesity. He explained that scientists already know that a mutation in one of five specific genes in the human body—humans have 30,000 genes in all—results in massive obesity and an enormous hunger. “All five of those genes have an impact on the brain, so obesity is really being governed by appetite and metabolic rate that is regulated by the brain,” he said. One of the five genes carries the instruction for making a hormone, called leptin. Fat secretes leptin, which travels through the bloodstream to the brain and provides the signal to stop eating, he recounted. “When animals, whether mice or humans, have a mutation that causes deletion of that gene, they become massively obese.”

Interestingly, most of the brain’s neurons are insensitive to leptin, but not the small subset of the brain’s nerve cells called obesity neurons. These neurons have receptors for the hormone. When a mutation occurs in the gene for the leptin receptor, the brain no longer registers leptin’s signal to stop eating, and appetite skyrockets.
One of the greatest hurdles to Dr. MacKenzie’s research was separating the obesity neurons from the millions of other neurons in the brain, he said. “What we did was develop a way to genetically label those cells in mice and make them fluoresce green. Then, we use a method called laser-capture microdissection that allows us to pick up fluorescing cells individually. Once we have them, we can extract their RNA, and from that RNA determine which genes are made in that cell.” Dr. MacKenzie’s research group is one of the few teams worldwide that is putting all the pieces together: genetically labeling the neurons, harvesting them with the microdissection technique, and conducting the global gene analysis.

The researcher’s job now is to learn exactly how the receptor controls the function of the neuron. “If you can understand how that receptor regulates that activity of the cell, you may have many other avenues in the cell that you can manipulate to have the same functional impact on the cell as activation of that receptor,” he said. “That would open up a whole variety of new drug targets.”

Drs. Granneman and Leff are taking a somewhat different tack. “The current thinking is that fat tissue serves as a buffer for excess energy and when a person gets to a certain level of obesity, the fat just can’t be stored the way it normally is and instead starts to accumulate in muscle and in other tissues that normally don’t get fat. That change is probably a key event in producing insulin resistance,” Dr. Granneman said. “We’re trying to understand the nature of the signal and how it might alter the buffering capacity of the animal and the ability of the animal to deal with that excess lipid.”

Dr. Leff is mainly interested in transcription factors, the sets of proteins that turn genes on and off in response to various signals. His work centers on a transcription factor called peroxisome proliferator-activated receptor-gamma, or PPAR-g, that also serves as a receptor for a commonly prescribed class of anti-diabetic drugs called the thiazolidinediones. “We’re specifically studying human mutations in the gene that encodes PPAR-g. The fairly small number of people who have the mutation also have the syndrome called lipodystrophy. In lipodystrophy, the patients have less than the normal amount of adipose tissue, yet all have diabetes.” By understanding the molecular details of these mutations, his research group will gain a view into the molecular causes of diabetes.

“Right now, the molecular causes of run-of-the-mill, ‘normal’ diabetes are really poorly understood. If we can understand what exactly PPAR-g does, and what other molecular components of the cell it interacts with, it broadens our knowledge of what all of the important components of diabetes are and gives us new places to look for potential drug targets.” One of the ways he is investigating PPAR-g is through transgenic mice. “By manipulating the mouse PPAR-g gene, we’ve generated animals in the lab that are either more or less susceptible to diabetes.” It took about three years to create the animals, and his group has just begun to conduct experiments and collect useful data.

Dr. Granneman’s research group is particularly studying whether they can alter the function of the adipose tissue from storing the excess energy to burning it. “With a certain drug treatment that we’re using on animals, we can quadruple the metabolism of the storage form of adipose tissue, so it goes from a metabolically inert storage tissue to a tissue that’s really metabolically active and burns up the energy.” Although the drug treatment is unsafe for humans because of its side effects, it does present possibilities, he said. “If we understood the cellular mechanism for switching the function of the adipose tissue from storage to energy-burning, then we might be able to induce the same consequence through another way that wouldn’t have the side effects of the drug.”

Through pioneering work, the
Wayne Medicine / 2004

The CIMER group worked together at a pharmaceutical company before joining WSU in 2001.

research group has what Dr. Granneman calls “really good strong leads into the genetic program that converts fat from a storage form to an oxidative form.” He added, “We’ve been able to validate our findings using knockout mice, gene transfer into adipocytes (fat cells) and other types of technologies.”

Dr. MacKenzie said his colleagues’ work hold promise for future drug development. “Once you know the gene program and which genes are being induced or shut down to cause this transformation, you can figure out the metabolic pathway that’s involved. Then, all these different stages in the drug pathway become potential drug targets to induce the change in fat tissue.”

Dr. Granneman’s group is currently in the process of discovering and further confirming the potential drug targets. He explained, “The value of a target really is directly proportional with its degree of validation, and the more you can show that it’s really a rate-limiting step, or a key metabolic link in the chain that produces the desired effect, the more valuable the target will be.” That, he said, is where the drug-industry background becomes important. “You really have to know how to whittle down your list of drug targets and rank them according to what’s ‘druggable.’”

Dr. MacKenzie agreed, “That’s what’s different about us. If we didn’t have the background that we have, we might easily get lost in so many of the cell-biology questions that come along. Instead, we’re always tuned into how to turn this into something..."
practical, because we really want to come up with something that’s workable at the end of the day.”

Although CIMER only started at the end of 2001, Drs. MacKenzie, Granneman and Leff’s relationship goes back about two decades. MacKenzie and Leff were researchers at the pharmaceutical company Parke-Davis (now part of Pfizer), and knew Granneman as a researcher at Wayne State University. In 1998, Dr. Granneman took a leave from the university (although he continued to run a research program at Wayne State) and spent three years as part of Drs. MacKenzie and Leff’s research group at Parke-Davis. When Pfizer bought out Parke-Davis, WSU psychiatry chair Thomas Uhde invited the three researchers to WSU to form a new center to study obesity and diabetes. The center received initial funding from the Fund for Medical Research in Education, and the three CIMER researchers presently receive funding for their individual projects from the National Institutes of Health and the American Diabetes Association. CIMER is now completing its move to the Lande Research Building on the School of Medicine campus. It will put the three researchers close together, allow for easier collaborations, and provide space for the fourth researcher, who will be added to CIMER within the next year.

In addition, CIMER submitted a proposal for and received a $3.5 million, three-year grant from the Michigan Life Sciences Corridor to form the Michigan Diabetes Research Consortium with scientists from the University of Michigan and Michigan State University. Like CIMER, consortium research will emphasize the general theme of how obesity progresses to diabetes, and which defects occur in key cells in the body. Dr. Granneman noted, “The Life Sciences Corridor is a big effort in Michigan to get economic development out of the universities. We filled that bill perfectly, because we had both industry and academic experience, and could bring it all together in an important disease area for Michigan: obesity and diabetes.”
DETROIT: A CITY OF GIRTH

It’s quite likely that almost all the kids in your elementary school class were skinny as rails. That’s not true anymore, and it has health professionals – especially those in Detroit – very worried. “I think our society is sitting on a time bomb,” remarked Paulos Berhanu, M.D., who directs the Division of Endocrinology, Diabetes and Metabolism in the Department of Internal Medicine.

According to national surveys, Detroit is near the top of the list for metropolitan areas with the most obese residents, and far too many of those overweight individuals are children, Dr. Berhanu said. Statistics reveal that the number of obese adults has risen from 12 percent of the population in 1991 to 21 percent in 2001 – from about one in 10 to one in every five adults. Similarly, the National Health and Nutrition Examination Survey (NHANES) showed an increase in obesity among boys and girls aged 12-19. “From 1988–94 to 1999–2000, the number of obese children rose in all ethnic categories, but especially among ethnic minorities. If you look at just African-American girls, about 25 percent are now overweight, and the problem continues to get worse” he said. The data hit home in Detroit, where the majority population is African American.

“Adolescent obesity is very important, because these are the children who are at risk for developing type 2 diabetes at a young age,” Dr. Berhanu said, adding that overweight individuals are also at increased risk for high blood pressure, cardiovascular disease, heart attacks, stroke, and a variety of other dangerous, debilitating and sometimes fatal conditions.

