Summer 2012

Advance (Summer 2012) - The Connection of Mind and Body: Improving Quality of Life for Terminally Ill People

University of Tennessee Medical Center
University of Tennessee Graduate School of Medicine

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On the Horizon: Healing Chronic Wounds with a Unique Gas

Research Spotlight: Advances in Imaging and Assessing Alzheimer’s Disease

Studies in Brief:
- Using PET-CT for Better Bronchoscopies
- Slowing the Progression of Prostate Cancer

Clinical Trials

The Connection of Mind and Body
Improving Quality of Life for Terminally Ill People

Summer 2012
Spirit of Discovery...
Observations

“If you would understand anything, observe its beginning and its development.”

Aristotle

The purpose of Advance is to highlight research at the UT Graduate School of Medicine. While we look forward to a bright future, there are important insights if we harken back to the glorious days of early research at our institution. Dr. Alan Solomon, Dr. Wahid Hanna and Dr. Carmen Lozzi kindly shared with me some of the signature achievements of the researchers at the Graduate School of Medicine from the mid-1960s to the mid-1990s.

During this period, the Birth Defects Center was established and several novel chromosomal abnormalities were described. Our clinicians were among researchers at several centers who conducted the first clinical trials with L-DOPA for treatment of Parkinson’s disease. The favorable response in one of the subjects who participated in the study was instrumental in later funding and developing the Cole Neuroscience Center.

Other notable contributions include:

• Development of the K562 cell line from a patient with chronic myeloid leukemia that continues to be used to this day by researchers all over the world to study hematopoietic development;
• Discovery of thrombopoietin;
• Landmark studies on functional properties of erythropoietin, including experiments with NASA to elucidate the cause of anemia during space flight;
• Establishment of several clonal plasma cell lines that continue to provide important insights into the pathogenesis of multiple myeloma; and
• Development of a monoclonal antibody (11-1F4) that specifically binds to amyloid fibrils and is capable of lysing amyloid deposits. The National Cancer Institute has developed a chimeric derivative of this antibody for Phase I clinical trials in humans.

Only a few of the major scientific contributions are mentioned. The list of achievements is long and truly impressive. Scientists currently working at the Graduate School of Medicine celebrate the efforts of our senior colleagues and are proud of their many achievements and valuable contributions to medical science. The cadre of researchers at the Graduate School of Medicine build on what has already been accomplished with the goal of providing novel treatments for treating human illnesses and raising the research enterprise to even greater heights in the future.

The articles in this issue of Advance shine the spotlight on our talented researchers and their current accomplishments. These professionals have the ideal platform to build on our past successes!

Rajiv Dhand, M.D., FCCP, FACP, FAARC
Professor of Medicine
Chair, Department of Medicine

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Advance is produced by the University of Tennessee Graduate School of Medicine. The mission of the digest is to spotlight research programs at the institution and explain how the work of our researchers impacts healthcare in East Tennessee and beyond.

Institutional Review Board
All research using human volunteers follow stringent federal regulations that require a review by an Institutional Review Board (IRB) before it is approved. The IRB committee is comprised of physicians, pharmacists, scientists, researchers and non-scientific community representatives. The members review research protocol to ensure protections are in place.

Faculty from the UT Graduate School of Medicine influence medical care across the world by publishing and presenting. For a comprehensive list of publications and presentations, visit http://gsm.utmck.edu/scholars.

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After you speak with Eric Carlson for just a few minutes, you will ask yourself, “What drives this man?” His energy level is astounding, so is he fueled by strong coffee? His strategic planning is grounded yet visionary; has his love of college football or background in competitive tennis developed his strategic ability? The walls of his office proclaim his academic pursuits, so does intellectual curiosity drive him? His desk is covered by photos of family; is it they who define him? Yes.

All of these factors (minus the coffee; his energy is all his own) influence him. But then you hear him speak again and again about his patients, about improving the health of his patients, about educating his patients, about learning all he can about the diseases that impact his patients.

