Like a busy tangle of highways, the central nervous system transports messages from the brain to points throughout the body, prompting a variety of physical functions. When there are road blocks, however, a neurological traffic jam develops, and the messages are stuck in place. Nerve fibers in the brain, spinal cord and optic nerve are the key conduit for the electrical impulses of brain-body communication. Surrounding these fibers is a thin layer of insulating protein and fatty material called myelin. Scientists believe multiple sclerosis may be an abnormal autoimmune reaction in which the patient’s own immune cells, which normally patrol the body's systems seeking to repel outside infectious agents, initiate an attack on the patient's myelin. A destructive process called demyelination ensues. Lesions — scarring and bare spots — form along the nerves, inhibiting communication between the brain and the body, and impairing physical function.

Hillel Panitch, M.D., and his colleagues work to free the tie-ups caused by multiple sclerosis.

CLEARING THE NEUROLOGIC TRAFFIC JAM

by JENNIFER NACHBUR

photography by RAJ CHAWLA
According to the National MS Society, onset of the disease typically occurs between the ages of 20 and 50, and about 70 percent of MS patients are women. Of the approximately 400,000 diagnosed cases in the United States, roughly 2,500 are in Vermont. In fact, Vermont has one of the highest prevalence rates in the country with an MS rate of one person per 500 people in the general population — twice the U.S. average. Hillel Panitch, M.D., professor of neurology and director of the Multiple Sclerosis Center, explains that several factors are believed to contribute to this statistic, including genetics, exposure to viral infections, such as herpes and Epstein-Barr, and geography. Those of northern European and especially Scandinavian heritage, as well as people in northern-tier states like Vermont and Minnesota, are particularly at risk. Epidemiologic studies, says Panitch, show a link to exposure to sunlight (and possibly one of its important components, Vitamin D) and related distance from the equator.

A 30-year veteran in the MS field, Panitch embarked on his research career as a neurology resident at the University of California in San Francisco, then further delved into the science of the disease as a postdoctoral fellow in neurovirology at Johns Hopkins University, moving on to serve as a senior staff fellow with the Neuroimmunology Branch of the National Institutes of Health. As a neurology professor and principal investigator at the University of Maryland, he had a leading role in studying several breakthrough therapies that radically changed the lives of MS patients. Approved in the early and mid-1990s, these interferon-based treatments, which help control the immune system, offered the first-ever option for halting the progression of MS.

“There was nothing 15 years ago to help patients,” admits Panitch. “Now there are six approved drugs, and MS is among the more treatable neurological diseases.”

In 2000, Panitch joined the College of Medicine faculty and established the Multiple Sclerosis Center at Fletcher Allen Health Care. UVM’s association with MS treatment stretches back to the 1960s, when former chairs of the Department of Neurology George Schumacher, M.D., and Charles Poser, M.D., developed sets of criteria still commonly used throughout the field to make a clinical diagnosis of MS.

Charlene Young is one of about 700 MS patients from Vermont and upstate New York who are treated at the Multiple Sclerosis Center. Fourteen years ago, the Jericho, Vt. resident was plagued by a variety of symptoms, including a profound loss of balance, weakness in her left foot and leg and toe spasms. At just 41 years of age, she learned she had multiple sclerosis.

Most MS patients have the relapsing-remitting version of the disease, in which symptoms come and go in discrete episodes, but Young is afflicted with a rarer version. Called primary progressive, this type of MS only strikes about 10 to 15 percent of patients and is characterized by persistent symptoms that with time progress in seriousness. Her issues, in addition to the weakness and balance problems common in MS, include a combination of stiffness and involuntary muscle contractions called spasticity. Now 55 years old, Young has had to make adjustments over the past 14 years, including designing and building a one-story home with her husband, Larry, two years ago to accommodate her physical needs.

“You learn to take care of yourself, make changes in daily living and do things in short spurts,” she explains. She has been on the staff at Fletcher Allen’s primary care practice at Aesculapian Medical Center in South Burlington, Vt. for 18 years. Young currently works four days a week as a scheduler/practice support specialist, and takes time off to get treatments and tests as needed.

Clinical trials for primary progressive MS were non-existent until a few years ago, when the first study ever sponsored by an American pharmaceutical company was launched. “I waited a very long time — about 12 years,” recalls Young.

Young took part in a study of rituximab, a monoclonal antibody that can be closely targeted on B cells, one of the types of immune cells thought to play a role in demyelination. Though the clinical trial was double-blind placebo-controlled, Young believes she received the actual drug due to a noticeable improvement in her symptoms. Now, after completing her participation in the clinical trial, Young is officially “on drug,” receiving the therapy via intravenous infusion in the hematology/oncology outpatient clinic twice in January and then two more times in July.

“You treat symptoms, not the disease,” says Young, who in addition to her rituximab therapy also takes an anti-spasmodic drug called baclofen and another drug to help alleviate the fatigue element of her MS.