Dr. Berhanu came to Wayne State a year ago. He traded a secure position at the University of Colorado, which is located in the leanest state in the nation, for the opportunity to make a difference in diabetes prevention and care in Detroit. Still, he said, the extent of the problem in Detroit was stunning. “Until I came to Wayne State and walked through Detroit Receiving Hospital, I had never seen so many relatively young adults walking with canes because of complications from hypertension, strokes and cardiovascular disease. I certainly didn’t see anything of this magnitude in Colorado.” The problem is highlighted by two of his current patients that include a young woman who had a heart attack at age 28, and another woman who required coronary artery bypass surgery at age 29 because of clogged arteries. “The risk factors were the same for both of them: hypertension, type 2 diabetes, dyslipidemia – all of those factors that come with obesity. These are patients who are young, but are already disabled.”

To those Michigan residents who believe obesity is only a problem for the patients, Dr. Berhanu countered, “At the end of the day when those young people come in with their heart attacks, they are your problems and they are my problems, because we have to pay for it through Medicare, higher health insurance premiums, disability costs, lost economic productivity, and loss of our competitiveness in the global economy.”

While the picture may look bleak, he believes Detroit and Michigan can rebound. “The very first requirement is that we recognize that there’s something major we need to change. I think the problem of obesity is one area that everybody agrees needs to change, because it’s galloping as an epidemic.” Fortunately, he said, the Detroit area already has the infrastructure in place. “We have the institution, we have the clinical people, and we have the talented researchers in such groups as CIMER (see related story). Now we need to – we must – get the community, the business leaders and the political leaders involved, put the resources in place, and create a vision to synergize everything.”

He added, “We have no choice but to move forward, because the alternative is unacceptable.”

Dr. Berhanu helps Detroit fight the obesity epidemic.
When Dr. Hong lectures, he prefers using pictures instead of narratives to explain electrophysiology. He believes visualization is a key to genius minds.
Visualization and divergent thinking are keys to nurturing a genius mind.
What do the true genius minds have in common? Albert Einstein, Richard Feynman and Stephen Hawking are all brilliant physicists, of course. But what unites them? How do they think? And most importantly: Is it possible for ordinary people to think in genius ways?

Absolutely, says Felix Hong, M.D., Ph.D., who believes the secret of genius lies in visual thinking, an expansive short-term memory and trust in intuition. He also believes these elements can be taught and learned in common folks as well. Although these traits were probably innate to the true geniuses of our time, the same principles could be practiced and mastered to raise the intelligence bar for people of every IQ.

“These elements may not necessarily produce great test-taking students, but they nurture great problem-solvers, and the retention of knowledge is longer lasting and far more important,” Dr. Hong said.

While growing up in a strict educational system in Asia, Dr. Hong learned to excel at school, but he always felt like there was more to learn and there was a better way to do it. After decades as a professor of physiology at Wayne State University, he began to study advanced thinkers and came to some conclusions.

In teaching young scientists and physicians the electrophysiology of nerve membranes, Dr. Hong has tried to institute picture-based learning as an alternative to traditional rule-based learning methods. He admits it is difficult for some people, especially medical students, to throw out their old modes of thinking, but has plenty of evidence (including Mozart and Einstein) to show that this mind habit can become an important part of a person’s reasoning ability.

Critics say although it is interesting to know how a genius thinks, advanced thinking applies to only an elite few. They say you can’t apply that type of reasoning to a person of average intelligence. Dr. Hong doesn’t think that visualization automatically begets a genius. He does, however, think it could help everybody think deeper, more clearly and more openly, regardless of their original level of intellect.

Dr. Hong says, “Most literature on genius minds classifies two categories: genius versus non-genius. A genius is a creative thinker and non-genius is a traditional thinker. I believe there’s a gray scale that exists between genius and non-genius. If there is an actual method of thinking that can increase your understanding and reasoning ability, and if that method can be taught and learned, why wouldn’t...

**IN HIS OWN LECTURES, DR. HONG FAVORS THE WISDOM OF VISUAL LEARNING.**

**“REMEMBER, PHYSICAL DIAGNOSIS IS STILL PARTLY SCIENCE AND PARTLY ART, REQUIRING AN OVERALL JUDGMENT BASED ON CONFLICTING INFORMATION. THAT IS WHY COMPUTERS haven’t taken the place of doctors.”**
we try it? It may not work for everybody, but I have seen students who were blown away by the results in their test scores and in their own increased mental capacity. It is not impossible to master this way of thinking.”

A picture is worth more than a thousand words

Einstein, Feynman and Hawking all called themselves visual thinkers. Abstract thinking in science actually demands concrete visualization of fictional scenarios. To assign a picture to an atomic structure, to create a diagram explaining an electrophysiological reaction, or to “see” how the earth could have been created from a mass explosion are perfect examples of picture-based reasoning.

Dr. Hong explains visualization as taking something you know and using it like a template or metaphor to make sense of that which you might not otherwise conceive. Picture-based learning, he says, requires parallel processing, while its opposite, rule-based learning, requires linear or sequential processing.

A simplified comparison can be seen in a creative chef versus a strict recipe follower. A picture-based cook might gather ingredients based on what flavors were complementary in past meals. He may remember liking the combination of rosemary with thyme or garlic with oregano. A rule-based cook would have a hard time improvising an alternative ingredient if it did not fit the recipe exactly as written.

In his own lectures, Dr. Hong tries to provide information for both learners, but of course, favors the wisdom of visual learning. He points to a lecture about muscles that he presents in two ways. The first is a four-frame cartoon that shows two concurrent processes at work. It is a conceptual diagram of balanced, concurrent systems and takes about 15 minutes to explain. The second option for linear thinkers is a two-page narrative of each process, but the interaction of the two processes is much harder to verbalize. Dr. Hong says the people who learn the picture actually understand the process better and can take it one step further to make educated guesses about insults to the system or other unforeseen situations. The people who learn the narrative can spout out key words and learn to make associations when they hear them specifically, but they may never have a clear visualization of the process at work, and are less likely to remember it later in their careers.

“Saying that I hate standardized tests is an understatement,” Dr. Hong said. “They teach people to think in a box. In my opinion, learning to think by practicing on multiple choice questions is like learning to ride a bicycle with training wheels permanently attached. Why? Because multiple choice questions often contain most of the clues or hints, whereas problem solving in real life requires active gathering of clues or hint.” A deep thinker, an outstanding physician and an inquisitive scientist should be able to generate new rules from old knowledge, he said.

Picture-based learning implies that you don’t reinvent the wheel each time you think about similar types of questions, and furthermore, that you recognize patterns in problems across disciplinary fields. The lessons you learn in electrical engineering can apply to physiology. Similarly, watching how lotus leaves overtake a pond is mathematical exponential functioning at work. An equation that says lotus leaves in a pond double the coverage of the pond over a 24 hour period gives a great visual understanding. And the example of a lotus leaf is much easier to remember than abstract equations calculating population growth, doubling time and growth curves. So, the same pattern at work in your backyard garden is regularly used by urban planners to estimate population growth.

The difference is: the linear thinker would memorize the mathematical equation, but would get completely stuck if she forgot one element of the equation. A visual thinker could recall the picture behind the mathematical derivation and be able to reason through it, without knowing the equation at all. Instead, the visual learner understands the reasoning behind the equation. The mathematical actualities can
always be confirmed later for verification, but it needn’t stymie one’s attempt at processing the problem. Attempting difficult problems becomes a practiced, habitual personality trait of many ultra-intelligent people. And as Dr. Hong says, there is much more interesting wisdom in the attempt rather than the solution itself.

Super-powered RAM gives wide solution assortment

Being able to visualize something is just one part of the genius hardwiring. Part two is being able to shuffle through loads and loads of templates, memories and patterns to see if there is a good fit or potentially existing answer to a problem that was previously encountered. In computer speak, this short-term storage capacity is called RAM (random-access memory) and the shuffling through all theoretically possible solutions is called search space.

A chess player, for example, must consider a nearly infinite number of possible moves, countermoves and unpredictables in trying to outsmart an opponent. But this search-and-match for possible moves is not undirected or random. A player limits the number of combinations to explore, does it in a reasonable length of time and then does a mental comparison before choosing the best move. People who can explore and store many combinations in RAM are at an advantage, because they are choosing from a sufficiently larger search space. The RAM allows them to pay attention to several concurrent events, which is essentially, parallel processing.

