

Paying Tribute to A Leader in Academic Neurology and Peripheral Neuropathy

BY JAMIE TALAN

ARTICLE IN BRIEF

Experts in the field of peripheral neuropathy gathered to pay tribute to Dr. Jack Griffin, a leader in the field of academic neurology, in January.

Give Jack Griffin, MD, five minutes with a foot and he could with great skill, compassion and certainty diagnose a peripheral neuropathy. The professor of neurology and neuroscience at Johns Hopkins University is credited with helping to change the course of treatment for Guillain-Barré syndrome (GBS) and putting skin biopsies on the diagnostic map for peripheral neuropathies.

One day, neurologists will carry a tuning fork, reflex hammer, and a punch skin biopsy, Dr. Griffin has said to colleagues over the past decade.

The idea of looking to skin for evidence of small caliber nerve fiber damage is indicative of the way John Wesley Griffin's mind works. His interests in all forms of human nature were obvious from a very young age. He was agile on the field — as the first baseman for a Nebraska farm league in high school — and nimble in mind as a double major in chemistry/zoology and Russian studies. He graduated in three years so he could start his medical training

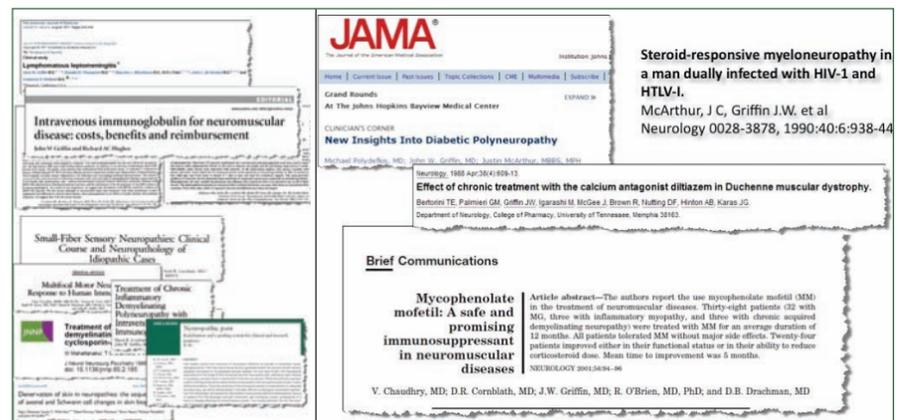
at Stanford. He entered his neurology residency at Johns Hopkins and has basically never left. He spent a decade there as chairman of neurology. His colleagues said that his love affair with axons and Schwann cells led to remarkable changes in the field.

At Johns Hopkins in January, the first scientific celebration of 2011 was in full swing at the Sheldon Auditorium at the Bloomberg School of Public Health where hundreds of colleagues from all corridors of Dr. Griffin's life showed up to talk about peripheral neuropathies. There were many of his long-ago neurology fellows who shared his penchant for axons as well as comrades in residency to young doctors continuing to work the bench in the Griffin lab.

'A SUPERB NEUROLOGICAL DETECTIVE'

The two days of science and stories was aptly titled: The Friends of the Axon, the Schwann Cell & Jack Griffin Scientific Symposium. In addition to listening to more than a dozen scientific talks, those in attendance shared snippets of a life that undeniably altered the practice of neurology.

"Most men would be happy with any one of these achievements," said Justin McArthur, MBBS, MPH, director of neurology at Johns Hopkins, whose



DR. JACK GRIFFIN has edited major textbooks on peripheral neuropathies and published more than 300 papers on the mechanisms of degeneration and of axonal protection in nerve disease, mechanisms underlying painful nerve diseases, and the acquired demyelinating neuropathies.

introductory slides traced Dr. Griffin's exemplar as a clinician, with work that prompted the development of plasmapheresis as a proven therapy for GBS. That treatment came on the heels of Dr. Griffin's discovery that the condition was triggered by the body's inflammatory attack on peripheral nerves.

"Jack has had a hand in developing about 15 different treatments and diagnostics," said Dr. McArthur. "He is a superb neurological detective."

The name of Jack Griffin's farm team was the Lincoln Optimists. It speaks

to the very nature of the neurologist, Dr. McArthur added. "With his patients, it is always, 'you will recover.' With his research, it is 'this is going to work.' There is a tremendous positive spirit that has been felt throughout his career."

