Widow on a mission to attract minorities to clinical studies

Phyllis Jefferson read every dementia study she could after her husband was diagnosed with the disease.

She attended support group meetings and sought answers from doctors on how best to treat the condition.

What medicines could help? Would they be safe to take with the cocktail of other medications he was prescribed for his previous kidney transplant?

To Mrs. Jefferson’s surprise, doctors couldn’t definitely answer many of her biggest questions, particularly how certain treatments have affected other African-Americans like her husband.

The problem? Not enough minorities are participating in research designed to learn more about a disease that has no known cure and has a higher risk of developing in African-Americans.

“There is so much ignorance about the disease,” said Mrs. Jefferson, whose husband died last year at age 67 after battling dementia for less than five years.

Mrs. Jefferson is now taking up the battle against Alzheimer’s and other dementias in a new way as part of a UT Southwestern Alzheimer’s Disease Center community advisory committee that reaches out to African-Americans to encourage minorities to participate in studies. Although her husband received treatment elsewhere, Mrs. Jefferson is also volunteering for some of the Center’s clinical trials as a control subject who doesn’t have the disease.

“If I can say that I participate in clinical studies, it may encourage other people of color to participate,” said Mrs. Jefferson, a Dallas resident and CEO of P. Jefferson Consulting Services in Dallas.

Like many research institutions across the country, UT Southwestern aims to boost the number of minorities who participate in Alzheimer’s studies. Part of that effort includes the advisory committee, which is run through UTSW’s Brain Smart University community outreach project and holds public panel discussions every few months.

To date, African-Americans and Hispanics comprise 14 percent of participants in UTSW dementia studies. Nationally, dementia studies have about 20 percent representation from these groups, according to the National Alzheimer’s Coordinating Center.

“It’s really in its infancy, in terms of our understanding of cognitive disorders among diverse cultural groups,” said Dr. C. Munro Cullum, Professor of Psychiatry, Neurological Surgery, Neurology and Neurotherapeutics, and Rehabilitation Counseling, who holds the Pam Blumenthal Distinguished Professorship in Clinical Psychology.

Dr. Cullum said numerous factors that may alter how dementia affects minority patients have yet to be researched with enough data to draw solid conclusions, including those with co-existing conditions such as kidney disease, as Mrs. Jefferson’s husband had. He was a kidney transplant recipient for 22 years before being diagnosed with dementia.

“There just aren’t enough... Continued on page 6 »
FALL FORUM: UTSW experts to discuss cardiovascular aging as a risk factor for Alzheimer’s disease

For more than 20 years, researchers have focused on the beta-amyloid clumps found in Alzheimer’s disease—riddled brains, with billions of dollars spent searching for a cure. However, Dr. Ben Levine, also Professor of Internal Medicine and holder of the Distinguished Professorship in Exercise Sciences at UT Southwestern, points to multiple studies that show the risk of cognitive impairment and dementia is about 50 percent lower for those who exercise aggressively.

Dr. Levine revisited a groundbreaking UT Southwestern study reported in 1966. When five healthy young men were put to bed for three weeks, their physical conditioning plummeted (although it recovered with two months of training).

Thirty years later, those same men were brought back to the lab for retesting. “What we found was that not a single person – not one – was in worse shape 30 years later than they were after three weeks of bedrest in their 30s. So three weeks of bedrest was worse for the body’s ability to do physical work than 30 years of aging,” Dr. Levine said.

While the heart muscle typically stiffens in middle age, then contracts and atrophies in later years, the Institute’s research has found that 65- to 70-year-olds who train regularly can have the heart and blood vessel conditions of healthy 30-year-olds. Committed training for four to five days a week over a lifetime can have major effects on the aging of the heart and blood vessels.

According to Dr. Levine, for those who haven’t been running races and swimming laps, there is still hope. A clinical study recently completed at the Institute, in which participants underwent physical training for two years, showed that men and women ages 40 to 60 reversed a substantial amount of sedentary aging symptoms. “They came pretty darn close to people who had exercised their whole life,” Dr. Levine said.

However, he warned, “There’s a sweet spot in late middle age where you can actually reverse it. If you wait too long – roughly in the 70s or later – you can’t.”

In January, Dr. Zhang and his team were awarded a $15 million National Institutes of Health grant to continue research into the heart-brain connection.

WHO: UT Southwestern’s Dr. Rong Zhang, Associate Professor of Neurology and Neurotherapeutics and Internal Medicine, and Dr. Benjamin Levine, Professor of Internal Medicine
WHAT: 2016 Alzheimer’s Fall Public Forum
WHERE: Simmons Biomedical Research Building, 6000 Harry Hines Blvd, Dallas, Texas
NOTEWORTHY: The forum is free to the public and there is complimentary valet parking. Please confirm attendance by calling 214-648-2344.

