WHAT KEEPS MD/PHDS HUMMING THROUGH 8 YEARS OF MED AND GRAD SCHOOL?

(AND THAT'S NOT COUNTING RESIDENCY)

BY MEGHAN HOLOHAN

PORTRAITS BY FRANK WALSH

A few years ago, student David Volk walked into Western Psychiatric Institute and Clinic and headed up to the ninth floor—the schizophrenia ward.

As soon as he arrived, he was told to help with James Morris' diagnostic interview.

There's a metal surveillance bug implanted in my left leg, which travels around my body transmitting information, Morris told Volk instead of answering the question he was asked.

I used to play in the WNBA, but Michael Jordan has kept me from being a superstar, he said.

Morris wasn't making any sense. His paranoid and grandiose delusions strongly suggested a diagnosis of



"I might have been the only person to have chosen pathology having never done any pathology," Clayton Wiley says, laughing a little. He'd like Pitt MD/PhDs to plan their careers more intelligently.

schizophrenia. Other than that, all Volk knew about Morris he had learned from his intake records. The previous night, Morris (not his real name) had been on the streets of Pittsburgh screaming at people passing by. He'd been erratic, threatening. His behavior landed him in WPIC's emergency department.

The staff in the ED wanted to admit him. Morris refused. *I don't need to be in the hospital. I can stay with my father.* He struggled as he was involuntarily admitted.

It didn't seem like Morris had been eating. And the rags that covered his lanky frame indicated that he might not be able to care for himself. Morris had probably been living on the streets.

After being interviewed by Volk for a while, Morris started crying.

"I just want to go home."

Home was his father's house, Morris insisted. Yet, Morris didn't know where his father lived. Volk (MD/PhD '04) thought that Morris might feel better if he could return to his father's place. A patient man of medium build with gold-rimmed glasses, Volk had just started his psychiatry rotation. He'd spent the past five years doing schizophrenia research in the lab of David Lewis, professor of psychiatry and neuroscience. Now he was meeting a fellow man who had the disease he'd studied in such detail. Morris was exactly the kind of person Volk wanted to help with his research. Here at the hospital, instead of examining diseased brain tissue, Volk was witnessing a manifestation of all those things he had studied—a person with a complex, debilitating, lifelong disorder.

Morris was the "translational element" that Volk had heard so much about as an MD/PhD student at the University of Pittsburgh.

The number of physician-scientists is decreasing in the United States during a time when research funding from the National Institutes of Health (NIH) for physicians who conduct basic science research has doubled since 1998, says Clayton Wiley, director of neuropathology and the MD/PhD program at the University of Pittsburgh.

"Biomedicine has become a much more complicated science," Wiley says, explaining that in the past 50 years, new fields such as molecular and structural biology have emerged. And the amount of medical and scientific information has grown exponentially.

When Jonas Salk's team scrambled for a killed polio vaccine, they were working with a "fairly simple disease," albeit deadly, notes Wiley. To make the vaccine, they had to replicate the virus. In the face of the modern HIV epidemic, scientists will draw on the enormous advances of the past few decades. To develop a vaccine, they'll need to understand the genes of the virus and how the virus interacts with the host. Likewise, scientists are, of course, using these tools to tackle age-old puzzles of medicine, like the herpes virus.

Wiley believes MD/PhDs, in particular, can play a valuable role in this scientific landscape. They're specifically trained to handle the depth and details of basic science research and translate those into practical bedside care.

He notes that the Association of American Medical Colleges has invited MD/PhD programs to be more actively involved in the organization because the association realized that physician-scientists are increasingly becoming leaders in medical education.

"A lot of institutions think of the MSTP [medical scientist training program] as a seed," says Bert Shapiro, a PhD who directs the medical scientist training program of the

National Institute of General Medical Sciences (NIGMS) for the National Institutes of Health. "It is a good way to get triple-threat faculty members who know medicine, research, and are good academicians."

There are 120 MD/PhD programs in the United States, and the NIH has selected 39 programs to support in light of the strength of those institutions' research programs, among other criteria. The NIH list includes the University of Pittsburgh School of Medicine program, founded in 1983.

The agency funds about a fifth of the students at Pitt. The School of Medicine finds money to fully fund the other students. Since Wiley took over the program eight years ago, the number of students has increased from four to 12 in each entering class. Without support from the NIH or the school, those MD/PhD students—who go to school for an average of eight years before starting their residency training—would graduate at least a quarter of a million dollars in debt.