Dr. Hong, a music aficionado and great lover of symphonies and Mozart in particular, believes in the truth of music therapist Don Campbell’s controversial book, “The Mozart Effect.” The book says listening to Mozart music can unlock the creative spirit, help babies expand their minds and help students perform better. After inspection of Mozart scores, Dr. Hong said, “I found peculiarities in the late symphonies (numbers 21-41) that may be conducive to the enhancement of parallel processing capability. The effect is primarily an enhancement on the capacity of the short-term or working memory instead of the long-term memory.”

Mozart often ran two or more melodies concurrently rather than successively, demanding more of the listeners’ parallel processing. “The melodies could not be classified as dominant or subordinate, primary or supporting, but instead appear equally attractive, demanding a subconsciously divided attention. By necessity,” Dr. Hong said, “the listeners must place all concurrently running melodies in the short-term memory, thus, at least temporarily, giving up the habit of a one-track mind. It is hard to imagine that prolonged training as such will not have an effect on the mind’s spatial capability.”

Dr. Hong says he would trade his long-term memory for short-term memory any day. “Most people regard the capacity of the long-term memory as the primary determinant of cognitive abilities. I personally hold a different opinion. I believe the short-term memory is more important in creative problem solving, because the long-term items can be looked up later. The short-term allows you to search, compare, discard and select the best choice out of a wide range of answers.”

For example, a student with a great long-term memory might have learned all 50 of the United States and be able to recite them in alphabetical order for the rest of his life. But a student who visits the states, assigns personality and traits to them, and learns about their geography and climate will have much more input in deciding on a good vacation spot in February, or where to go if you want to see the ocean, or choosing a bustling city to start a new business. The list of states resides in a person’s ROM (read-only memory) or hard disks, but the search for good information about the states takes place in the RAM. Which student really knows the states? And what is more useful in life: recitation of facts or understanding their meaning? Do you want a doctor who can recite all the cancer drugs on the market or one who can analyze the choices and choose the one that is best for your particular diagnosis?

Dr. Hong points out the distinctions coined by Max Wertheimer who classified reproductive thinking as “blind” or senseless thinking and productive thinking as truly insightful. “Reproductive thinking manipulates mental structures, but does not generate new mental structures, whereas productive thinking does both,” Dr. Hong said. An
Members of the Royal Airforce Mission had a dilemma when they tried to design a “bouncing bomb” during World War II. They needed a bomb which, when dropped from precisely 60-feet altitude, would skip across the water, hit the side of a dam and detonate after sinking. They couldn’t get the angles just right, but had a sudden awakening while watching an opera in London one evening. After looking at the spotlights angled at the singers on stage, Barnes Wallis had a perfect picture for his plane. Using picture-based reasoning, engineers could apply similar principles to very different situations.

expansive short-term memory allows productive thinking, or the ability to add layers of information, relevance and function to things you already know.

Of course, all scholars are required to go back and test their possible solutions with rigorous rules and standards to verify their accuracy, but that is done after a creative search for best-possible solutions, Dr. Hong said. The tested, mechanical rule-based standards have their place in this stage of verification, but they are clearly preceded by free association and creativity—and that part is far more important.

Demystifying intuition and redefining it as recognition

Many psychologists have referred to the highly creative nature of geniuses, but most dismiss it as subjective in nature and therefore, hard to study or pinpoint. It is said that Nobel Prize winners have great intuition, inspiration and insight—but those words have represented an intangible nature of knowledge that has eluded scholars.

Genius mathematician Henri Poincaré tried to explain his thought process in the early 1900s and described great introspection and intuitive feelings. “It is by logic that we prove, but by intuition that we discover,” he said. He seemed unable to verbalize what made him think differently than his peers.

Dr. Hong suggests that by changing the word “intuition” to “picture-based pattern recognition” we can finally demystify what it really is. Many great scientists and scholars from Andrew Wiles (who solved Fermat’s Last Theorem in mathematics) to Alexander Fleming (who serendipitously discovered penicillin) admit to having experienced the “aha phenomenon” or the “eureka” experience. That is, after studying, thinking about and even obsessing over something for a long time, the answer suddenly and overwhelmingly came to them in an unusual moment, when they weren’t actually concentrating on it at all.

Dr. Hong says it is because geniuses have multi-track, multi-task minds with a remarkable ability to keep many ideas at the forefront, and then slightly pushed out of consciousness and then suddenly recallable again. When their attention to the problem is diffuse, they often stumble across something familiar, a template they’ve been searching for, a pattern between a previously solved problem and this one they are working on, and “aha,” it all fits.
This is not random chance or good luck, Dr. Hong said. It is parallel processing, even at a subconscious level. It is that constant search for a creative solution that must exist but hasn’t yet been explored. It is the recognition and transfer of rules across the boundary of disciplines.

"Intuition is simply picture-based pattern recognition," Dr. Hong said. "It is highly advanced free association—a mental linkage of superficially dissimilar but fundamentally related pictures or patterns. It is a subtle and creative match of patterns that others have missed."

For that reason, Dr. Hong often tells his students to stop concentrating for a while, to not try "too hard," and to walk away from a problem to allow incubation.

Are we dumbing down our doctors?
What does this mean for medical students who for all these years have been at the top of their classes, ahead of the curves, and in the top percentiles for all standardized tests?

"Widely used standardized testing further encourages students to use deductive reasoning at the expense of inductive reasoning, to discourage exploration and to encourage learning within the confines of narrative thoughts presented by the teacher, to ruin the good habit of verification, and to foster a passive work ethic."

What about evidence-based medicine, a major paradigm shift in medical practice that assigns tested, uniform practices to different diagnoses? In this practice, rules are assigned to treating various conditions, based on 30 years of accepted clinical research. "I do not object to the use of evidence-based medicine as a supplementary and complementary approach by physicians who still can call the ultimate shot," Dr. Hong said.

The fact is, according to Dr. Hong, rule-based standards in evidence-based medicine could eventually lead to mental rigidity and dogmatism. (For example, all people with sore throats get treatment X no matter what.) When it comes to training physicians, simply having them assign a predestined rule to a pre-screened condition ignores their need to cope with novel situations or novel processes when they arise, as they surely will. "Remember, physical diagnosis is still partly science and partly art, requiring an overall judgment based on conflicting information," Dr. Hong said. "That is why computers haven’t taken the place of doctors. Digital computing cannot tolerate bugs or imperfections. Human reasoning is required to weigh consequences, make conditional jumps, assign importance and priority to competing symptoms and analyze the overall situation."

The habit of making such
The value of picture-based learning can be applied to something as simple as tying a shoelace. Imagine writing instructions for tying a shoe. It would be nearly nonsensical. Directions would be much clearer through pictures and demonstrations. This is the case in many instances, according to Dr. Hong.

"WHEN CREATIVITY AND CRITICAL THINKING TAKE OVER ROTE MEMORIZATION IN EDUCATION, OUR FUTURE PHYSICIANS AND FUTURE PATIENTS WILL BENEFIT EQUALLY IN HEALTH CARE AND IN LIFE."

attempts at complex reasoning can make a big difference in solving all problems: whether it’s how one protein reacts with another, whether or not to take a new job, or how to fix the plumbing in the bathroom. The truth for physicians is: the problems are not that simple. They are all complex with much at stake.

Medical students must be hard workers in order to get accepted into highly competitive academic programs, but not all hard workers are geniuses. By contrast, all geniuses are creative problem-solvers. This makes Dr. Hong wonder where the emphasis should fall in a medical curriculum. After interviews with many of his former students, Dr. Hong repeatedly observed that B students often remember topics learned more than a year ago, but some A students forget as if they had never taken the course.

Dr. Hong fears that premed and medical students have increasingly levitated towards the use of their left brain at the expense of their right brain. “The danger is that our students will be trained like robots and education reduced to the fabrication of examination-taking machines.” Dr. Hong said it is most important that students grasp what is crucial in any given problem and why it is crucial. Educators need to train people how to think, not what to think.

“When creativity and critical thinking take over rote memorization in education, our future physicians and future patients will benefit equally in health care and in life,” Dr. Hong said. “The ‘aha’ phenomenon will happen more regularly, because our minds will be trained and prepared for it.”

So, might there be a genius Nobel Prize winner hiding away in Wayne State’s Scott Hall? Play a Mozart symphony in the background, allow some incubation time and intuition, and we may just see.

