

Gregory Holmes, M.D.: Myth buster

By Laura Stephenson Carter

The hero of the week is Chicago White Sox trainer Herm Schneider, who saved first baseman Greg Walker's life by prying his mouth open with scissors to keep him from swallowing his tongue after Walker suffered a seizure during pregame warm-ups." So reads the "Inside Baseball" column in the August 15, 1988, issue of *Sports Illustrated* (SI).

Epilepsy expert (and sports fan) Dr. Gregory Holmes wasted no time in shooting off a stern letter to the editor, which SI published a month later. "While Schneider deserves praise for his willingness to help, his actions were incorrect and could have caused Walker considerable harm," Holmes wrote. "It is a myth that you can swallow your tongue during a seizure. You cannot swallow your tongue during a seizure," he emphasized. "What's more, the mouth should never be pried open, and especially not with a sharp object."

Holmes, who since 2002 has been a professor of medicine and of pediatrics at DMS and chief of neurology DHMC, admits that seizures can be terrifying to watch. Even for someone like him who has seen thousands of them. He's spent his career treating people with epilepsy, doing research on the underpinnings of the disorder, and trying to dispel some of the myths that surround it.

"The problem is you can't do much, which makes it very frightening," says Holmes, who is a past president of the American Epilepsy Society. "You don't want [people having a seizure] to hurt themselves. Don't stick anything in their mouth," he cautions. "Just turn them on their side and wait for it to end."

Epilepsy is one of the most misunderstood disorders, Holmes says. People think it's contagious, that it causes mental derangement, that someone with epilepsy can't live a normal life. And then there's that persistent swallowing-their-tongue myth. It's all untrue.

Holmes's first encounter with epilepsy was when he was in high school. A fellow student "unfortunately had a couple of grand mal seizures in the classroom and fell out of her seat, urinating and jerking," he says. "What was really bad was the teacher didn't know what

Grew up: Toledo, Ohio

Education: Washington and Lee University '70 (B.S.); University of Virginia School of Medicine '74 (M.D.)

Training: Yale (pediatrics); University of Virginia (pediatric neurology); Institut National de la Santé et de la Recherche Médicale, Paris (visiting research scientist)

Previous position: Professor of Neurology at Harvard and Director of the Center for Research in Pediatric Epilepsy at Children's Hospital, Boston (and before that, posts at the Medical College of Georgia, from 1986 to 1988, and the University of Connecticut, from 1979 to 1986)

Favorite neckties: Any that picture Mickey Mouse

Favorite sports: "I love the Red Sox and Patriots, but my favorite is college football. I am a big University of Virginia fan, although they are usually terrible."

"The problem is you can't do much [about a seizure], which makes it very frightening," says Holmes, who is a past president of the American Epilepsy Society.

to do." The other students learned to ignore the girl's seizures and "pretended it wasn't happening. But . . . then we tried to ignore her when she wasn't having a seizure. So she became an outcast and had no friends in the class, even though she was a really nice girl. It was this terrible feeling of ignorance, knowing that something bad was happening. We just didn't want to be around her.

"I was just as scared as everyone else," Holmes admits. "But I wasn't scared to go into medicine. I wanted to learn more so I wouldn't be scared."

As Holmes embarked on his medical training in the early 1970s, the field of epilepsy treatment was evolving rapidly. Through the 1960s, people with epilepsy typically relied on a couple of drugs—dilantin and phenobarbital—to control their seizures, but those drugs had unpleasant side effects. Since then, new and more effective medications have been developed. "There's a lot more interest in understanding the mechanisms of epilepsy, and that led directly to treatments," Holmes says. Today's approach to epilepsy "makes a lot of sense once you understand how seizures occur," he adds.

Epilepsy—which affects more than two million people in the United States, according to the National Institute of Neurological Disorders and Stroke—is a brain disorder in which clusters of nerve cells, or neurons, fire electrical impulses at higher-than-normal rates. This is what causes the seizures. But not all seizures are of the so-called grand mal, or tonic-clonic, type that Holmes observed in his high-school classmate all those years ago. Some can be as mild as staring off into space for a few moments.

