

Multiple System Atrophy

Managing orthostatic hypotension in MSA.

BY NORRA MACREADY

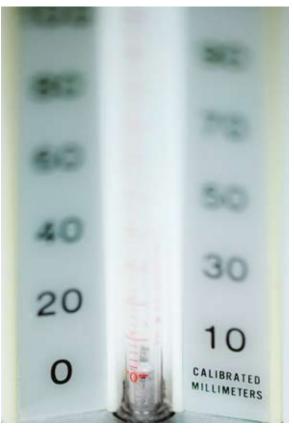
y the end of her life, Sylvia Summers could not stand for more than a few seconds without fainting. Don, her husband, dreaded when she would get up from bed to use the bathroom, which happened five or six times a night. "She might lose consciousness while sitting on the commode," he recalls.

Sylvia had multiple system atrophy (MSA), a progressive, degenerative neurological disorder affecting parts of the brain that control balance, coordination, and "autonomic" or automatic functions such as blood pressure, sweating, and elimination. The average life expectancy for people with MSA is seven to 10 years.

Formerly known as Shy-Drager Syndrome, MSA currently afflicts 25,000 to 75,000 Americans. "Many cases are never diagnosed correctly because it can look a lot like Parkinson's

disease," says David Robertson, M.D., professor of neurology at Vanderbilt University Medical Center in Nashville, TN. "Twenty-five years ago, MSA was considered an extreme form of Parkinson's disease," Dr. Robertson notes. In fact, he believes that one of the patients originally described by Dr. Parkinson himself may actually have been suffering from MSA. Sylvia Summers had symptoms for five years and saw many other physicians before she found Dr. Robertson, who finally gave her an accurate diagnosis.

Doctors still don't know what causes MSA. "It seems to just strike people randomly," Dr. Robertson says. He's cared for about 700 people with MSA since 1976 but has not detected any unifying feature in his patients. There does



not appear to be a genetic connection. "At the end of the day, there really is nothing to substantiate any specific risk," says Paola Sandroni, M.D., associate professor of neurology at the Mayo Medical Center in Rochester, MN. "At the moment, all we can say is, it's just bad luck."

One characteristic feature of MSA is an accumulation of slender fibers or filaments called glial cytoplasmic inclusions, or GCIs, in the cells of affected portions of the brain. One component of the GCIs is a protein called alpha synuclein. This protein is also found in the brains of people with Parkinson's disease and Alzheimer's disease and is thought to play a role in the development of those disorders, as well as multiple system atrophy.

SYMPTOMS OF MSA

The symptoms of MSA reflect its impact on the autonomic nervous system. Patients often have urinary incontinence or the opposite—a problem with emptying the bladder, Dr. Sandroni says. They may also have severe constipation. An inability to sweat, which is another common symptom of the disease, makes it difficult to regulate body temperature. As a result, these patients are at high risk of heat stroke. The motor symptoms of MSA include diminished facial animation stiffness clumsiness slow movements, and decreased manual dexterity, all of which result from the loss of balance and coordination. (These symptoms are seen in Parkinson's disease, as well.) Sleep disorders and problems with speaking and swallowing can also be part of the MSA picture. And as the disease progresses, patients of-

ten have trouble breathing while asleep; this is due to signals from the sleep centers in the brain becoming weaker and weaker. Death usually comes when the person simply stops breathing.

ORTHOSTATIC HYPOTENSION

One of the most troubling symptoms of MSA is orthostatic hypotension, in which the blood pressure plummets every time the patient tries to stand up. As Sylvia and Don Summers discovered, the result often is an almost immediate loss of consciousness. Orthostatic hypotension is "one of the hallmarks of MSA, and it's definitely one of the earliest and most common symptoms," Dr. Sandroni says. Interestingly, blood pressure while sitting or standing usually remains normal or even a bit high.

MSA has no cure yet, but doctors do have a variety of tools at their disposal for helping patients manage their symptoms. For orthostatic hypotension, management relies on a combination of lifestyle adjustments and medication. Nondrug interventions include exercise, adjusting salt and fluid intake, diet, stress management, and changing one's sleep position.

"We begin by telling the patient to stay in good physical condition so they can maintain the pumping action of the leg muscles," Dr. Sandroni explains. When you stand up, blood flows down to the veins in the legs. Healthy people compensate for this almost instantaneously through a complex interaction of neurologic, cardiovascular, and hormonal or endocrine responses, which operate together to keep blood flowing up to the brain.

This interplay deteriorates in MSA, but one way to prevent blood from pooling in the legs is by maintaining leg muscle tone. By squeezing the veins in the legs, toned leg muscles prevent blood from pooling in the lower extremities and keep it moving to the brain. As the MSA progresses and patients become too ill to exercise, support garments around the legs or abdomen can achieve a similar result.

Adjusting one's salt and fluid intake can also help. Just as decreasing salt intake may lower blood pressure, increasing salt can raise it, Dr. Robertson says. So consuming more salt is one way people with MSA can minimize or avoid orthostatic hypotension. Dr. Robertson also advises patients to drink about 16 ounces of water just before going out or performing a task. Their blood pressure will start to rise within 10 minutes and be at its height within 30 minutes. The effect wears off in about 90 minutes.

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tients monitor their diet, practice stress management, and adjust their sleep position. Large, heavy meals can exacerbate orthostatic hypotension by diverting blood from the brain to the digestive tract in order to digest all that food. Eating smaller, more frequent meals helps ensure a more even supply of blood to the brain. At the Mayo Clinic, Dr. Sandroni and her colleagues also advise their patients to avoid stressors such as excessive heat exposure, which may exacerbate the symptoms of MSA. Finally, sleeping with the head elevated helps some people with orthostatic hypotension.

DRUG TREATMENTS

Drug treatment similarly is aimed at maintaining blood pressure and bloodvessel tone. The drug midodrine works on the blood vessels themselves to keep them constricted, which maintains blood pressure. "It has been proven effective," says Phillip Low, M.D., professor of neurology at the Mayo Medical Center. Pyridostigmine improves impulse transmission through the autonomic nervous system. Midodrine and pyridostigmine may be prescribed individually or together. A third drug, droxidopa, is in clinical trials in North America and Europe for the treatment of orthostatic hypotension. It is already in use in Japan and Southeast Asia.

Currently, the treatment of MSA mostly focuses on managing symptoms such as orthostatic hypotension. How-

ever, three clinical trials of drugs that may alter its course have started or are about to start this year, Dr. Low points out. One involves an immune protein called intravenous immunoglobulin (IVIG), on the theory that MSA may result from an autoimmune process. Also in the works is a trial with rasagiline, which currently

is used in the treatment of Parkinson's disease. The precise action of rasagiline is still not known, Dr. Low explains, but it is thought to protect cells against oxidative stress. "There is some evidence that early administration may prevent MSA from progressing, which leads us to hope that it might provide a form of neuroprotection."

In the third trial, which is being funded by the National Institutes of Health, Dr. Low and his colleagues will study the antibiotic rifampicin, which has long been used to treat tuberculosis. Recent animal studies have suggested that rifampicin prevents the formation of the GCI fibrils that infiltrate the brain cells of people with MSA. All in all, he says, "these approaches are quite ambitious and aim to affect the natural history of the disease."

Norra MacReady is a medical journalist and book author whose health articles have appeared in The Economist, Glamour, and WebMD: The Magazine.

FIND OUT MORE

For more information about OH and MSA, including the droxidopa clinical trials, contact the Shy-Drager Syndrome/MSA Support Group at **shy-drager.org** or call 1-866-737-4999. Don Summers is the founder and president.