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FOR THE DIRECTOR
Roger N. Rosenberg, M.D.

For the past 28 years, it has been my honor and privilege to serve as the Director of the Alzheimer’s Disease Center at UT Southwestern. During that time, significant research, innovative educational programs, and superb clinical research projects targeting Alzheimer’s and other neurodegenerative diseases have been achieved at our National Institutes of Health (NIH)-funded Center.

Support from the Friends of the Alzheimer’s Disease Center has been a major factor in this success. Preliminary grants of more than $1 million have been awarded to junior faculty over the past two decades by the Friends. These funds have generated many more NIH and peer-reviewed grants to our faculty, making them truly committed scientists studying the complexities of this disease.

More than 13 years ago, I began my research to develop a DNA vaccine as a potential therapy to delay or prevent Alzheimer’s disease. I want to express my sincerest gratitude to my friends and benefactors who have made this progress possible including: the M.B. and Edna Zale Foundation, ABE (Brunsky) Zale, Donald and Barbara Zale, the Rudman Foundation, The Rudman Partnership, the McCune Foundation, AWARE, the Presbyterian Village North Foundation, Dr. and Mrs. Freiberger, and Denker families.

Your generous support has made it possible for us to publish more than 12 papers documenting the DNA structure of the vaccine and its effectiveness to produce high levels of anti-amyloid beta 42 [Ab42] antibody to reduce amyloid-containing plaques in the brains of Alzheimer’s animal models. Further, the vaccine elicited a noninflammatory immune response in three species of animals, an FDA requirement in advance of human trials.

These data have been the result of the dedicated and creative research efforts of colleagues in my laboratory. At the Alzheimer’s Association International Conference in Toronto in July, Dr. Doris Lambracht-Washington, Instructor of Neurology and Neurotherapeutics, and I presented two papers describing our most recent results. One study shows that the vaccine reduced both amyloid-containing plaques and phospho-tau in the brains of Alzheimer’s mouse models. The second paper revealed that monkeys and rabbits immunized with the vaccine remained healthy and that high levels of the anti-Ab42 antibody were produced with a noninflammatory response.

This vaccine has potential to be given as a vaccination, at risk for Alzheimer’s disease to delay or prevent it. The next step is to develop a Phase 1 clinical trial to evaluate safety, toxicity, and tolerability of the vaccine in humans. We are grateful to the Chairs of the Friends of the ADC over the past 20 years, including Billie Leigh Rippey (the first Chair), Tommy Thomsen, Stuart Bumpus, Sarah Losinger, Bill Montgomery, Charron Denker, Harvey Mitchell, and Bonnie Smith.

Special thanks go to Ruben Esquivel, Vice President for Community and Corporate Relations at UT Southwestern, who worked closely with me to inaugurate the Friends group 19 years ago, shepherding the idea to propose to UTSW administration.

I am also grateful to all of our dedicated research colleagues at the Center, including our leadership. Special thanks go out to Carol Hall, Director of Development, who has helped organize the twice-yearly educational forums and laboratory tours for Friends members. For decades, she has been a dedicated, tireless champion of our work to maximize grant application and educational programs.

The future for Alzheimer’s disease research looks bright and promising. We have learned a critical amount of information about the biology and natural history of the disease – and important research into developing therapies is only just beginning.

Thank you everyone again for your continued support.

FALL FORUM Continued from page 2

a four-site, phase II clinical trial to determine whether exercise, other alone or in combination with medication to reduce blood pressure and cholesterol, can improve neurocognitive function in older adults at high risk of developing Alzheimer’s.

The study will follow 640 trial participants over two years. They will undergo electrocardiograms, brain MRIs, and cognitive tests, and breathe into large plastic bags while exercising to measure the volume of oxygen they consume, and hence their level of aerobic fitness. The Pennington Biomedical Research Center at Louisiana State University; Washington University in St. Louis; and the University of Kansas are also participating in the study.

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Thank you everyone again for your continued support.
FUNDING THE FIGHT
Friends award $130,000 to two UTSW researchers

Since its inception in 1996, the Friends of the Alzheimer's Disease Center has donated more than $1 million toward UT Southwestern Medical Center-led investigations into Alzheimer's and other neurodegenerative diseases. These critical gifts help early-career researchers get started on important projects and attract additional funding from other governmental groups and supporters. Earlier this year, the Friends awarded $65,000 grants to Dr. Doris Lambracht-Washington and Dr. Lenora Volk to further research aimed at curing Alzheimer's.