Seizures are just this incredible spread of synchronous electrical activity," says Holmes. As a result, "cells that were not normally supposed to wire together do wire together." Epilepsy can be caused by illness, tumors, brain damage due to head injury or stroke, or abnormal brain development; in some cases, there may be genetic factors involved. It's usually diagnosed using information obtained from the person's medical history, a physical examination, and an electroencephalogram (EEG), in which electrodes placed on the scalp

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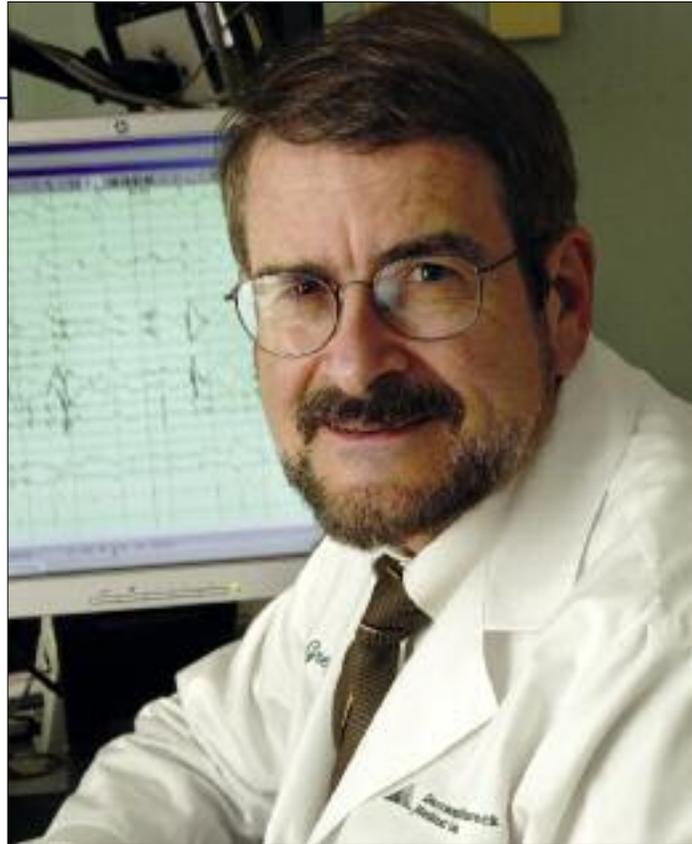
measure the brain's electrical activity and help pinpoint where the seizure is originating—a spot known as the seizure focus.

Even though there have been improvements in medications since the 1960s, the new drugs still don't help about 30 percent of people with epilepsy, Holmes explains. Surgery, such as a procedure to remove the seizure focus, may help some of those people. The surgery has "gotten better and better," thanks to improved technology to locate the focus, such as MRI scanning and better EEG recording methods, he says.

In fact, the University of Virginia, where Holmes earned his M.D. and also did a residency in pediatric neurology, was one of the first medical centers in the nation to continuously monitor EEGs, while videotaping patients, to see how their brain activity corresponded with their seizures. In 1997, the Food and Drug Administration approved a device called a vagus nerve stimulator—a pacemaker-like apparatus implanted in the chest that reduces seizures by delivering periodic small shocks to the brain via the vagus nerve.

Holmes actually began working in health care even before he entered medical school. One summer while he was in college, he participated in a program that recruited undergraduates to work in mental institutions; he was posted at Fairfield Hills State Hospital in Newtown, Conn. "They would assign us several patients," he says. "You'd work with the psychologist or the psychiatrist. He'd give you a game plan on what to do, how to interact with the patients, and the treatment goals." And at night, Holmes volunteered at Connecticut's Southbury Training School, for the mentally retarded. Years later, during his residency in pediatrics at Yale, he returned to the training school to treat patients with epilepsy. The work with epilepsy led him into neurology and sparked his interest in developmental neurobiology. He soon began doing research on how seizures affect the developing brain. And he continued to see patients.