Young is grateful to have had the chance to participate in the clinical trial, with a personal understanding of what that access can mean to someone dealing with MS. “We’re lucky to have someone so cutting-edge and dedicated to bringing trials to patients as Dr. Panitch,” she says.

Neurology Chair and Physician Leader Robert Hamill, M.D., agrees. “We were very fortunate to have been able to recruit Dr. Panitch, who is one of the most highly regarded neurologists in the field of multiple sclerosis,” to Vermont,” says Hamill. “He established the MS Center as an important site for
Two of Panitch’s associates complement his efforts to ensure that patients like Young continue to lead quality lives and find successful treatments. Yang Mao-Draayer, M.D., Ph.D., is an assistant professor and attending physician in neurology, who completed a residency at Fletcher Allen and an MS fellowship with Panitch. She sees MS patients in the clinic and conducts laboratory-based research with support from UVM’s Center of Biomedical Research Excellence neuroscience grant, as well as institutional and industry funding. Through her work, Mao-Draayer hopes to identify how naturally-occurring protective factors in immune cells like T-cells interact with neural stem cells to repair the damage of demyelination. To do this, the group is comparing immune cells in normal and MS patients’ blood.

Mao-Draayer describes neural stem cells as “fire fighters” and “construction workers,” based on their tendency to go to where the “fire” or damage is, put out the fire and then try to rebuild the area. Lab associate Julia Cambron, a third-year M.D./Ph.D. student, studies what factors promote the survival of the neural stem cells and the interactions between immune cells and stem cells.

“To understand how patients respond to different treatment, our lab team and my technician Eugene Scharf have been trying to identify intrinsic neuroprotective factors from patients’ immune cells,” explains Mao-Draayer. “Our goal is to find a potential novel therapy that could help to repair the nerve damage.”

Forming new alliances and programs that lead to better care is MS fellow Dr. Angela Applebee’s goal. A graduate of the University of South Dakota Sanford School of Medicine and former Fletcher Allen neurology resident, she assists Panitch with clinical research and patient care, as well as teaching neurology residents about the history, identification and treatment of MS. Among Applebee’s many projects are several new clinical initiatives, including a spasticity clinic and a collaboration with the Department of Radiology on a regular MS/MRI conference that keeps neurologists updated on the latest sequences in the imaging technology critical to assessing MS lesions. In her research capacity, she attends national conferences and trial meetings with Panitch and serves as a co-author on his study papers.

“This fellowship allows me to work with a world-renowned expert, who knows the historical facts, because he was part of the founding of all the medications that became available in the 90’s,” says Applebee, reflecting on her work with Panitch as she sits in her office in the Neurology Clinic.

With seven to eight active clinical trials running and another five or so soon-to-launch, Panitch and the MS Center are busy, to say the least, and dependent on the support of Mao-Draayer, Applebee, and a highly capable staff to keep things running smoothly. MS patient Charlene Young describes Sandra McGrath, MS, F.N.P., a nurse practitioner who works directly with patients, as “my resource — she gives me all the information I need.” Patty Krusinski, the principal MS study coordinator, is in charge of making sure clinical trials run smoothly. Amy Savage, R.N., a clinical research nurse in the Office of Clinical Trials, works part-time as an MS study coordinator and is managing one of the new oral treatment trials, which, according to Panitch, is the latest trend in MS clinical research.

“MS patients are interested in oral drugs versus injection or I.V.,” says Panitch, “because oral is so much easier.” A total of four oral medication trials are getting ready to launch, three of which are for established MS patients and another for people with pre-MS conditions.

Even without oral medications, there is no shortage of treatments. However, the costs of these breakthrough therapies run an estimated $20,000 annually, says Panitch, which is making it harder to treat people, even those covered by insurance. Another challenge to Panitch and his colleagues in the MS field is the very way trials are conducted.

MS clinical studies mostly include untreated or relapsed patients. In 2007, Panitch, who serves on the National MS Society Medical Advisory Board, participated in an MS Society task force discussion on the ethics of conducting placebo-controlled trials, since MS patients randomized to a placebo group do not get treatment.

For a person facing an MS diagnosis today, the outlook and options are very different than those of just a generation ago. Thanks to passionate clinical specialists like Hillel Panitch and the six therapies that they have helped develop in that time — Avonex, Betaferon, Rebif, Copaxone, Novantrone and Tysabri — this one-time death sentence has evolved into a chronic condition that, though still complex to treat, offers patients like Charlene Young the possibility of a quality life. Two summers ago, a dozen years after her initial diagnosis, Young took up kayaking — adapting to her equipment by sitting on top of the craft to make getting on and off easier — and enjoyed it all summer long. “I need to focus on the glass being half full,” says Young, who is hopeful that her therapy will successfully slow or halt the progression of her MS. “I’d like to be in the same place when I’m 65.”