Dr. McArthur became aware of that spirit soon after he completed his residency in 1985. Dr. Griffin was already well known in neurology as a great mentor, providing the canvas to any number of willing residents eager to do research. Word spread that Dr. McArthur and his wife Julie had a

Continued on page 9

Imaging Biomarker, Alzheimer Disease

Continued from page 7

evaluation than the mere presence of an association. For a predictive biomarker, the question is not just whether that factor relates to the outcome of the disease but what its incremental contribution is in predicting who will get the disease and when."

"It would be nice to have blood biomarkers," said Ronald C. Petersen, MD, PhD, the Cora Kanow Professor of Alzheimer's Disease Research at the Mayo Clinic and director of the Mayo Alzheimer's Disease Research Center and the Mayo Study of Aging. "The hope is to stratify normal older people into different risk groups. Those in the highest risk group could get



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MRI, PET, CSF, spinal taps and now a blood test. Theoretically, this latest finding means that blood reflects what is going on in the CSF and in the brain."

But John C. Morris, MD, director of the Alzheimer's Disease Research Center at Washington University School of Medicine in St. Louis, MO, wonders whether such a blood test would be able to pick up individual differences. "This was a study of almost 1,000 people. The amount of Abeta in plasma is so small that it is hard to tell whether it is going up or down over time."

The biomarker was tested in normal elderly people. The next step, said Dr. Morris, is to conduct a similar study to assess its power in predicting AD.

Others have tried and the results have been mixed, he pointed out.

Dr. Yaffe and her colleagues used a relatively new Abeta assay developed by Innogenetics, a Belgium company. Dr. Yaffe said it is more sensitive than earlier tests. •

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Jack Griffin

Continued from page 8

new child and Dr. Griffin drew a big smile and handed his young colleague a sheet of paper. On it, Dr. Griffin had written a poem.

"His kindness is not saved for people in his circle," Dr. McArthur said. "It is in his periphery. It is something I will never forget. It is always his way to create a warm community here."

Anne Louise Oaklander, MD, PhD, associate professor of neurology at Harvard's Massachusetts General Hospital and a member of the *Neurology Today* editorial advisory board, applied for a postdoctoral fellowship with Dr. Griffin in 1991 when she was chief resident in neurology at the University of Medicine and Dentistry of New Jersey. While most neurologists focused on neurons, Dr. Griffin was breaking new ground studying the entire nerve ecosystem, including non-neuronal cells such as Schwann cells and macrophages, showing that they also contributed to neurological diseases. Dr. Oaklander's doctoral research on cellular changes during nerve injury had put them in contact, and he invited her to interview at Johns Hopkins.

"We had a delightful time looking at slides, talking about patients," Dr. Oaklander said. "He treated me as if I were already one of his fellows. When I returned home, my husband asked if I had gotten an offer, and I confessed that I didn't know. We were so busy it never came up." So she arranged a second train-trip to Baltimore. When Dr. Griffin saw her again, he was perplexed. "What brings you back so soon?" Dr. Oaklander replied that she wasn't sure if he had offered her the job. He looked at her with surprise. "Of course I did," he said. "Wasn't it clear?" That two-trip job offer began her career in peripheral nerve.

UNRAVELING A MYSTERY IN CHINA

Dr. Griffin has always been a dealmaker. In the 1980s when several Johns Hopkins neurologists learned of a mysterious paralysis among young people in rural villages of Northern China, he gathered a number of his colleagues and convinced them that their skills were needed abroad. The humanitarian effort would last a decade, with yearly trips to the rural countryside. As a neuropathologist, he understood that there was a detective story afoot. Children were dying of a neuropathy and he began to methodically work every angle. Many of the children were sick in the summer months. They needed round-the-clock care in a region with very little access to treatments. The only way to help

DR. JACK GRIFFIN: 'MOMENTUM IN FIELD IS BUILDING'

Jack Griffin, MD, said that the two days spent listening to the research from his colleagues was gratifying and exciting. "I can see that the work done on peripheral nerve diseases will help unravel what is going on in the central nervous system," said Dr. Griffin, the Distinguished Service Professor in the departments of neurology, neuroscience and pathology.

He added that the momentum in the field is building. He was particularly excited to hear his colleagues talk about axons and Schwann cells, which his work showed have an incredibly intimate interaction and dependency with nerve cells. He is also hopeful about the work in protection of nerve fibers and regeneration. "It is realistic to imagine that it is possible to remyelinate and repair the central nervous system. The potential for repair is very evident from experimental work," he said. "We are moving towards better protection of injured nerves."

Dr. Griffin said it was great fun listening to his colleagues "overgenerous comments." Of course, he remembers his Chinese collaborators talking about the American scientists in their native language. When asked if there was that *eureka* moment in the rural villages, he said no. "We snuck up on it," he said. "We knew right away that the physiology was different from what we knew as classical Guillain-Barré. It was a pure motor axonal degeneration. Our challenge was then to figure out how and why it happened."