Dr. Hong says intuition is the uncanny ability to recognize a subtle match where average people fail. The value of visualization is illustrated here in molecular recognition which is accomplished by matching a finite number of recognition sites. It’s not easy for everybody to see, but people trained in picture-based learning may be more likely to make the match.
Dr. Steffes went to the Home Depot and Michael’s Crafts to get supplies for a mock OR. He built a box and made a lifelike stomach and intestines so training surgeons can practice using a camera and monitor to operate without actually seeing inside the body.
Judy Coyle, a Harper University Hospital bariatric surgery patient who has lost 75 pounds, is anxious to speak to the other members of her post-surgery support group. They’re gathered together in the Carl Sandburg Library in Livonia, Mich., just two days before Thanksgiving.

“I just did my first three-mile walk!” exclaims Coyle, 57, a Highland resident who used to own a local bridal shop. “And I’m thinking about starting yoga. Before my surgery, I was a ‘buffet professional.’ Now my quality of life is so much better. I can get on the floor and play with my grandchildren. That’s the joy of my life.”

The other members of the group, all of whom have suffered from morbid obesity, nod knowingly. Each one of them has a similar success story following gastric bypass surgery. In gastric bypass surgery, the stomach is stapled, creating a small pouch. A rerouted portion of the small intestine is attached to the pouch. Ultimately, the capacity of the stomach is reduced to about 3-7 ounces. Many patients maintain a long-term weight loss of about 100 pounds.

One man in the support group says he’s lost so much weight following surgery that his mid-size Taurus sedan now feels like a much larger Mercury Grand Marquis. Another says that prior to the surgery, he couldn’t fit into a restaurant booth; now he not only can slide in easily, he’s walking up to seven miles a day. The wife of one member sheds a tear as she demonstrates how she can put her arms around her once-overweight spouse for the first
time in their marriage.

Renee Potrafka, 37, is attending the meeting with her husband Ives, 49. Like the others in the room, both have undergone bariatric surgery at Harper University Hospital. Renee, a biology teacher at Father Gabriel Richard High School in Ann Arbor, pulls some dramatic evidence of her weight loss out of her pocket: her before-and-after school ID photos. In the 2002 picture, she carried 260 pounds on a 5’4” frame. Today, she’s down to 178 pounds, just 40 pounds shy of what she weighed in high school and her ultimate weight-loss goal.

Sitting in the circle and quietly listening to these stories is John Webber, M.D., a Wayne State University assistant professor of surgery and a key member of the Minimally Invasive Surgery Program affiliated with Harper University Hospital and the Wayne State University School of Medicine.

He is here tonight to answer a seemingly endless stream of questions, ranging from which medications the post-surgery patients can tolerate to plastic surgery options that will help them to get rid of excess skin and achieve a more pleasing shape.

Nearly all of them started the relationship with the Harper bariatrics program by calling and saying “I want the surgery that (singer) Carnie Wilson or (TV weatherman) Al Roker had.” As Dr. Webber points out, overweight celebrities who have undergone gastric bypass surgery have popularized the procedure. Even so, the office rejects about half of the patients who inquire about the surgery, most notably the super-obese and those under age 18.

Dr. Webber and Chris Steffes, M.D., a Wayne State University associate professor of surgery, run one of two comprehensive bariatric surgery programs at Harper University Hospital. A second program is run by Michael Wood, M.D., a Wayne State University clinical professor of surgery. More than 400 people last year turned to WSU surgeons at Harper University Hospital for bariatric surgeries.

“I would encourage every one of you to get into a routine exercise program,” advises Dr. Webber, a fit-looking 40-year-old who manages to be strict yet supportive with his patients. “We’ve given you a start, but as you all realize, the surgery is just one step. You must change your behavior in order to succeed. It takes a motivated patient to be successful.”

He reminds the group that morbid obesity is a chronic disease, meaning that its symptoms build slowly over an extended period of time. An estimated 5-10 million Americans are considered morbidly obese. The Harper Bariatrics (www.harperbariatrics.com) Website highlights the fact that obesity is a medical problem that caused approximately 300,000 deaths in the U.S. last year.

Obesity becomes “morbid” when it reaches the point of significantly increasing the risk of one or more obesity-related health conditions or serious diseases that can result either in physical disability or even death.
Drs. Webber and Steffes operate as a team when it comes to laparoscopic bariatric surgery. They are a fascinating pair who combine experience with enthusiasm. In addition, both have just returned from 90-day tours of duty in Iraq where they served as trauma surgeons.

So committed are they to developing the Minimally Invasive Bariatric Surgery Program that they have set up a mock operating room in their offices on the fourth floor of the Harper Professional Building. Dr. Steffes went to the Home Depot and Michael’s Crafts to get the supplies he needed to create the operating room and a lifelike stomach and intestines.

“Our job is to train Wayne State residents to do this operation,” said Dr. Steffes, 43. “It’s our obligation to make this something we can teach. Just think about it. Operating-room time is $45 a minute. The cost is free in the mock OR. The idea of the mock OR needs to be expanded to the whole medical school. There’s not the time or the money for students to learn this on a live patient. I think of it this way: The public expects you’ve flown the simulator before you take off in the 747. Mock training will become more important in the medical profession.

“In addition, I’m looking for the role of this type of surgery in health care. We are helping patients with diabetes, high blood pressure and other complications of obesity. And we’re saving money for the economy. Let’s keep the big picture in mind. Why else are we getting into this complicated business? We have to help society and train residents in 21st century operations. Bariatric surgery is a necessity. We need to move in this area. I’m looking to push the envelope laparoscopically. Right now,
we’re redefining ourselves.”

Both surgeons often oversee Wayne State University Medical School residents as they practice manipulating the tiny video camera that is inserted through a small incision into the rubber abdomen. They teach residents to view the procedure on a separate video monitor and work on improving their hand-eye coordination. Like most laparoscopic surgeons, they say this approach gives the surgeon better visualization and access to key anatomical structures.

This approach is considered less invasive than "open" bariatric surgery because it replaces the need for one long incision to open the abdomen.

Both Dr. Steffes and Dr. Webber say they are proponents of laparoscopic gastric bypass surgery because it results in a shorter hospital stay and an earlier return to work, along with less post-operative pain and decreased incidence of incisional hernia, wound infection and wound complications. The patients in the support group say they prefer it over open gastric bypass surgery because it’s also more cosmetically appealing. To prove that point, Renee Potrafka lifts up her sweater and shows the group her five tiny abdominal incisions.

In early 2004, the WSU doctors will also begin to offer so-called “lap band” bariatric surgery.

“We are looking at some way to help patients who need a ‘bridge operation’ and who can’t go through the entire reworking of their digestive system,” explained Dr. Steffes.

He pulls a doughnut-shaped ring with a long white tube attached to it out of a desk drawer in his office to demonstrate. The ring — a constrictive band — is put on the top of the stomach. The tubing is connected to a port under the skin. Physicians can then adjust how tightly the band constricts the stomach and limits food intake by injecting fluid into the port. Dr. Steffes says the lap band procedure can be done in about 20 minutes in the operating room, as opposed to about three hours for laparoscopic gastric bypass. However, it will require adjustment on a regular basis — about every few weeks for the first couple of months.

And, it’s not a miracle cure.

“The message is that the surgery is the easy part,” said Dr. Steffes. “I tell patients that you don’t get this operation and magically lose weight. You can’t continue to eat chili dogs ten at a time. The surgery is the start of a life change that includes diet, exercise, nutrition, vitamins and taking personal responsibility for your weight loss.”

The message seems to have gotten through to the patients meeting in the library just hours before the biggest eating feast in America. Ives Potrafka points out that the Harper Bariatrics Message Board has been barraged by a flurry of email questions about Thanksgiving and how to avoid the pitfalls of overeating or eating the wrong foods. The newest member of the group — a woman just two months past her bariatric surgery — asks: “Is there anything we should avoid during the holidays?”

“Yes,” responds Coyle, who looks fit in a sweatshirt and jogging pants. “Avoid the holidays. Period.”

Dr. Webber sits back and grins.

“It makes me extremely happy to see people change their lives around from hiding in the house to being productive members of society,” he said. “Nothing gives me more joy in surgery than seeing a patient a year or two later and you don’t even recognize them. I love it when they tell their stories. It makes it all worth it to me.”