**2016 Grant Recipient
DORIS LAMBRACHT-WASHINGTON, PH.D.**

Dr. Doris Lambracht-Washington, Instructor of Neurology and Neurotherapeutics, is working with Dr. Roger Rosenberg, Director of the Alzheimer's Disease Center, on an immunotherapeutic approach to prevent Alzheimer's disease.

In recent years, great progress has been made in further development of a DNA amyloid beta 42 (Aβ42) vaccine developed by Dr. Rosenberg, also Professor of Neurology and Neurotherapeutics, and of Physiology, and holder of The Abe (Benny) Morris and William Zale Distinguished Chair in Neurology. “We found recently in an Alzheimer's disease mouse model (3xTg-AD), a mouse that develops plaques and tangles, that this vaccine may also prevent the development of neurofibrillary tangles,” Dr. Lambracht-Washington said. “The grant will be used to investigate this aspect in more detail. It is very exciting that the anti-Aβ42 immunotherapy with a DNA vaccine not only removes amyloid from the brain in mice models, but also shows significant changes in the other hallmark of Alzheimer's, tau hyperphosphorylation and tau tangles.” Pivotal research has linked abnormal aggregation of both proteins, tau and beta-amyloid, to Alzheimer's disease.

Dr. Lambracht-Washington has worked at UT Southwestern for 15 years, the last eight years in the lab of Dr. Rosenberg. She earned a master's in biology and then a master's in biology and then a doctorate in immunology/genetics, both at the University of Hannover in Germany. In 2003, Dr. Lambracht-Washington completed a postdoctoral fellowship at UT Southwestern in the lab of Prof. Kirsten Fischer-Lindahl, Professor Emeritus of Immunology.

**2016 Grant Recipient
LENORA VOLK, PH.D.**

Dr. Lenora Volk, Assistant Professor of Neuroscience and Psychiatry, has a personal link to the illness that she studies. “My grandfather, who also was a university professor, had Alzheimer’s disease. I have seen firsthand the toll that Alzheimer’s can take on a person and a family.”

Dr. Volk, who joined the UT Southwestern faculty in 2015, is studying the protein complex PICK1/KBRA, which she found during her postdoctoral studies to be important for neural communication and memory in adult mammals. Her research explores how human genetic data links this complex to variations in memory performance and Alzheimer’s disease. “Our current studies are aimed at understanding how this complex regulates neural communication, and why neurons from young animals are resilient to the loss of this complex while adult neurons are not,” Dr. Volk said.

Because the earliest stages of Alzheimer’s disease appear to reflect a disruption in communication between brain cells, she said, “understanding the mechanisms responsible for age-related decline in neural communication will likely be critical for developing effective treatments and diagnostics.”

After earning an undergraduate degree in biochemistry at Oklahoma State University, Dr. Volk earned a doctorate in neuroscience at UT Southwestern in the lab of Dr. Kimberly Huber, Professor of Neuroscience and a Southwestern Medical Foundation Scholar in Medical Research. She completed a postdoctoral fellowship in the lab of Dr. Richard Huganir at the Johns Hopkins University School of Medicine.

Neurogenerative conditions affect tens of millions of people worldwide. Alzheimer’s disease alone afflicts more than 5 million people in America and is the sixth leading cause of death in the United States, according to the Centers for Disease Control and Prevention.

In light of this significant health problem, the need to find cures, preventive therapies, or better treatments for neurodegenerative diseases compels researchers such as Dr. Marc Diamond, Director of the Alzheimer's Center and a Professor of Neurology and Neurotherapeutics, and his research team believe they have uncovered the answer: understanding how the tau protein aggregates in brain cells.

His potentially groundbreaking research focuses on identifying genetic targets to block the propagation of tau, which normally stabilizes the shape of brain cells but creates abnormal clumps within the cells in the presence of diseases such as Alzheimer’s.

Compelled by the potential of Dr. Diamond’s investigations, Cure Alzheimer’s Fund recently made its first donation to UT Southwestern in the amount of $150,000.

“Dr. Diamond is a highly respected researcher with whom we became familiar from his outstanding work at Washington University. When we heard that he would be continuing his career and Alzheimer's research at UT Southwestern, our scientific advisory board was excited to seek out ways to support his current research on better understanding the functions of tau,” said Mr. Timothy Lykken, President and CEO of Cure Alzheimer’s Fund. “What he is going after is a critically important, and heretofore not clearly understood, aspect of Alzheimer's pathology. If he can crack this case, so to speak, it will be a huge contribution to the field of Alzheimer's research.”