Today, he cares for patients with epilepsy at DHMC and, for one week every summer, at Camp Wee Kan Tu in Duxbury, Mass. The camp, run by the Epilepsy Foundation of Massachusetts and Rhode Island, is both educational and fun. "Many of [the campers] have nev-



Dartmouth's Greg Holmes, now a nationally known expert in epilepsy, recalls feeling helpless and scared when a high-school classmate had an epileptic seizure during class.

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er known anyone else to have epilepsy," explains Holmes, nor seen a seizure before. "If we make it so it's not such a big deal, they don't see it as a big deal for themselves." He confesses that he'd love to start an epilepsy camp in New Hampshire some day.

What he doesn't love, however, is the fact that 10 percent of children with epilepsy suffer eventual cognitive decline. "We see a lot of children that just dwindle in front of our eyes," he says sadly. "The first time they come in to see you—they've had a couple of seizures, and they look pretty good." Then as their epilepsy progresses and they continue to have seizures, "they go from being the best in their class, to just getting through, to where they don't go on to the next grade, [to] requiring special education. It's pretty tragic."

But, he continues, it is difficult for doctors to determine whether it is the seizures themselves, or the medications used to treat them, that are affecting the brain. There are so many variables, including the age of onset of the seizures, as well as their length, duration, and cause, that it's hard to sort out what's causing what.

That's where his research comes in. In the lab, at least, the variables can be controlled or eliminated. "We think that seizures in the developing brain may have much different consequences than in the adult brain, in which the circuits are pretty well formed," explains Holmes. In a child's brain, if "there's too much aberrant electrical activity, it can really screw up the circuitry. They may never recover."

In one study, Holmes's research team is working with rats in an effort to understand the association between recurrent seizures and spatial memory. Spatial memory is tested using a Morris water maze, a shallow pool containing a platform hidden just beneath the water's surface. After repeated trials, the rats learn to use external cues to find the platform every time, no matter where they have been dropped in the pool. The rats also wear tiny electrode-studded caps that measure signals from their spatial-memory neurons.

"We have found that rats, even with very brief seizures, have im-

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pairments of spatial memory,” says Holmes. “We were surprised at how profound the defects were.” In addition, the signals from their spatial-memory neurons are less stable than normal and show less precise firing patterns and lower firing rates.

The findings suggest that in humans, “even brief seizures can dramatically alter the brain’s function, and we’re not sure how permanent this is,” Holmes adds. “Nevertheless, if you’re having seizures you’re probably not thinking correctly. Your memory is going to be screwed up.” For instance, he explains, children who’ve had a brief seizure may not be quite right for a day or so afterwards and can demonstrate impaired learning.

Of course Holmes has served on the requisite editorial boards; churned out hundreds of journal articles, abstracts, and book chapters; and held leadership positions on national committees and societies. He has traveled the world giving lectures on epilepsy. At DHMC, he hopes to turn the Section of Neurology into a department. He sees patients on a regular basis. And he’s running several clinical trials to test new therapies for epilepsy. DHMC is one of the major centers in New England testing a responsive neurostimulator system, a device that is implanted on the surface of the brain and that can detect oncoming seizures and deliver shocks to stop them before they happen.

Still, Holmes is frustrated that he doesn’t have time to do hands-on research any more. He used to enjoy day-to-day laboratory work, and he continues to follow his lab’s progress exploring epilepsy’s long-term consequences on the developing brain; discovering novel ways to alter brain excitability; determining which parts of the brain are impaired following seizures; and investigating how seizures affect learning, memory, and decision-making processes. Now, however, the actual experiments are done by others.

But he does make time to ensure that people with epilepsy are treated with respect. And to dispel all those myths. As he wrote in his letter to *SI*: “While [grand mal seizures] are frightening and everyone feels the need to ‘do something,’ the first goal should be not to do anything harmful.” ■

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