It all becomes clear. Yes, he’s inspired by family and faith, and he is a lifelong learner. But to what end? Eric Carlson, D.M.D., M.D., is mostly driven by his desire to succeed on behalf of his patients. He is the chair of the Department of Oral and Maxillofacial Surgery at the Graduate School of Medicine and a cancer surgeon. He is a teacher of residents and fellows, and he is a clinical researcher. His educational curriculum, the research he conducts and the plans he makes translate immediately to his patients.

A Perfect Storm
Carlson grew up in Massachusetts and initially chose to study dentistry.

“I knew during dental school that I’d broaden my career,” he says. “I have a strong sense of curiosity, and I’m motivated by a challenge. The inquisitive mind is the stimulated mind.” He then graduated medical school and obtained residency training in oral and maxillofacial surgery and general surgery followed by a fellowship in oral/head and neck surgery.

A challenge is what he faced when he joined the Graduate School of Medicine in 2002. He characterizes his choice to come to Knoxville with a weather analogy:

“My educational vision matched that of Jim Neutens [Dean of the Graduate School of Medicine], and my clinical vision matched John
Bell’s [physician and director of the University of Tennessee Medical Center Cancer Institute]. It was a perfect storm.”

As chair, he has developed the Oral and Maxillofacial Surgery department and residency and fellowship programs into nationally renowned programs. For the past three years, in fact, his residency program has received the highest number of applications of any program in the country. Part of his strategic plan for the department is to expand the residency program from a four-year to a six-year program that will also permit his residents to earn the doctor of medicine degree.

“Education is my life,” Carlson says simply. And he’s not just talking about educating young doctors. He spends a great deal of time educating his patients, as well. He believes an educated patient is far more prepared than merely an informed patient and can make educated decisions about his or her treatment.

Inspiration and Intellectual Curiosity

Like education, translational research satisfies his intellectual curiosity, as well. His strategic plans for the department include performance of nationally recognized clinical and basic science research, and currently he is investigating squamous cell carcinoma of the oral cavity associated with human papillomavirus. He is researching why at the molecular level, it can kill one patient but spare another with cure realized.

“I want to know why this happens,” Carlson says. “If we can characterize cancer at the molecular level, we can offer personalized approaches to cancer treatment and possibly realize better outcomes for our patients.”

He loves a challenge, and he is driven by the desire to improve the health of his patients. As a result, he works many long hours but still calls his job “fun.” When he’s not at work, he spends his free time almost exclusively with the people in the photographs on his desk: his two daughters, beautiful wife and father, who is his role model.

“My father taught me that anything worth doing is worth doing well,” Carlson says.

He admits that he has probably spent more time at work than with his beloved family, but he has tried to create balance in his life by making time for them along the way. During his daughters’ childhood, for example, he sometimes brought them to work with him, and occasionally they could observe surgeries. No doubt due to this influence as well as that of his wife, a nurse who, he says, has faithfully supported him for 24 years, one of his daughters has chosen to study veterinary medicine, and the other, who just graduated from high school, believes she will study nursing. Will they have the same compassion for their patients that has been modeled by their father?

“I love my job,” this father, surgeon, teacher and researcher says. “I want to make a difference in my patients’ lives. I will use the tremendous resources at the [University of Tennessee] Medical Center; I will continue to learn; and I will do research on behalf of my patients. When their outcomes are better, my job is more fulfilling,” he says.
Our brains register pain in at least eight ways. To Ragi Doggweiler, M.D., they represent many different opportunities to help chronically and terminally ill patients improve their quality of life.

Personal life experiences brought Doggweiler to embrace a new research study she now is leading, and the study, itself, has deeply emotional roots. Brothers, John and Ward Flynn, grew up in Florida as independent, sometimes quarrelsome brothers. After decades apart pursuing their own careers in healthcare education and administration, Ward was diagnosed with terminal colon cancer, and the brothers reunited. Using their experience in healthcare, they set to work together, and with Ward as the visionary and John as the implementer, their work reached John Bell, M.D., Professor, Department of Surgery, Surgical Oncology, and Director of the University of Tennessee Medical Center Cancer Institute.