THE HARPER BARIATRICS (WWW.HARPERBARIATRICS.COM) WEBSITE HIGHLIGHTS

THE FACT THAT OBESITY IS A MEDICAL PROBLEM THAT CAUSED APPROXIMATELY 300,000 DEATHS IN THE U.S. LAST YEAR.
World-Class Doctors. World-Class Care.

Congratulations to the 102 members of the Wayne State University Physician Group who were recognized by Best Doctors Inc. for providing quality care when it matters most.

The Wayne State University Physician Group is proud to partner with the Detroit Medical Center in providing quality care. For more information about the Wayne State University Physician Group please call 1-877-WSU-DOCS or visit www.wsupg.org.
Dr. Honn, who was recently named distinguished professor, holds 13 patents for various compounds and methods.
WHEN IT COMES TO HIS RESEARCH FINDINGS, Kenneth Honn, Ph.D., is stubborn. “I’ve been fighting dogma forever, but I absolutely will not give up,” said this internationally known cancer researcher. “The things we’re working on just turn out to be controversial, so what are you going to do?”

In his 20-plus years at Wayne State, Dr. Honn has become the most-cited researcher at the university according to the last study done, and frequently receives more external funding in a single year than many faculty members receive in their entire careers. This professor of radiation oncology and pathology, and adjunct professor of chemistry has also introduced and helped develop what has become one of the hottest areas in cancer research today. It all derives from a simple philosophy, he said. “Like I tell my students, you just have to follow your instincts.”

Dr. Honn is perhaps best known as the man who put the cancer-research spotlight on eicosanoids, a large and diverse group of 20-carbon fatty acids, including several that are active in preventing the spread of cancer. His research group is also heavily invested in the study of a number of transmembrane proteins known as integrins. The group found that some integrins serve as receptors in tumor cells and facilitate their movement to other parts of the body. One of Dr. Honn’s latest interests - and one that is sure to spur some new arguments - is his assertion that low-dose radiation may actually do more harm than good in treating cancer by enhancing the spread of cancer known as metastasis.

His work has always turned heads and sometimes turned up noses, he said. But, Dr. Honn’s choice for a research field paid off early on in his career. By 1979, just a year after earning his doctorate from the WSU biological sciences department and joining the WSU faculty, he had already found that some eicosanoids were active against the spread of cancer, or metastasis. “The whole thing with eicosanoids, cancer and metastasis really took off,” Dr. Honn recalled. His first projects centered on the roles of two eicosanoids, thromboxane and prostacyclin, in fighting tumor-cell progression. Thromboxane regulates the activity of platelets, which veer from their normal function in blood clotting to one of promoting metastasis in tumor cells. Prostacyclin, on the other hand, inhibits platelet function and tumor cell adhesion to the endothelial lining of the blood vessels, and therefore hinders metastasis.
In 1981, Dr. Honn published his results in two papers— one of them with cancer researcher Dr. Bonnie Sloane — in the journal *Science*. In the same year, he also received two grants from the National Institutes of Health (NIH) and another from the American Cancer Society. In 2003 alone, for example, Dr. Honn had a staggering 10 active research grants totaling $1.4 million. He typically has two NIH and several other grants in any given year. His funding has remained reliable.

His 1981 findings led to a relationship with a German pharmaceutical company, which began making long-lived analogs of prostacyclin that it planned to test as anticancer agents. Although translational research is a buzzword now, relationships between academic and industry were few and far between in the early 1980s. “Think about it,” Dr. Honn said. “In ’81 nobody was thinking about translational research, but that’s what we were doing.”

The thromboxane work is still continuing. Dr. Honn’s research group recently found that cancer cells express the enzyme that makes thromboxane. “In a paper that was just accepted in the *American Journal of Pathology*, we report that we cloned thromboxane synthase from prostate cancer, and it plays a role in motility. We found that the highest expression of the enzyme is in cells that are undergoing perineural invasion, which is how the cancer cells escape from the prostate along a nerve path. We’re quite excited about this,” he said. He noted that WSU pathologists David Grignon and Mingxian Che collaborated on the paper.

By the late 1980s, Dr. Honn’s research turned toward 12-lipoxygenase, a member of another group of eicosanoids, that he suspected was “very important in terms of tumor-cell growth and metastasis. We later discovered the effects on proliferation were actually prevention of apoptosis and stimulation of angiogenesis,” he said. Both are critical for metastasis. Normal cells undergo apoptosis, or programmed cell death, but tumor cells are adept at avoiding it. In addition, tumor cells require an entire network of new blood vessels, which occur via angiogenesis.

Dr. Honn began working with WSU chemists Larry Marnett and Carl Johnson, and the three men collaborated with another pharmaceutical company on developing drugs to shut down 12-lipoxygenase. Marnett left the university and now heads a research institute at Vanderbilt University and Johnson just retired from Wayne State, but Dr. Honn has continued to study 12-lipoxygenase, currently working with a local biotech company to test newly designed compounds. He commented, “We’re hoping that within a year, we’ll be in a phase I clinical trial with these 12-lipoxygenase inhibitors.”

A particularly fortuitous discovery, and one that surprised even Dr. Honn, came from Irma Grossi, a graduate student in his research group. “We were looking at the receptors on platelets that were responsible for the interaction between the platelet and the tumor cell, and the hot area of research at that time was integrins, some of which mediate platelet-platelet adhesion,” he explained. Grossi conducted some experiments and reported to Dr. Honn that she had found a particular form of an integrin on the tumor cells. No one had ever reported the occurrence, and Dr. Honn was highly skeptical until her repeated experiments and steadfastness convinced him.

Another fortuitous discovery was made by then postdoctoral student Dr. Mohit Trikha. He was following up on the project started by Dr. Grossi’s finding when he discovered that tumor cells produced truncated integrins, shorter versions of the full length receptors which were secreted by the tumor cell. He and Dr. Honn postulated that these truncated integrins were anti-adhesion molecules.

Once again, Dr. Honn faced opposition to his group’s findings, as well as an associated grant proposal on the topic. “Once dogma gets established, it’s just incredibly hard to break through. But we got more data, put the proposal back in, had to go back and get more data, put in the proposal again, and finally it got funded.” The extra effort was well worth it, he said. “We were right. We were absolutely right. And now, there are numerous researchers looking at integrins and discovering truncated forms.”

Besides the novelty of their discovery, Honn said truncated integrins are important because of their function. Through experiments conducted in collab-
oration with WSU and Karmanos Cancer Institute professor Avraham Raz, Dr. Honn said, “We showed that the full-length integrin goes to the leading edge of the cell where attachment is important and the truncated integrin goes to the trailing edge of the cell where detachment is important. Consider that when the cell moves, it has to grab on at the leading edge, but detach at the trailing edge. That means that the truncated integrin functions as an anti-adhesion molecule to facilitate tumor-cell movement.”

He added, “This is a totally new mechanism for cell movement. Plus, we have found that there’s a correlation with the stage and the grade of prostate cancer and the production of the truncated integrin. Now we’re now looking to see if we can measure the truncated integrin in blood and see whether it can be used as some sort of a diagnostic feature not only in prostate cancer, but also in other types of cancer, specifically head, neck and lung cancers.” Dr. Honn and the university were awarded two patents on these discoveries and another for the use of specific antibodies to detect their presence in tumor tissue.

Another major research emphasis among Dr. Honn’s 13-member research group is a study that spans both eicosanoids and integrins. It began when graduate student Keqin Tang was working on her doctoral thesis on the proteins that interact with and may regulate 12-lipoxygenase. “With Russell Finley in the Center for Molecular Medicine and Genetics here at Wayne State, she discovered four proteins that specifically interacted with the 12-lipoxygenase, and one of them was the cytoplasmic tail of an integrin, so it brought our integrin work and our eicosanoid work together,” he said. The study is especially interesting because this particular truncated integrin, called beta 4, has been shown to be involved in neck-cancer metastasis.

The research group is now investigating the possibility that the association between 12-lipoxygenase and beta 4 integrin serves as a signal to produce another compound, called 12-HETE, that dissolves a structure (the hemidesmosome) anchoring the tumor cell to the extracellular matrix. Without the anchors, the cells can travel to new areas of the body.