DR. JACK GRIFFIN

the children breathe was for family members to take turns with Ambu bags. The children's peripheral nerves were badly damaged.

The first hint was that it was summer. Family members seem to have a lot of diarrheal illnesses. Cultures finally revealed a bacterium found in chicken feces. Chickens, it turned out, lived in very close proximity to the humans tending them. That would explain why this epidemic was found in rural villages and not in cities. The bacterial infection damaged peripheral nerves. Not only would their efforts spare these families but it would also help shine a light on how antibodies waged against *Campylobacter jejuni* could trigger an autoimmune response against the peripheral nerve.

The efforts of this small band of scientists would pay off big time in understanding conditions that behaved like GBS. Arthur K. Asbury, MD, the Van Meter Professor of Neurology at the University of Pennsylvania and an expert on peripheral neuropathy, said that it was known that GBS was a disorder of damage to the myelin sheath. But when the neurologists began looking at the pathology of the nerves from the patients in Northern China they saw that the insulation was fine. Surprisingly, it was the axon that was hard hit by the condition. They were looking at a new disease. Dr. Griffin and his colleagues coined the term for the condition, acute motor axonal neuropathy or AMAN.

"No one ever considered the axon," said Dr. Asbury.

Guy McKhann, MD, the founding director of the Department of Neurology in 1969 and a collaborator on the epidemiological puzzle in rural China, agrees. "We would never have figured it out," said Dr. McKhann, who had initially recruited Jack Griffin from Stanford when he was hired to direct the new neurology department. "Jack is very good at listening and evaluating new information as it comes along."

"What we learned in China changed our whole view of Guillain-Barré," Dr. Asbury added. The immune system abnormality led to the thinking that plasmapheresis might help and it did, Dr. Asbury said. While such a treatment would never make it to the rural villages in Northern China, an education effort to help keep the chickens out of the homes paid off. Over the years, the syndrome has virtually dropped away.

Dr. Griffin didn't just go to China with his smarts as a neuropathologist and epidemiologist. Before he ever left the US, he began to teach himself Mandarin so that he could work with his foreign colleagues. "He knew how to understand what was said but he never would let on," recalled Dr. Asbury. "It became a joke. He would listen to the scientists talking about us or the work and he would raise his eyebrows. We would just laugh."

"Jack is the epitome of a clinician scientist," added Dr. McKhann. "He takes the problems of the patients back to the lab to study and what he finds he brings back to the patients." Johns Hopkins Medical School Dean Edward Miller, MD, said that Dr. Griffin was "practicing translational medicine before it was even a term."

David S. Zee, MD, professor of neurology, otolaryngology, head and neck surgery, ophthalmology, and neuroscience at Hopkins, has known Dr. Griffin since their residency days. They worked at the NINDS together for a few years post residency. There, he recalled that a patient came in with progressive spastic paraparesis and Dr. Griffin asked the young man whether he'd been away on vacation. His skin was tan and it was the middle of winter in Bethesda. The patient said that he had not been away and there was no explanation for his tan. "Well, that got Jack thinking," said Dr. Zee. He ran some tests and identified an adrenal problem and wrote two papers describing the syndrome, adrenomyeloneuropathy.

Dr. Griffin's colleagues came from far and wide to participate in the recent symposium. His most recent deal has been a lifetime dream to create a place where scientists can work on neurological puzzles with abandon. In 2007, Johns Hopkins opened the Brain Science Institute and Jack Griffin stepped into his natural role as founding director.

It has become a place where science can thrive on the funding of donors and researchers with ideas do not have to worry that their thoughts are too far off the beaten track of federal funding. Scientists there can study how the brain responds to the sounds of a symphony or how nerves fire when looking at a particular piece of art. There is also a strong effort to develop new compounds for a range of neurological diseases.

Dr. Miller announced at the recent symposium that Hopkins will now have a named Jack Griffin directorship at the Brain Science Institute.

The measure of a man goes well beyond the named lectures, which are many, and the seats that Dr. Griffin filled as a member of the National Advisory Council to the NINDS, chair of the Burroughs Wellcome Fund Program in Translational Research, past president of the Peripheral Nerve Society and the Society for Experimental Neuropathology, and president of the American Neurological Association.

For the real show, his colleagues agreed, one must watch Jack Griffin reach down to touch a foot, ponder, test, think and finally shake his head in gratitude that a simple foot can tell such a complex story. •