“One day, John [Bell] sent me an e-mail he had received from John Flynn,” Doggweiler says. “He thought I might be interested in it.”
Doggweiler, an associate professor at the UT Graduate School of Medicine and a neuro-urologist at UT Medical Center, is searching for ways to improve the quality of life for her patients who suffer from chronic pelvic pain. She believes that combining holistic approaches to patient care with standard medical protocols could make a difference. To that end, over the past 10 years, she earned certifications in several areas of integrative medicine, and last year, she started a Mind-Body Skills Group. The field of integrative medicine recognizes the connection of body and mind to achieve optimal care for the patient.

So Doggweiler was, indeed, interested in the e-mail John Bell had received from John Flynn. Seems the Flynn brothers had started the Institute for the Quality of Life, or i-QoL, to study how patients and caregivers manage terminal diseases and how quality of life can be preserved and improved. It is an instructional program including a “calculator” that tracks a patient’s quality of life in real time.

“The scientific, evidence-based approach to healthcare naturally focuses almost exclusively on the health of the body,” says Ward Flynn. “My brother and I believe i-QoL is the first rational integration of conventional healthcare and complementary care. [Health of the] body, mind, heart, spirit and setting is critical for optimal healing.”

As part of a collaboration with the Cancer Institute, the calculator will be used to monitor patients during their treatment courses and will help to choose alternative approaches that will be available in the Cancer Institute, including mindfulness training, acupuncture, yoga and exercise, food studies and more.

“To get healing, we have to approach care from many points of view,” Doggweiler says. “Self-care skills and a supportive environment can assist an individual to achieve a higher level of physical, emotional and spiritual wellness while navigating the experience of disease. With this approach, physicians will see better results, and the patient will experience a higher quality of life. Mind-body medicine, grounded in a respectful, therapeutic partnership, should be a central element in the care of every person.”

Why This Matters:
Western medicine is beginning to recognize a connection between the mind and body and how to use it for the best care possible for patients. Research to better understand this connection can lead to improved quality of life for people who are chronically or terminally ill.
Medical researchers believe Alzheimer’s disease is caused or worsened by amyloid deposits in the brain that contribute to memory loss. Amyloid is a term that describes an abnormal state whereby many different types of proteins and sugar molecules can misfold and form hair-like fibrils that deposit in vital body organs causing devastation and eventual death.

Seeing amyloid in the brain is imperative to diagnosing and staging Alzheimer’s disease, and for those who suffer from Alzheimer’s or other forms of amyloid-related dementia, diagnosing the severity of the condition aids in treatment decisions and patients’ quality of life.

John Dougherty, M.D., is part of a multi-disciplinary and multi-institutional team who are investigating ways to see amyloid and measure the severity of cognitive impairment.

“Up to 60 percent of patients with early indicators of Alzheimer’s disease go undiagnosed in the primary care setting,” says Dougherty. “We are making progress to improve that number.”

Dougherty is the director of the Cole Neuroscience Center at the University of Tennessee Medical Center (Memory Disorder Program), and an associate professor of Medicine in Neurology at the Graduate School of Medicine. He and others are combining imaging technology with new assessment tools to determine a reliable way to diagnose and stage cognitive diseases.

In their research, the team is evaluating a novel brain amyloid radioimaging agent AVID-45 (Amyvid™ Avid Radiopharmaceutical) in patients who have been diagnosed with early Alzheimer’s disease or mild cognitive impairment. The researchers also are using an interactive computerized self-test developed by Dougherty and his colleagues at the University of Tennessee,
The aim of the study is to determine if the extent of brain amyloid seen by radioimaging correlates with test results.

The online test, called alzselftest™, is an affordable, readily accessible screening device that can be self administered or administered by physicians, caregivers or family members. It evaluates orientation, visual-spatial abilities, verbal fluency, memory, attention and executive processing.

The test also is used in conjunction with a driving simulator at UT Knoxville that predicts impaired driving ability in patients with Alzheimer’s disease.