While that work is continuing, Dr. Honn believes he now has evidence that deals a serious blow to the low-dose radiation treatment, called hyperfractionation, that is becoming popular among radiation oncologists. “I wondered whether radiation increases 12-lipoxygenase activity so we get more 12-HETE produced. If that’s the case, it could be that low-dose radiation actually increases the metastatic ability of tumor cells,” he said. “We looked through the literature and, lo and behold, there was anecdotal evidence that you actually get a worse outcome in some cases with low-dose radiation, because you get more metastasis.” He said his group’s experiments now indicate radiation at low doses used in hyperfractionation stimulates protein synthesis for 12-lipoxygenase. “If you take those irradiated cells and inject them into the tail vein of a mouse, you see a great increase in metastasis.” Besides its potential effect on hyperfractionation, the work may have implications for new anti-cancer drugs, he said. “We actually just discovered that our 12-lipoxygenase inhibitors sensitize prostate tumor cells to radiation, and I’m talking about a two-fold sensitization, which is phenomenal. Plus, we have evidence that it will probably work in head and neck cancer, and in lung cancer, too.” Assistant Professor Daotai Nie, who is a member of Honn’s research group, is working under a grant from the Department of Defense to review a series of the inhibitors, and hopefully add one more cancer-treatment option to the growing drug arsenal.

With such an active research endeavor, several hundred publications, a long tally of grants, Dr. Honn’s vita is enormous. When asked if he’ll always remain busy in his scientific pursuits and adamant about his findings, Dr. Honn simply replied, “Sure. Why not?”

![FIGURE 3: Cancer cells express the enzyme that makes thromboxane and thromboxane synthase plays a role in motility.](image)

![FIGURE 4: Collaborations among the research teams of Dr. Honn and Dr. Russell Finley forged the discovery of four proteins that specifically interacted with the 12-lipoxygenase, and one of them was the cytoplasmic tail of an integrin, bringing Dr. Honn’s integrin and eicosanoid work together. The truncated integrin, called beta 4, is involved in neck-cancer metastasis.](image)
New radioactive tracers can tell within weeks whether cancer treatments are effective

BY LESLIE MERTZ

Cancer specialists hear the questions again and again from patients and their family members: Is the treatment working? Is the tumor going away? Until now, specialists needed at least two months, and often much more, before they could make that assessment. A new method of tumor evaluation, however, provides answers to those queries in as little as two weeks after the initiation of chemotherapy, and allows the health-care professionals to adjust the treatment accordingly.
Dr. Shields’ method of evaluating cancer therapy success is different than most. Instead of concentrating on size, he looks for evidence of life in the tumor using developmental techniques to image tumor metabolism.
"Commonly used techniques, like magnetic resonance imaging (NMR) and computed tomography (CT), tell you where the suspected tumor is, how big it is, and whether it’s getting bigger or smaller over time. That information is very useful, but it only goes so far," said Anthony Shields, M.D., Ph.D., professor of internal medicine at Wayne State, and associate center director of clinical research at the Karmanos Cancer Institute. “It doesn’t tell you whether it’s malignant or not, whether it’s even a tumor or not, and from my perspective as somebody treating cancer, it doesn’t tell me very much about how it’s responding to treatment.” That’s because a tumor’s size can be misleading, he said. “A tumor can shrink substantially, but everything that’s left may be completely alive and ready to grow back at a moment’s notice. On the other hand, we often see lumps that don’t change in size, but what’s inside is dead.”

Dr. Shields’ method is different. Instead of concentrating on size, he looks for evidence of life in the tumor. “My area of research for the last 20 years has been the development of techniques to image tumor metabolism. I focus on imaging cell growth, and whether the machinery for DNA synthesis and cell growth is still active. With that information, I can monitor changes in response to therapy.”

He has developed a series of targeted, radioactive chemicals, called tracers, that travel right to the site of the tumor. These tracers, when viewed with a positron emission tomography (PET) scanner, provide high-contrast images of metabolism. The images yield the information necessary to determine whether a cancerous tumor is alive or dead, and growing or shrinking. “According to our preliminary data, these tracers can tell us whether a tumor is responding to treatment within a couple of weeks.”

The early assessment can make a world of difference to a patient, he noted. “With current methods, we need at least two months to determine if the chemotherapy is working, which means that we may be giving the patient something that is very toxic besides being ineffective. The tumor may even be growing during that time period,” he said. “And these days, drugs can easily cost several thousand dollars per patient per month, so you have toxicity, time lost, and cost while you’re treating somebody with something that’s ineffective.”

The early recognition of treatment failure has become especially significant now that physicians have a number of cancer-treatment options, he said. “We’ve got second- and third-line drugs approved, so if the first one doesn’t work, we can switch to the second one or the third one.” As head of the development therapeutics program at the Karmanos Cancer Institute, Dr. Shields is well aware of the array of up-and-coming treatments. “We have more than 300 new drugs in the pipeline nationwide for treating cancer.”

In the past, most chemotherapeutic drugs were cytotoxins that not only poisoned tumor cells but also normal cells, he said. “That’s why people used to get so sick with them. Now, more and more of our drugs are targeted — they attack a specific pathway to the tumor or cell, and try to turn it off. The advantage is that it’s a lot more specific, and it can be a lot less toxic. The problem is evaluating how well they work.” As an example, he mentioned a number of new drugs that are designed to slow a tumor’s growth. “The tumor stops growing, but it doesn’t shrink much,” he said, pointing out that MRI and CT scans of tumor size would be insufficient to judge the effectiveness of one of these drugs. Anti-vascular agents also require new evaluation methods. This set of drugs blocks blood from flowing to and nourishing tumor cells. “With these agents, we don’t always immediately see the response in the tumor’s size. With newer MRI techniques and PET, however, we can actually measure blood flow.”

One of just a handful of medical oncologists worldwide who are developing tracers for imaging tumor growth, Dr. Shields makes his tracers from slightly modified forms of the naturally occurring compound called thymidine. “Thymidine is one of the four bases used in making DNA, and replicating cells — cells that are growing and dividing — make a lot of DNA, so they take..."
Dr. Shields has developed a series of targeted, radioactive chemicals, called tracers, that travel right to the site of the tumor and can tell whether a tumor is responding to treatment within a couple of weeks.

Up and use thymidine.” The challenge was to make a radioactive form of the compound that would show up on PET scans. “What we did was make a radioactive atom called fluorine-18 in our cyclotron here on campus and attach it to these forms of thymidine.”

They then inject the tracer intravenously into a patient while the patient is on the PET scanner. “From the outside, the PET scanner looks pretty much like a CAT scanner,” he said. “The difference is that a CAT scanner uses X-ray beams coming from the outside to go through the patient to take pictures. With our method, the tracer goes to the tumor and releases its radioactivity there, because the tumor is growing so fast and using so much thymidine. The scanner picks up that radioactive beam and converts it to an image.”

To extract data from the image, Dr. Shields turns to Otto Musik, Ph.D., the lead physicist at the PET Center. “The PET scanners produce large amounts of data — hundreds of images — during a single scan. We can’t just look at the images of tumor metabolism, we have to have a number, so we can determine the rate of growth now vs. the rate of growth in two weeks,” he said. “For instance, in breast cancer we find that if the growth rate drops by 20 percent or more in three weeks, the outcome is very good. With Otto, we’ve developed techniques to change the series of images into quantitative information that gives us those percentages.”

Dr. Shields has designed a variety of tracers for use with different tumor types. “I’ve spent a lot of time with a tracer called FLT, or fluorothymidine. This one is looking very good for breast cancer, brain tumors and lung cancer. Another thymidine tracer, called FMAU, works on prostate cancer,” he said. Although they didn’t make the original FMAU compound, Shields and colleague Dr. Thomas Mangner, found a new way to synthesize the compound, making it much longer-lasting than the original. Dr. Mangner, WSU associate professor of radiology, also directs the PET Center at Children’s Hospital of Michigan, where Shields conducts much of his research. Dr. Shields developed FLT with colleagues at the University of Washington. In addition, he and his four-person research group work with several clinicians, including Drs. Andrew Sloan, assistant professor of neurosurgery, and Philip Philip, a professor of internal medicine.