"The crucial thing here is getting people early and giving them a chance to get thoroughly trained. You get highly accomplished and motivated researchers," says Shapiro, who is also branch chief of cell biology at NIGMS. Even though MD/PhD students have a lot of experience, they typically are a couple of years behind on the career ladder. Wiley notes the average physician-scientist gets a faculty position at the age of 37 and first investigator award from the NIH at 44. He is hoping that with new curriculum changes going into effect, Pitt students will be able to graduate in seven years and get into the workforce earlier.

Wiley pursued his degrees in the early days of physician-scientist training programs. After completing his undergraduate degree at the University of Chicago in 1976, he headed to the University of California, San Diego, to attend its MD/PhD program. His experience is similar to many who've matriculated through such a program. He completed two years of medical school, then spent four years doing neuroscience research, and when he finally returned to med school he was overwhelmed. He'd had no clinical training for four years. And his first rotation was surgery. Shortly after he started, he received a note:

"Dr. Wiley is a concern to the Department of Surgery."

It was difficult for Wiley to finish that rotation. He didn't understand the surgery residents, and they didn't understand him. He'd just spent four years devoted to the specifics of scientific investigation, asking the same question over and over in different ways to yield the best response. Suddenly he was expected to think like a clinician—to come up with an answer on his feet, then and there, with little time for weighing options. It was not a smooth transition.

It was the summer of 2002, 4:30 in the morning, and David Volk's alarm clock was squawking.

He pulled himself out of bed to get ready for his surgery rotation. He felt like he had just closed his Lawrence's *Essentials of General Surgery,* but that was at midnight. Ahead was another morning of relentless questions about the mechanisms of wound healing or some other clinical subject he hoped he could remember. Just a week before, as a researcher, he'd been contributing to the emerging body of knowledge about cognitive dysfunction among schizophrenic patients. But this morning, he was a third-year med student and a surgery newbie. All that he knew about schizophrenia would be of little help.

Volk felt much like Wiley did at the start of his surgery residency—there is some disconnect between being a PhD student and being a medical student.

But Wiley and his staff are making the disconnect less palpable. Students in the MD/PhD program at Pitt can participate in longitudinal clinics while they pursue their doctoral research. Spending a half day each week in the clinic helps sharpen fledgling doctoring skills. In addition, students can now dive into an eight-week clinical rotation after their second year of medical school, before they start their research years.

Fortunately for Volk, he was in the first class of MD/PhD students to benefit from these clinical programs. NIH's Shapiro expects that longitudinal clinics like Pitt's will become a trend. Both Pitt and the University of California, San Diego, have incorporated clinical experience during time typically allotted for doctoral research—and that approach is all the buzz at national meetings of MD/PhD program directors.

Wiley readily admits that his experience in a physician-scientist program informs how he has helped Pitt's program evolve. After being dumped into a surgery rotation, Wiley only had three months to decide what specialty he would pursue. He knew that surgery wasn't his calling but wasn't sure of much else.

"I might have been the only person to have chosen pathology having never done any pathology," he says, laughing a little. Wiley is a tall man with perfectly placed brown, silver, and gray hair. He folds his hands when he talks.

He thought pathology would be a good match with the graduate work he'd pursued in neurology.

"It was not intelligent," he admits about how he chose to specialize in pathology. "It was more luck than planning."

Sitting in his office more than 20 years later, Wiley makes it seem like there was little thought behind his career choice. In fact, almost every Pitt MD/PhD student makes the program seem like it is easy—like it is just a matter of perfect planning. And that certainly

YOU'VE GOT A FRIEND

When Genevieve Gorny's fiancé broke his foot, she didn't know how she was going to move her furniture by herself to her third-floor apartment. She had just moved to Pittsburgh from Duluth, Minn., to start the University of Pittsburgh School of Medicine's Medical Scientist Training Program. She hardly knew a soul in Pittsburgh, but she knew Russ Traister, a second-year grad student in the program who'd been assigned as her student mentor. Gorny had been paired with Traister because they shared an interest in biochemistry and molecular genetics. She stayed at his house when she visited campus, and he told her about all the great restaurants. Soon, he was at her service again, helping her lug a couch and heavy desks up the steps of her Highland Park apartment building.

