

Gene Therapy for Diabetic Neuropathy

By Peggy Peck

First diabetes left his legs numb and then it became a real pain, says Frank Giaramita — so constant that he could no longer “walk the land” for his work as a real estate appraiser. Giaramita, 56, of Saugus, Mass., has diabetic peripheral neuropathy, a type of nerve damage caused by diabetes. Although it primarily affects the legs, diabetic neuropathy can also cause pain in the arms, hands and fingers.

“It began with numbness in my legs more than 10 years ago,” he recalled. The numbness progressed to sharp pain — like a Charley horse that never goes away. He also started having problems with balance and coordination, and, eventually, Giaramita found he could no longer work.

When Giaramita read a newspaper article about a research study investigating gene therapy as an effective treatment, he immediately contacted the study’s lead researcher

Allan H. Ropper, M.D, chairman of the department of Neurology at Tufts University in Boston to enroll in the \$10.2 million National Institutes of Health-funded study.

Diabetic neuropathy is a common complication of diabetes. High blood sugar levels result in blockages in the tiny vessels that supply blood to the nerves, causing nerve damage, Dr. Ropper explains. He and other neurologists have theorized that the best way to treat diabetic neuropathy is to try to regrow that network of tiny vessels, the microvasculature, to improve circulation and undo the nerve damage.

In earlier studies with heart patients at Tufts, researchers had found that a growth factor called vascular endothelial growth factor or VEGF promoted the growth of cells that helped replace damaged or blocked vessels, Dr. Ropper said. Patients who received VEGF experienced improved blood flow to



Research volunteer Frank Giaramita, shown here with his wife, Diane, is seeking relief from the disabling pain in his legs.

the heart and legs. They also experienced improved nerve conduction in the legs, Dr. Ropper said. Nerve conduction refers to the complex communication system that allows signals to be sent from nerve endings to the brain. These messages control not only limb pain but also limb motion.

In the diabetic neuropathy study, Giaramita and other participants receive injections in their thighs and calves every two weeks of a gene that instructs the body to make VEGF. Only one leg is injected so that Dr. Ropper and colleagues can compare the effect of treatment in an individual patient.

Since this is a “blinded study” — only half of the participants receive the active substance, so the results can be compared — Giaramita doesn’t know whether

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he received VEGF or a placebo (or inactive substance). He will undergo testing including nerve conduction studies over the next year to determine if there are changes in the microvasculature or in the ability of the nerves to send and receive signals.

Since VEGF promotes cell growth, there is always a concern that it will also trigger unwanted abnormalities — such as cancer cells. For that reason the patients are also carefully monitored with regular blood tests to detect any abnormal cells, says Dr. Ropper.

Giaramita completed the treatment last spring. Although he doesn't know if he received active gene therapy or simply a placebo, he says, "I personally felt that my leg was stronger and I seemed to be getting some nerve impulses."

Why did Giaramita enroll in this study? The bot-

tom line, he says, is that "this is the only study that is examining a real treatment to get at the cause of neuropathy — not just treat the pain." He said he carefully assessed the treatment risks and decided: "nothing is given to you free. You have to take some risks to gain and if you're not willing to do that, then don't complain."

The study is ongoing and participants are still needed. People interested in volunteering should contact clinical coordinator Karen Visnaw, R.N. at Karen_Visnaw@cchcs.org. NN

Peggy Peck is a freelance science and health writer whose articles appear in medical journals, magazines and Web sites, including Reuters Health, WebMD, Medscape, and many more.

Spotlight on the Neuropathy Association

Ronnie Chalif, an artist who developed peripheral neuropathy, founded the Neuropathy Association 10 years ago. She banded together with three fellow patients, because, she says, "at that time, we didn't have any answers or any support." There are now nearly 100,000 members, and 250 support groups nationwide.

The non-profit organization's fast growth attests to the prevalence of peripheral neuropathy, says Donald G. Jacob, Ed.D., the association's executive director.

"Most people associate peripheral neuropathy with diabetes, but that only accounts for 1 out of 3 cases. For the remaining two-thirds, there could be 150 different causes: chemotherapy, autoimmune diseases, tumors, heredity and other injuries," he adds.

The disorder is caused by damage to the peripheral nervous system, the network that transmits information from the brain and spinal cord (the central nervous system) to every other part of the body. Depending on which nerves are damaged, the disorder can cause numbness, tingling, prick-



ing sensations, burning pain, muscle wasting and paralysis.

The organization awards \$50,000 grants for research,

lobbies the National Institutes of Health for more research dollars, and is establishing a national network of "neuropathy centers" at medical institutions around the country.

It also raises awareness about the disorder, with the help of its national spokesperson, Mother Delores Hart. Now a cloistered nun, she starred in such 1950s and 60s movie classics as "Where the Boys Are," and, with Elvis Presley in "King Creole."

"We plan to have a fund-raising dinner in Hollywood reuniting Mother Delores with many of the stars of her era. That will help bring our cause to the forefront," says Dr. Jacob.

For more information, visit www.neuropathy.org or contact the organization at this address:

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