Besides the PET/tracer combination’s use in evaluating cancer treatment, Dr. Shields believes it may also speed the transit of new cancer drugs through clinical trials. “Cancer is not one disease; it’s more than a hundred diseases,” he said. “Even among patients with the same type of cancer, like breast or colon cancer, their tumors may be mutated in different ways, and different genes may be activated. More and more, we’re going to be tailoring our therapy based on how an individual’s system uses a drug and on the metabolism of that person’s tumor.”

Current drug-approval trials are very expensive and time-consuming, in part because they require testing in such large patient pools, he said. “Development of a new drug costs $800 million on average. That works if you’ve got a blockbuster drug that you can give to thousands and thousands of patients. If, however, you’re tailoring a drug for a couple thousand patients nationwide who have this kind of cancer and who have this kind of genetic abnormality, you can’t afford to do that. We need to speed up the trials, and understand much more rapidly whether the drug is working. Imaging is the way to go.”

For now, however, the tracers themselves are going through patient trials. “We’ve already studied more than a hundred patients with FLT, FMAU is going into patient trials, and we’re testing another tracer, called FAU, as an imaging agent and a therapeutic drug. I’ve met already with the U.S. Food and Drug Administration, and we’re working on getting national approval to use these tracers.”
Ph.D. STUDENT IS KEEPING SCIENCE COOL

BY AMY DICRESCO
Her friends in corporate jobs sometimes giggle at Pamela Osenkowski's “dorky science job,” but she just laughs. “I know, I know,” she said. “Sometimes scientists get too involved in their work and forget that there is life outside of the lab. Luckily, graduate students here not only support my science, but also make a point to talk about the real world too!”

While her friends had more traditional jobs to support them through college, Osenkowski studied turtle populations in the University of Michigan-Dearborn’s Natural Area, explored the cellular basis and genetics of tobacco plants, and created small peptide inhibitors for the Henry Ford Health System. A strong science student in high school, Osenkowski earned a bachelor’s degree in biology from the University of Michigan in 2000 and has a dual interest in animal and cell-based research.

At age 24, Osenkowski is a shining star in Wayne State University’s Graduate Program. She is just beginning the fourth year of her Ph.D. program in cancer biology, and she has already published several papers, been honored with a Scholar-in-Training Award from the American Association for Cancer Research, a Novartis Award at the Matrix Metalloproteinase Gordon Conference, and first prize at the WSU Graduate Student Research Day competition.

Under the tutelage of Dr. Rafael Fridman, professor of pathology, Osenkowski studies MT1-MMP (membrane type 1-matrix metalloproteinase), an enzyme that is over-expressed in cancer and may contribute to metastasis, the deadly aspect of cancer progression.

“I chose to study cancer biology because there is a huge incidence of it in my family,” she said. “In my lifetime alone, I lost my grandma, grandpa and uncle to colon, lung and brain cancer.” After a rotation with Dr. Shahriar Mobashery, who studied the kinetics of MMPs, Osenkowski partnered with Dr. Fridman to study the cellular basis of MMPs.

“I study MT1-MMP regulation on the cell surface,” she said. “Since MT1-MMP is complexly regulated on the cell surface, I generate MT1-MMP mutants to better understand the structure/function relationships of this enzyme. The mechanisms of regulation I am currently studying include autocatalytic processing, shedding, and internalization. Understanding the delicate balance between these different mechanisms, and determining if there is a preferred regulatory mechanism during specific biological conditions will give us valuable insight into one of the most prominent proteases in cancer.”

“I am fortunate to have Pam working with me,” Dr. Fridman said. “She is a brilliant scientist who works hard and with enthusiasm. Every day, she has new things coming around and it is for me the best time of the day when we discuss results and new ideas. Pam always finds a way to overcome every difficulty with tenacity, knowledge and optimism. It makes me feel proud to see how Pam has become a mature and insightful scientist. I am sure that Pam’s future is bright.”

Several senior MMP investigators from across the country have already taken an interest in Osenkowski’s research and drive and are recruiting her for post-doctoral fellowship positions upon her degree completion in 2005. She is interested in job possibilities in Vancouver, British Columbia, and California, but her long-shot dream is to do biology-based research for NASA and be part of the space station program. She has applied for a research position there, but won’t have an answer until closer to graduation.

“Pam is, indeed, among our best as we look at the many successes within our graduate training programs. Her enthusiasm for science and her work is contagious, and everyone associated with her finds themselves caught-up in that enthusiasm!” said Kenneth Palmer, Ph.D., associate dean for graduate programs at WSU. “Pam has a very promising research career ahead of her.”

Osenkowski, who was once quite intimidated by the scientific exchanges of her professors, is now joining in the mix and stirring up discussions of her own. She says Dr. Fridman and the WSU graduate program have been great in preparing her for a career in science. But still, if she works hard, she sees it only fit to play hard.

She continues her mission to keep science cool. For instance, she “shook things up” when she took control of the pathology department’s holiday party. “Everyone actually sang karaoke and stayed until the end!” she said. And she has initiated summertime “Pathology in the Park” events. “We have to get out of those labs sometimes,” she insists.

In addition, her research awards have allowed her to travel to scientific meetings and see fun places. She will be attending a protease meeting in Italy this May and is working on data collection now to submit.

Italy in May? That doesn’t sound so dorky, now does it? ☔
Few Ph.D. candidates complete their degree with a full spectrum of research experience to their credit. Grant Blouse is an exception. By the time he earned his doctorate in pharmacology from the Wayne State University School of Medicine in 2003, he had already secured a full-time research job, contributed to a winning National Institutes of Health grant, published and presented 20 research papers and abstracts and accepted an adjunct professorship to teach students the following semester.

“He is a brilliant student,” said Bonnie Sloane, Ph.D., professor and chair of pharmacology, who encouraged Dr. Blouse to do his doctoral work in the Department of Pharmacology. “Grant has an enthusiastic approach to science and life. His research is basic but fundamental to understanding how a protease and its inhibitor interact. The protease in this case is tPA (tissue plasminogen activator), an enzyme that is given as the leading thrombolytic therapy for dissolving blood clots in patients presenting with a myocardial infarction or stroke. Therefore Grant’s analyses provide information that could be used to modify the tPA treatment presently used therapeutically or to design new synthetic inhibitors that regulate the function of tPA’s natural inhibitor, PAI-1.”

In 1998, Dr. Blouse moved to Detroit to work as a senior research assistant at the Henry Ford Health System after completing his master’s degree in biochemistry at Clemson University in South Carolina. He was excited to be involved in a research laboratory studying fibrinolysis, which involves enzymes breaking down proteins in the blood clotting process.

He uses molecular biology and protein engineering to uncover the mysterious mechanisms of proteases and inhibitors—specifically, PAI-1, the inhibitor of tPA. Because tPA is used as a drug to dissolve blood clots, his work has tremendous impact on possible new drug designs for cardiovascular disease.

“It’s like a mousetrap mechanism where the mouse is the protease and the PAI-1 is the trap. When the mouse goes to get the cheese, the inhibitor snaps into action, and the mouse or protease gets stopped dead in its tracks,” Dr. Blouse said. In other words, if the tPA isn’t allowed to function freely because the PAI-1 gets in the way, major problems cascade from the impending cell and tissue damage.

Even with the responsibilities of a full-time job, Dr. Blouse quickly began to think about pursuing his Ph.D. and looked to Wayne State University after meeting Dr. Bonnie Sloane at the first meeting of the International Proteolysis Society, an organization she founded to bring together scientists with the same research interests. Shortly thereafter, Blouse enrolled in the Wayne State graduate program. He completed his coursework at WSU, but did all his laboratory research at Henry Ford under the tutelage of biochemist Joseph Shore, Ph.D., who headed the biochemical research division.

“I received a great education in chemistry at Clemson University, but Wayne State focused a little more on the direct translation from science to medicine and that really interested me. Just the fact that the Ph.D. program is part of the School of Medicine, not the College of Science, speaks volumes about the biomedical translational work that is encouraged,” he said.

Dr. Blouse’s cardiovascular work has taken a slightly new turn recently, as he discovered that PAI-1 also plays a role in cancer migration and metastasis. Thus far, there are no clinically useful drugs to modulate PAI-1 function and researchers are now looking to develop novel therapeutic strategies that could stop cancer in its earliest stages.