Cure Alzheimer’s Fund is a nonprofit organization based in Massachusetts dedicated to funding research with the highest probability of preventing, slowing, or reversing Alzheimer's disease. Since it was founded in 2004, the Fund has distributed more than $40 million to support 186 projects in 85 labs around the world.

“We are engaged in mechanistic studies to try to find cellular factors that control the transcellular propagation of pathological forms of tau. This financial support makes it possible to carry out higher-risk projects that would not ordinarily be funded by the National Institutes of Health,” said Dr. Diamond, who was recruited to UT Southwestern in 2014 from Washington University in St. Louis and holds the Distinguished Chair in Basic Brain Injury and Repair. “The significance of this research is very high – we anticipate that if we can identify these factors, we can then design drugs to block them and thus prevent the progression of Alzheimer’s disease.”

Ramping up the battle against these conditions is critical. Experts estimate that Alzheimer’s disease develops in a new person every 67 seconds, meaning there are more than 50 new cases every hour and nearly 1,300 new cases every day.

Dr. Daniel K. Podolsky, President of UT Southwestern, said, “One of our top research priorities at UT Southwestern is understanding the basic mechanisms of brain diseases like Alzheimer’s. The work of Dr. Diamond and his team exemplifies how UT Southwestern is pushing the frontiers of medicine to pave the way for new therapies. The generous support of organizations like Cure Alzheimer’s Fund expedites this mission.”

Dr. Podolsky holds the Philip O’Bryan Montgomery, Jr., M.D. Distinguished Presidential Chair in Academic Administration, and the Doris and Bryan Wildenthal Distinguished Chair in Medical Science.
Working toward a test for Alzheimer’s risk detection

Dr. Dwight German envisions a day when anyone age 60 or older can walk into a doctor's office for a blood test that detects risk of developing Alzheimer's disease. The test would flag signs of potential trouble and prompt further examinations before the disease takes hold. In some cases, the solution could be as simple as drinking mineral oil.

The research of Dr. German, Professor of Psychiatry at UT Southwestern, indicates that the science to make this happen already exists. A test he helped develop several years ago has been further substantiated to show that people with certain protein-level changes in the blood are more likely to develop Alzheimer’s.

It may be on the market within the next few years for patients seen by a primary care doctor.

“You’d like to have a test that’s going to tell you that maybe in 10 years you’re going to be in big trouble unless you do something today,” said Dr. German, who collaborated on developing the blood test with Dr. Sid O’Bryant, Interim Executive Director of the Institute for Aging & Alzheimer’s Disease Research at the University of North Texas Health Science Center.

Dr. German’s work on early detection could be vital as other scientists at UT Southwestern seek methods to slow or stop the spread of toxic proteins associated with Alzheimer’s, such as beta-amyloid and tau, which are blamed for destroying groups of neurons in the brain.

Some of Dr. German’s recent research has focused on DDT, a pesticide widely used in the 1940s that he found may be linked to Alzheimer’s. His group reported that a DDT metabolite exists in high levels in the blood of some Alzheimer’s patients, and the higher the pesticide levels, the lower the patients’ cognitive abilities.

Dr. German’s next step is to study whether the pesticide actually produced brain damage in patients who had Alzheimer’s. Based upon these findings, he said, doctors could better identify at-risk individuals before symptoms arise and prescribe mineral oil, which research shows reduces the DDT-related pesticide in the blood.

“It looks like this pesticide exposure may play a role in getting the disease,” said Dr. German.

The U.S. banned DDT in 1972 after scientists found it was an environmental hazard and could potentially harm people. Immigrants from countries that still use DDT have high levels of DDE in their blood, which is the metabolite of DDT, and it remains in the body for decades.

Using data from the National Health and Nutrition Examination Survey, Dr. German’s colleagues found that Mexican-Americans have three times higher levels of DDE in their blood than non-Hispanic whites. Mexican-Americans also develop Alzheimer’s disease at an earlier age than non-Hispanic whites.

Dr. German’s group plans to examine whether the higher blood levels of DDE are related to the earlier onset of disease in Mexican-Americans.

Jefferson

Continued on page 7

patients that fall into that category for us to even know what the implications are at this stage,” he said.

Dr. Cullom, also a member of the Division of Psychology, Director of the Neuropsychology Program at UT Southwestern, and a Clinical Core Leader in the UTSW Alzheimer’s Disease Center, attributes the shortage of minority participants, in part, to a lack of awareness among some who don’t recognize symptoms of the disease and, therefore, don’t approach doctors for help.

Mrs. Jefferson said others are simply reluctant to volunteer.

“If we’re going to find a cure, we’re going to have to start trusting the medical industry to do that,” Mrs. Jefferson said. “And so by having a panel of African-Americans at these educational opportunities, when they hear our story they’re more likely to believe us.”