“We want to promote early diagnosis of Alzheimer’s disease, so the many people who are undiagnosed can be diagnosed and receive treatment early, when it is most effective,” Dougherty says. Research has indicated that alzselftest™ is 95% accurate in diagnosing Alzheimer’s disease and 97% accurate in detecting mild cognitive impairment.

These and other efforts are part of a comprehensive Alzheimer’s Disease Diagnosis and Treatment Center soon to be operational that will combine the resources of the UT Graduate School of Medicine and University of Tennessee Medical Center. The new program would provide not only diagnostic and treatment services for patients and support services for their caregivers, but it also would involve the faculty and students at UT Knoxville’s colleges of Nursing; Social Work; and Education, Health and Human Sciences.

As part of the Center’s mission, Jon Wall, Ph.D., a professor and director of Preclinical and Diagnostic Molecular Imaging Laboratory, and his associates are commercializing a new peptide, p5, that will be used as an imaging agent for Alzheimer’s disease and other amyloid-associated illnesses.

For information about the alzselftest™, visit www.alzselftest.com.

**Why this matters:** These important strides in the understanding of Alzheimer’s and other amyloid diseases enable us to diagnose more accurately and bring us closer to prevention and cures of these devastating diseases.
Clinical trials are medical research that helps bring new devices, vaccines or drugs more quickly to patients. They are monitored by the Institutional Review Board (IRB), a group of medical professionals and community representatives who ensure stringent adherence to federal regulations and protection for trial volunteers.

The academic medical center environment at the UT Graduate School of Medicine and University of Tennessee Medical Center enables and encourages physicians to conduct clinical trials to seek improved care for their patients. The professionals in the Maternal Fetal Medicine department at UT Medical Center have several trials under way.

Craig Towers, M.D., is the principal investigator in a trial studying testing of fetal lung maturity. The objective of the trial is to ascertain the accuracy of the lamellar body count in amniotic fluid containing blood. Little research exists on the effect that maternal blood has on the lamellar body count, which is a well-established test for fetal lung maturity. This clinical trial will examine the effect of maternal blood on the test in amniotic fluid in women who are not on heparin therapy to determine if the presence of blood skews the results. This test currently is enrolling.

The Maternal Fetal Medicine department, headed by Bobby Howard, M.D., also is studying a drug to stop labor. Howard is leading the study that is comparing intravenous and oral administrations of an oxytocin receptor antagonist being developed for the treatment of pre-term labor in healthy, pregnant women. Pre-term birth is the largest single cause of infant morbidity and mortality. The first phase of this trial has been completed, and the next phase will offer enrollment soon.

A study comparing two treatments to induce labor has recently concluded. More than 20% of pregnant women in the U.S. require medical intervention to induce labor, and the rate is continuing to rise. Mark Hennessy, M.D., and his team compared two vaginal inserts to find a safer and more effective means to induce active labor. For more information about the Maternal Fetal Medicine studies, contact Stephanie Porter, 865-305-8888.

Clinical trials provide answers to patients and physicians and help develop new treatments for a variety of medical conditions.
Researchers at the UT Graduate School of Medicine and University of Tennessee Knoxville are studying the effects of Zyflamend™ to slow or halt the progression of prostate cancer. Zyflamend™ is a commercially available herbal supplement that has been shown to slow or halt the progression of certain prostate cancer cells. UT Graduate School of Medicine physicians, Frederick Klein, M.D., chief of the Division of Urological Surgery, and Wesley White, M.D., director of Laparoscopic and Robotic Urologic Surgery, and other members of the Department of Urology, along with UT Knoxville researchers, Jay Whelan, Ph.D., head of the Department of Nutrition, and Paul Terry, Ph.D., associate professor of Public Health, are collaborating on the study.

Other than skin cancer, prostate cancer is the most commonly diagnosed malignancy among men. The American Cancer Society estimates more than 200,000 men in the U.S. will be diagnosed with prostate cancer in 2012. One in six American men will develop it, and more than 30,000 will die of prostate cancer this year.