The Pitt MD/PhD program prides itself on its student community. Students may pursue a wide range of studies, but they're brought together through their service on program-wide committees, with plenty from which to choose: There's a committee that organizes the annual retreat, one that interviews prospective students, one that organizes a weekend for visiting applicants, and then some. Student mentors don't just give advice on great hangouts; they are resources for finding a good preceptor for a longitudinal clinic or figuring out how to handle those first years of med school. And the student community, Gorny points out, is one of the reasons she decided on Pittsburgh. *—MH*



Patient interaction kept the scholarly fires burning for David Volk as he pursued eight years of medical and graduate school.

enters into it.

"The biggest question is, 'How does one person do two jobs?'" notes Wiley.

To help students figure out how to juggle two professional lives, Wiley has added advising sessions to the program since he assumed its directorship in 1996. As a student, Wiley didn't have the opportunity to meet with career counselors or a mentor specially appointed to guide him. However, at Pitt, each student is paired with a career adviser and a research adviser. While some students joke that they are advised to death, most of them agree that the counseling helps.

Shapiro rattles off a list of Pitt's strengths as a physician-scientist training program, including a large pool of applicants, which has increased during Wiley's tenure from 40 applications to 300 every year. He also mentions Pitt's nationally recognized programs like neuroscience, cognitive neuroscience, biomedical engineering, and transplantation. He lauds Pitt's partnerships with Carnegie Mellon University, enabling the training program to take advantage of CMU's strengths like robotics and social and decision sciences. (About 5 percent of Pitt students are pursuing less traditional MD/PhDs in fields like public policy.) But the quality Shapiro mentions first: "They have a very strong staff. Clayton Wiley is outstanding as a leader and role model."

Planning and clinics help, still the patients they work with are often the biggest motivators for students, as Volk has found.

When Morris first arrived at WPIC, his appearance and his smell—which was so penetrating that several showers and new clothes couldn't disguise it—indicated that he'd been living on the streets for some time. Volk knew it would be easier for Morris to live with schizophrenia in a home with a caring guardian. So he tried to track down Morris' father, which wasn't easy. Morris didn't know his father's phone number. And he wasn't sure where his father lived.

Morris, caught in the middle of a psychotic episode, was unable to understand why he was in the hospital. He was agitated all the time. He was disheveled. Yet, he inspired Volk. "During my MD training I did a lot of work with people who were suffering. I want to find a way to ease that suffering," he says, looking back on his experience. Pitt administrators note that PhDs with MDs tend to keep their research focused on the human element more than other PhDs might.

Morris had decided not to take green pills; he was convinced that green pills were poisonous. So the WPIC staff searched for a medication that wasn't green but would help Morris. He'd been taking four milligrams of the antipsychotic risperidone; the two-milligram doses were red. So Morris was given two red pills, instead of one green one.

Red or green aside, there's no cure for schizophrenia. But often doctors can help patients manage symptoms of the disease, like psychotic delusions. Still, risperidone and other medications do little to manage other symptoms, such as impaired communication and cognitive skills, including the ability to organize thoughts.

Meeting Morris reinforced Volk's thoughts about the limitations of current treatments. It demonstrated how meaningfully his lab pursuits could change people's lives.

The entire four weeks Volk was at WPIC, Morris never recognized him, nor did he recall that Volk was a medical student.

This is almost exactly what Volk was trying to understand through his research. Why couldn't Morris remember him? What is different in the brain of a person with schizophrenia that obstructs memory?

Volk became interested in the brain and how it works after taking an undergraduate class in neuroscience. Then he came to Pitt as a Baylor University senior to complete a summer neuroscience research fellowship, a 10-week program that gives undergraduates an opportunity to pursue neuroscience research with a faculty member. He worked in David Lewis' WPIC lab studying abnormalities in the prefrontal cortex in schizophrenic patient brains. Lewis ended up becoming his PhD adviser.

Studies have shown that inhibitory neurons in the brain play a role in complex cognitive processes, like short-term, or working, memory. People with schizophrenia have impaired working memory. Volk's doctoral thesis examines the role that GABA (gamma-amino butyric acid) plays in the brains of people who suffer from schizophrenia. GABA is a neurotransmitter that influences memory formation in the brain, Volk notes.

To better explain what he is describing, Volk grabs a notebook and draws a diagram of neurons. On his left hand is a wedding band. (He met his wife, who is now a physician's assistant, in a lab, though he still argues that students in the medical scientist training program aren't cloistered in labs and libraries, despite what you might assume. In fact, Volk mustered enough spare time to teach Bible study classes at his church, play sports, and set out on an occasional camping trip.)