Witnessing the quick demise of her husband, Theodore Jefferson Jr., motivated her to spread the word in her church and the community about the need for minorities to help doctors understand Alzheimer’s—a disease twice as likely to develop in African-Americans as in whites.

She recalls her anxiety after her husband’s diagnosis in 2011 and watching his symptoms gradually worsen from forgetfulness to confusion. Before her eyes, the man she’d been married to for 36 years was disappearing. Then in March 2015, she had to put him in a memory care center, where he lived another five months—far shorter of the decade or longer that some dementia patients live.

Mrs. Jefferson’s new mission is to help UT Southwestern educate the public and get doctors the data needed to help the next Theodore Jefferson Jr. survive longer, or perhaps— one day—beat Alzheimer’s.

“Until I was on this journey,” she said, “I did not realize how cruel this disease was.”

As one of the newest members of the UT Southwestern’s Alzheimer’s Disease Center team, Dr. Trung Nguyen, Assistant Professor of Neurology and Neurotherapeutics, sees patients showing signs of cognitive impairment. He is now developing his first clinical study focused on dementia.

“I always find it interesting how people think, and what happens when that system goes awry,” Dr. Nguyen said. “There has been lots of work with biomarkers in this field, leading to better understanding of the disease process and develop strategies for earlier detection and treatment. It’s an exciting field.”

Specifically, Dr. Nguyen is studying dementia with Lewy bodies (DLB), the third most common type of dementia after Alzheimer’s disease and vascular dementia.

Dr. Nguyen’s research includes involvement in a clinical trial of the drug cilostazol, which is used to treat symptoms of cardiovascular disease. This is where he sees the connection to Alzheimer’s.

“Through my research activities, I have the opportunity to make the discoveries that can aid in halting the devastating Alzheimer’s disease,” Dr. Nguyen said.

A native of Shreveport, Louisiana, and a graduate of Louisiana State University, Dr. LoBue recently completed his internship at UT Southwestern in 2013. His doctoral dissertation on “Self-reported Head Injury: Associated Risk in Mild Cognitive Impairment and Progression to Alzheimer’s Disease”

“When I went into graduate school, I was intrigued by the complexities of the brain and why some individuals develop neurodegenerative disorders and others don’t,” he said. “Through my studies, I have found that while the cause of Alzheimer’s disease is unclear, there are some risk factors that may play a role in its process. My research activities have focused on exploring the implications of these risk factors.”

Dr. Trung Nguyen

BvB Dallas game carries the ball for Alzheimer’s research

When more than 200 young Dallas professionals took the field at the Cotton Bowl on Aug. 13, it was all in good fun. However, the ninth annual BvB Dallas Powder Puff Football Game had a serious goal: to tackle Alzheimer’s by raising both awareness of the disease and research funding.

This year’s event also meant a lot to Dr. Christian LoBue, whose postdoctoral research at UT Southwestern will be funded by the group’s fundraising efforts. Each $25 ticket sold for the game benefited BvB Dallas beneficiaries such as UT Southwestern as well as his doctoral dissertation on “Self-reported Head Injury: Associated Risk in Mild Cognitive Impairment and Progression to Alzheimer’s Disease.”

“When I went into graduate school, I was intrigued by the complexities of the brain and why some individuals develop neurodegenerative disorders and others don’t,” he said. “Through my studies, I have found that while the cause of Alzheimer’s disease is unclear, there are some risk factors that may play a role in its process. My research activities have focused on exploring the implications of these risk factors.”

More than 35 powder-puff games are played around the country, all to benefit Alzheimer’s research. BvB Dallas’ game is believed to be the largest both in terms of number of participants and dollars raised.

For more information about BvB Dallas, visit bvb.dallas.org.
JOIN THE FRIENDS OF THE ALZHEIMER’S DISEASE CENTER

The Friends of the Alzheimer’s Disease Center provide crucial support to UT Southwestern Medical Center’s most promising and passionate researchers working to unlock the mysteries of Alzheimer’s disease.

In addition to funding research through generous annual grants, the Friends sponsor a community-wide public forum every fall and spring where the latest breakthroughs and best information on Alzheimer’s disease are presented by leading experts from UT Southwestern and major medical centers nationwide.

Membership begins at $500 per year, per individual or couple. Your donation is tax deductible and truly makes a difference in the fight against Alzheimer’s disease.

To join the Friends of the Alzheimer’s Disease Center, call 214-648-2344. Your support safeguards vital research into enhancing quality of life through early detection and improving the lives of patients and their families who live courageously each day with Alzheimer’s disease.

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