Why this matters:
Given the aging population and prevalence of prostate cancer, a positive finding in this study would potentially allow patients of advanced age or those with significant additional diseases a non-invasive means of delaying prostate cancer progression.
Paul Branca is investigating noninvasive ways to perform bronchoscopies.

A conventional bronchoscopy is performed by inserting a bronchoscope into the airways and taking a look around. It provides doctors with a visual tour of the throat, larynx, trachea and lower airways and allows therapeutic maneuvers, such as taking specimens for biopsy. Limitations of this procedure, though, occur from the equipment, itself: It simply cannot see everything, particularly cancer.

In 2009, Paul Branca, M.D., Clinical Assistant Professor, Department of Medicine, and Chief of Critical Care Medicine, embarked on a study to find a better, noninvasive way to get a look inside to more accurately diagnose his patients’ airway conditions.

“We have one of the most sophisticated pieces of imaging technology in the world, and I believed it could be used to improve results of bronchoscopies,” Branca says, in reference to the PET-CT scanner at the University of Tennessee Medical Center.

Branca and his team compared 30 conventional bronchoscopies with 30 conducted noninvasively with PET-enhanced CT imaging. The PET-CT bronchoscopies used specially designed software that digitally reconstructed the airway structure, showing not only anatomical but also metabolic images of the airway.

“It is early in the study, but the results are promising,” Branca says. “I believe they tell us there is a better, less invasive way to perform bronchoscopies that could result in more accurate diagnoses for patients.”

Next, Branca will compile and analyze the results of the first study and seek to begin a clinical trial for a more comprehensive study.

**Why this matters:**
According to the American Thoracic Society, more than 500,000 bronchoscopies are performed each year in the U.S. to diagnose airway bleeding, difficulty in breathing, lung cancer and other problems. This research could lead to more accurate diagnoses for patients suffering with airway-related conditions.
Brian Daley and team members track surgical outcomes for better patient care.

It’s not all done with test tubes. Sometimes, research using paper and pencil and keen observation can help an institution improve patient care.

This is the case with a quality-improvement initiative used by the Department of Surgery. The American College of Surgeon’s National Surgical Quality Improvement Program (NSQIP) helps medical institutions track surgical procedures and results to identify preventable complications and improve surgical outcomes for patients.

The Department of Surgery has been using NSQIP since 2009, and to date, more than 1,600 surgical procedures have been analyzed.

“We are able to see analysis of our procedures, physicians and outcomes,” says Brian J. Daley, M.D., a professor in the Department of Surgery. “Improvements occur because we can quickly identify a problem and change our practice using evidence-based medicine and because we simply are more focused on problems and continually seek ways to solve them.”

Daley notes improvements have occurred in the rates of deep vein thrombosis, superficial wound infections and more.

Using NSQIP not only allows the department to track its own data, but the program also provides data from peer institutions with similar patients. This allows sharing of best practices, learning from each other.

The University of Tennessee Medical Center is part of a collaborative comprised of ten Tennessee hospitals using NSQIP together. Collaboration such as this increases the sharing of best practices, identifies region-specific trends and reduces costs associated with surgery and complications. Most recent results from this collaboration indicate significant improvement of surgical outcomes through reduction of rates of acute renal failure, infections and other complications.

**Why this matters:**
A relatively simple research tool can track problems and help institutions devise improvements. This means better surgical outcomes for patients.
Chronic wounds affect more people than heart attacks and strokes combined. Usually, chronic wounds result from diabetes, lower-extremity arterial disease, pressure ulcers and traumatic injuries, and more than 100,000 people die from complications from these wounds each year.

Chronic wounds are difficult to treat. Often, they contain complex bacteria, and much of the time, the patient’s immune system is weakened, further slowing eradication of infection.