On the notepad, Volk draws a circle with lines coming out of it, like a sun a child might color. *This is the chandelier neuron.* Volk connects the circle to a triangle. *A GABA receptor.* He explains further: Volk learned during his doctoral work, by studying the prefrontal cortex, that the brains of patients with schizophrenia don't appear to use GABA the same way healthy people's brains do. When he looked further, he discovered an important subpopulation of inhibitory neurons, called chandelier neurons, were particularly affected in schizophrenia. Those abnormal chandelier neurons could be the key to cognitive problems experienced by those with schizophrenia.

Volk continues to be fascinated with schizophrenia and hopes to continue studying it after he finishes his WPIC residency.

Whatever is responsible for disrupting the memories of schizophrenic patients, Volk witnessed the consequences firsthand as he got to know Morris. Occasionally, Morris would remember a tidbit about his life that Volk could use in search of the patient's father. Then after weeks of searching, Volk found the right phone number. When he called, Morris' father told him that his son hadn't lived with him for more than 10 years. And to Morris' surprise, his dad had remarried. Unfortunately, Morris wouldn't be able to live with his father and his father's new wife.

Volk soon finished his WPIC rotation and lost touch with Morris. Six months later, he started a rotation at Mayview State Hospital in Bridgeville. As he rounded one day, he saw a familiar face in the long-term mental care facility. It was Morris.

This time Morris was taking his medication. The stable, long-term environment clearly helped his condition. He was healthy and happy, no longer suffering from delusions. With regular medication, Morris could think a little more clearly.

Curiously, and to Volk's delight, Morris even recognized him. ■

CLINICALLY RELEVANT

As Lou Ghanem enters the Hillman Cancer Center, he sets down the dozen bagels he's carried in and looks at the patient lineup and progress reports. In the pocket of his white coat is a stack of note cards inked with information about the major causes of chest pain, details of clinical trials, among other facts he'd like at his fingertips in this clinic. He was nervous when he first started this clinical rotation.

It had been three years since he'd seen patients.

Ghanem is in his fourth year of the PhD segment of the medical scientist training program at Pitt. Today he is participating in one of two required longitudinal clinics, working with Suresh Ramalingam, assistant professor of medicine, in a lung cancer clinic. As soon as Ramalingam, whom his patients affectionately call Dr. Ram, enters the office, he begins peppering Ghanem with questions: "What are the major causes of chest pain? What are the different types of aneurysms?"

One of James Luketich's assistants pops into the room. Luketich—director of thoracic surgery and codirector of the lung center at Hillman—has a patient with a new case of lung cancer. He thinks the tumor has metastasized, and he wants Ramalingam to consult and take over as the oncologist.

Ghanem and Ramalingam look at the CAT scans. Then the two join Luketich in a room where the patient, Christopher Downy (not his real name), sits in a chair beside the exam table. Ramalingam sits beside him and gently questions him: "How do you feel? How is your breathing? Are you coughing? Do you feel differently than you did a year ago?"

After Downy answers the questions, he looks at Ramalingam and asks, "How bad is it?"

Downy's wife is sitting in the corner, balling up her fists, trying not to cry.

"I don't know yet," the physician answers.

Ghanem and Ramalingam return to the office, where Ramalingam confesses that he isn't feeling optimistic.

"If it's two primary tumors, can surgery work?" Ghanem asks.

"The question is, can he live with one lung?" Ramalingam says.

As Ghanem watched the doctor's compassionate interaction with Downy, he was torn. He wanted to observe, so that when he starts treating patients himself he'll know whether a hug or a handshake or encouraging words are the best way to comfort a patient dealing with a tragic situation. Still he was sad to be part of such a grave diagnosis.

Pitt is one of the few schools in the nation offering longitudinal clinics where MD/PhD students can practice clinical skills while pursuing their PhDs. That's likely to change, however, because word has spread about how valuable such clinics are for these students. At Pitt, each student takes two clinics. For each clinic, the student spends half a day each week for six months in a rotation, which is often more specialized than the typical med school rotation. Ghanem is pleased he can work in hematology and oncology.

"You can ask more clinically relevant questions [in the lab] if you have medical knowledge," Ghanem says. He works in the lab of Richard Steinman. With Steinman, an MD/PhD and faculty member in the Departments of Medicine and of Molecular Genetics and Biochemistry, Ghanem studies the mechanisms of normal white blood cell differentiation in leukemia.

Equally important to Ghanem, who suspects his clinical skills have lapsed somewhat: His time in the longitudinal clinic levels the playing field with his peers who are working on their MDs full-time. *—MH*