With academic partners in Detroit, Tennessee, Belgium and Denmark, Dr. Blouse is already making a name for himself. He has been appointed assistant staff investigator at Henry Ford and was a significant contributor in securing grants from the National Institutes of Health and the American Heart Association. He has trained research assistants, one of whom has gone on to graduate school in chemistry at Wayne State, and another to study virology at Harvard.

“I was lucky to work with mentors who really let me get my feet wet and help with all aspects of research: grant writing, bench work, teaching and administration. I think I have lots of options and possibilities in front of me now,” he said. ☃️
Medical student Brandy Watson is considering a career in surgery.
BRANDY WATSON NEVER CONSIDERED MEDICAL SCHOOL until her college biology professor told her she should. The mere suggestion turned Watson in a totally different direction toward a rewarding career in research and medicine.

“I was a hospitality business major at Michigan State University,” Watson said. “During my first year of college, I was taking an integrative biology class to satisfy a general education requirement. I was doing well in the class and was really interested in the material, and my professor finally asked, ‘Why are you in business school?’ I thought that for me, a career in business was more tangible than a career in medicine. But my professor convinced me otherwise, so I tried some pre-med classes my sophomore year, did well and kept on going.”

Although Watson said she always liked science in elementary and high school, she didn’t have any family members or friends in health professions and never considered it as an option for herself.

At MSU, she joined the LANE Premedical Society (Leaders Achieving Notable Education) and received the Outstanding Senior Award. In 2001, she earned a bachelor’s degree in integrative studies and social science with a concentration in health studies and cognate anthropology.

She took a year off after graduation and worked in the post-baccalaureate research program at the National Institutes of Health (NIH) in the Department of Allergy and Infectious Disease. “We were working on respiratory viruses—mainly RSV—and I was able to recover and make a virus that is used in a cystic fibrosis lab in North Carolina,” Watson said.

Upon her return to Detroit, she was awarded a Medical Alumni Scholarship which granted her full tuition to the Wayne State University School of Medicine. She gladly accepted and is currently in her second year of the four-year program. Although she really liked the work at the NIH, it was very technical and she began looking for a new research project that would have more immediate applications outside the laboratory.

During the summer of 2003, Watson worked with Dr. Bruce Berkowitz of WSU’s anatomy and ophthalmology departments. He studies diabetic retinopathy on rat models and suggested that Watson work on a project to test whether diabetes and hyperthyroidism create a combinatorial effect. Through her project, she was able to combine anatomy, cell biology, ophthalmology and radiology—all fields she wanted to become better acquainted with.

“Brandy did a good job in the short time she was in the lab,” Dr. Berkowitz said. Recognizing her determination and interests, he suggested even more for her. “In fact, after seeing her enthusiasm and contributions to the project, I discussed the possibility of her joining the M.D./Ph.D. program here so she could continue her lab work.”

“I look at the science in a different way,” Watson said. “I see the need to incorporate research into any medical practice. There is much to observe and learn.”

Watson hasn’t yet committed to a medical specialty, but she suspects she will choose something that deals with whole body systems, not just one isolated organ or system. So far, she likes surgery, and has a special interest in minority health research.

“I’m wide open to whatever comes along,” she said. And it seems that even if Watson thinks she can’t do something along the way, all she needs is a reminder that she can.
The victim of a drive-by shooting, Weusi Olusola turned his disabling injury into a campaign against violence.
“YOU’D BE SHOCKED to see how many hands go up when you ask a group of Detroit middle-school students: How many of you know somebody who’s been shot?” said Weusi (Wei) Olusola, the victim of a 1986 drive-by shooting and the survivor of a traumatic spinal cord injury that left him paralyzed below the waist.

Generic messages of violence prevention have reached a near saturation point with Detroit kids. But when the message is delivered by a hip black guy who was once destined for a professional basketball career and is now rapping from his wheelchair—the message packs a bit more punch.

“The misconception is: You get shot, you’re dead. The reality is: Most people who get shot live with an injury or impairment that changes everything. And we’re here to show you,” said Olusola.

After months of treatment and therapy at the Detroit Medical Center’s Rehabilitation Institute of Michigan (RIM) in the late 80s, Olusola met five others just like him—black, single men who suffered serious injuries from gunshots, gang activity and violence. They got together to film and produce “Wasted Dreams,” a video that told the stories of the five young men and was used as a violence prevention and awareness tool that targeted school children in Detroit. That effort led to the formation of Pioneers for Peace, a group that takes violence prevention programs on the road, into classrooms and to communities. Today, the group is comprised of 25 volunteers who use their disabilities to drive home this message to youngsters: The decisions you make and the situations you face can land you permanently in a wheelchair or a hospital bed or worse—if you put yourself in the way of violence.

“You may think it’s cool to be a thug, or it’s cool to live like a pimp, or that girl gangs are where you find your friends, but we have to break that way of thinking,” Olusola said. As one drug-dealer turned Pioneer for Peace detailed his daily routine, he noted that it’s not so cool to scoot up the stairs on his bottom because he can’t walk. And no matter how cool his clothes are, his mom has to help him get dressed every day because he can’t move his limbs. “These things you take for granted can be taken away from you very quickly,” he said.

Robin Hanks, Ph.D., assistant professor of physical medicine and rehabilitation leads the Southeastern Michigan Traumatic Brain Injury System at RIM, which is one of 16 centers of excellence for traumatic brain injury treatment and research. She says the Detroit center leads the state in the number of violence-related brain injuries. In other cities, violence-related incidents comprise about 12 percent of hospital admissions. At RIM, they comprise 45 percent. The figures are similar for traumatic spinal cord injuries.

One notable thing to come out of the research is the profile of a person likely to suffer a violent traumatic brain injury (TBI). Statistics show that risk increases with each element of this profile: an African-American male, who is unmarried, unemployed and had a prior TBI. “Survivors of violent and nonviolent TBI have similar functional outcomes; however, they differ in preinjury and postinjury socioeconomic characteristics, injury severity and postinjury community integration,” Dr. Hanks said.

Interestingly, she found that an unemployed person’s risk of involvement in a violent injury is three times greater. According to Dr. Hanks, “It suggests that individuals who may be living on the fringe of society, in a less traditional mode of activity, are at greatest risk.”

Research stats have defined the target population for Pioneers for Peace, but an understanding of his community already did that for Olusola. “We’re a youthful group, so we understand what kids are dealing with,” he said. “We’ve all been there.”
Olusola was 16 years old when he was standing outside a friend’s house where a birthday party was going on inside. Six hitmen hired by a drug kingpin drove by and shot at the wrong house, killing one child and injuring three others, including Wei. At that time, he was headed to college on a full basketball scholarship and there was talk of a possible professional career. It all changed in a split second with the firing of a gun.

“I’m sick of it,” he said to a gymnasium full of kids. “What’s wrong with our people? We come together to have a good time, but we have to handcuff people to keep them together. We need to get our lives in order. We aren’t trying to preach and we aren’t trying to change anybody. We’re trying to make you use your head and think.”

The Pioneers for Peace program is more than a video and motivational speech. The group has written grants to start after-school programs to provide recreational activities. They hold workshops on various topics like conflict resolution and living with disabilities. They are establishing student chapters at schools, and they have teamed up with Wayne County sheriffs, police officers, jails and the morgue to give kids a “reality tour” of what happens to violent criminals.

“We are teaching kids to handle situations in peaceful ways. We want them to know you don’t have to win in every situation, but you need to have control in every situation,” Olusola said.

“The incidence of violence in the United States has reached epidemic proportions. Violence is a major contributor to premature death, disability and injury. We are thrilled to support Pioneers for Peace because they are delivering personal messages of hope to poor, disenfranchised minorities who need some counteraction to the messages bombarding them from everywhere else,” Dr. Hanks said. “We have enough athletes and superstars, we need real advocates who can open youngsters’ eyes to the reality of violence across the city and across the nation.”

Although he isn’t happy about his injury, Pioneers for Peace co-founder Chris Lewis said, “I look at what has happened to me and I see it as a blessing in disguise, because had I not been shot, I would probably be in jail or dead today.” Instead, he is a community advocate, disabilities and all, who is working every day to triumph over tragedy.

“We are teaching kids to handle situations in peaceful ways. We want them to know you don’t have to win in every situation, but you need to have control in every situation.”