Michael Karlstad, Ph.D., a professor in the Department of Surgery, is working with Advanced Plasma Products in Knoxville using funds from a National Institutes of Health Small Business Innovation Research Phase I grant to develop and test a new way to treat chronic wounds. The new technology creates a unique antimicrobial gas that is directed onto a wound, thereby disinfecting it and stimulating wound healing but causing no harm to surrounding tissue. This is the only gaseous treatment for wound healing currently in development for commercial use.

“Advanced Plasma Products has developed a new technology using atmospheric plasma to treat chronic wounds,” Karlstad says. “We are providing histological analyses and are preparing to test the technology in animal studies. We are excited to be involved in this research because of the impact this technology can have for many patients.”

**Why this matters:**

More than five million people in the U.S. suffer from chronic wounds, and because of the increase of the rates of obesity and diabetes, the incidence of chronic wounds will grow. Current therapeutics have only limited success. This treatment could improve success with chronic wound healing, saving up to $20 billion each year in U.S. healthcare expenditures and improving patients’ quality of life.
Symposium Highlights Collaborations

A dozen research activities led by scientists from Oak Ridge National Laboratory, University of Tennessee Medical Center, UT Graduate School of Medicine and various departments at the University of Tennessee Knoxville were featured at a recent Neuroscience Symposium sponsored by the UT Graduate School of Medicine.

“The symposium offered an opportunity to connect with other professionals working in neuroscience to perhaps create new collaborations or find inspiration for a new avenue of research,” says Mitch Goldman, M.D., Assistant Dean for Research.

Topics included diagnostics for Alzheimer’s disease; forewarming of epileptic seizures; diagnosis of brain injury; risk factors for concussion; study of neurodegenerative disorders; networks for nerve regeneration; and more.

Study Using Crisis Checklists Funded

A collaborative study between the Center for Advanced Medical Simulation and Department of Anesthesiology has received funding from Cardinal Health Foundation’s E3 Grant Program. Funded is an implementation of surgical crisis checklists into the perioperative setting using electronic health records to improve patient outcomes. Crises in the surgical setting can include virtually anything from cardiac arrest to fires. Crisis checklists help the care team follow established protocols to preserve the patient’s health and ensure a positive outcome. Part of the study will include team training in the Center for Advanced Medical Simulation, giving the team simulated events in a high fidelity operating room environment simulation.

Nursing Presentation Awarded

A study presented by nurses from the UT Graduate School of Medicine and University of Tennessee Medical Center received top honors at the recent annual conference of the Society for Vascular Nursing. Tammy Seay, R.N., Susan Rawn, R.N., K. Renee Black, R.N., and Lauren Scarbro, R.N., received the Judith Troyer Caudle Award for their presentation, "A Retrospective Study of Rate of Infection among Dressings used in Endovascular Surgeries with Femoral Access Sites.” Although limited, the study showed a correlation between higher infection rates and the use of gauze after endovascular interventions. Further research will examine other dressings and determine how smoking affects post-operative infection rates.

Feline Study Receives Grant

A collaborative project investigating drug delivery using a substance similar to a contact lens has received funding from the Winn Feline Foundation. Chris Stephens, Ph.D., a research assistant professor in the Department of Surgery and the Center for Materials Processing at the UT College of Engineering, along with team members from the UT College of Veterinary Medicine and UT Department of Biomedical Engineering are developing a nanoparticle drug delivery method using a custom-fabricated contact lens in a feline model. The study is investigating ways to stop permanent corneal damage.

New Cancer Institute

Watch the next issue of Advance for details about the new 100,000-square-foot Cancer Institute opening this summer at University of Tennessee Medical Center. The new facility houses all outpatient oncology services under one roof, as well as education resources and cancer research.

Your Chance to Advance

The people at the UT Graduate School of Medicine would be happy to discuss our research programs and how your support can help advance healthcare. For information about philanthropic giving to the UT Graduate School of Medicine Office of Research, please contact the development office at 865-305-6611 or development@utmck.edu.

If you would like more information about any of the research programs described in this issue of Advance, please contact the UT Graduate School of Medicine at 865-305-9290 or visit us online: http://gsm.utmck.edu/research/main.cfm.

Thank you.