

CELIAC DISEASE AND PERIPHERAL NEUROPATHY

Norman Latov, M.D., Ph.D., Director
Peripheral Neuropathy Center

Weill College of Medicine
Cornell University, New York, NY

February 3, 2002 presentation to
Westchester Celiac Sprue Support Group

Summarized by Sue Goldstein

Dr. Norman Latov was introduced by Dr. Peter Green, who remarked that Dr. Latov is a world famous neurologist whose expertise is in peripheral neuropathy. Dr. Latov is conducting research work on celiac disease in his laboratory in collaboration with Dr. Green and Research Fellow, Armin Alaedini. They are hoping to make significant advances in the study of neurological manifestations of celiac disease.

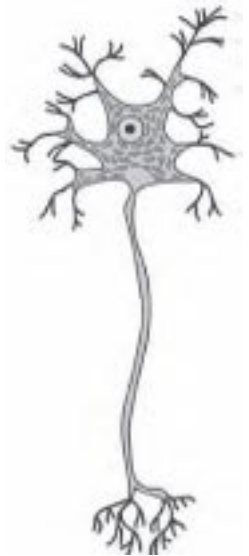
Dr. Latov began his talk by explaining that there isn't much known about the connection between neuropathy and celiac disease. He pointed out, though, that neuropathy is not unlike CD in some aspects. Although it is common, neuropathy is vastly underdiagnosed. There are many people who have it that don't know they have it, there is very little research being done, and people are coming together and trying to help themselves in support groups, as they do in CD.

PERIPHERAL NEUROPATHY

Neuropathy occurs when there is damage to the peripheral nerves. The peripheral nervous system is separate from the central nervous system, which is the brain and the spinal cord. The peripheral nerves are like wires leading from the spinal cord to the muscles, skin and internal organs, and they relay messages back and forth from the central nervous system to the muscles and skin. In addition, there are types of peripheral nerves – there are motor nerves which make the muscles move, sensory nerves which convey sensation, and autonomic nerves which control the gut, the heart, and other internal organs.

When you have neuropathy, these nerves are damaged, and the sort of symptoms that you have depend on which fibers are damaged. If you damage the motor nerves, you have muscle weakness and fatigue. If you damage the sensory nerves, you have numbness or a reduced sensation; you might cut yourself and not be aware of it. But most frequently, what you have is pain and bizarre types of sensations – burning, ice cold, prickly, stinging. Sometimes there is both spontaneous pain and lack of induced pain. There can be very confusing symptoms. The problem is that when you describe this to friends, family members or physicians, they look at you like you're crazy. Peripheral neuropathy is a diagnosis that is very commonly missed, and a diagnosis may be made that the patient is depressed or hypochondriatic.

Dr. Latov had recently read an article in the *New England Journal of Medicine* on hypochondriasis, a condition in which people pretend to have all sorts of illnesses they don't have. To introduce the subject, they discussed a patient who presented with belching and numbness and burning in the hands and feet. It was assumed that since nothing abnormal was found upon examination, the patient was hypochondriatic and had come to adopt her symptoms. Dr. Latov and colleagues thought it possible that the woman might have celiac disease and peripheral neuropathy. They wrote a letter to the editor of the publication and are hoping it will be published and will make physicians more aware of the conditions.



CELIAC DISEASE CONNECTION

There are many causes of peripheral neuropathy – lots of things that can damage the peripheral nerves. But the two things which are relevant to CD are nutrition and immunity. People with CD have nutritional deficits because of malabsorption; common causes of neuropathy are B12 deficiency, B1 deficiency, B6 deficiency, and Vitamin E deficiency. Neuropathies are also commonly caused by the immune system through autoimmune mechanisms. The immune system, which is supposed to protect you from infection and tumors, sometimes turns against the body and causes disease. At least some types of neuropathies are caused by the immune system.

Dr. Latov became involved with celiac disease when Dr. Green gave him a number of serum samples from CD patients to study. Dr. Latov, Dr. Alaedini and their laboratory looked at the samples because they are developing new assays for specific antibodies and proteins that are involved in autoimmunity.

Frequently in autoimmune neuropathy, there are antiganglioside antibodies. Gangliosides are molecules which are part sugar and part fat and are highly concentrated in the nervous system. Of the 21 samples studied, 6 had high levels of antibodies against ganglioside molecules. The 6 patients were called, 5 came in for an examination, and all of the 5 had neuropathy. A few of them had

(continued on next page)

CELIAC DISEASE AND PERIPHERAL NEUROPATHY... continued

painful neuropathies – they had pain in the arms and legs and didn't know they had neuropathy. Neuropathy was explained to these patients and they were treated.

Dr. Latov commented that 20-25% of people with CD might have neuropathy. It might be higher or lower; a larger sample needs to be studied to determine this. Some of the patients have been followed, and although it has just been a few months, it appears that these antibodies don't necessarily correlate with the severity of the CD as measured by anti-transglutaminase and anti-gliadin antibodies. The CD-related antibodies seem to be there, and they fluctuate in activity, though not necessarily in correlation with the other autoantibodies. It may be too early to draw conclusions, so this needs to be studied further.

Dr. Latov has been screening peripheral neuropathy patients for CD, and has already found several who have turned out to have positive serology and biopsy results. Dr. Latov and his colleagues are interested to find out if people who are kept on a gluten-free diet for a long period of time have improvement in the neuropathy and have changes in the levels of the antiganglioside antibodies.

There is also another interesting area to investigate. The villi in the stomach are lined with gangliosides, and one of the common targets of human ganglioside is a receptor for Cholera toxin. Cholera toxin typically attacks the villi in the stomach to cause diarrhea. It might be that these antiganglioside antibodies might contribute to gastrointestinal symptoms and perhaps explain why some people have gastrointestinal symptoms in the absence of other types of autoantibodies

Dr. Latov concluded his talk by saying that there is much to be studied, and that considerable research is needed. He stated that patient support groups can be helpful in getting research projects started.

SELECTED QUESTIONS AND ANSWERS

What is the treatment for peripheral neuropathy?

Dr. Latov tries to treat neuropathy on two levels: “We treat the symptoms, that is, if they have pain we give them medication to help with the pain, which helps. Pain can be a disease in itself. There isn't one medication that helps everyone, but there are 5 or 6 medications – with trial and error usually we can help just about everybody to reduce the pain. Then we try to find what causes the

neuropathy. In the case of celiac disease, we're trying to follow the gluten-free diet. We're trying to see if the neuropathy gets better if the diet changes. And if that doesn't work, we'll probably go on to try antiinflammatory medications, because those types of medications would help the neuropathy if we think it's autoimmune. Gammaglobulin is an antiinflammatory agent which we've used with a few people with celiac disease and neuropathies, when at the time we didn't know they had celiac disease. We found out later when we started looking. And the 2 or 3 people we treated really did not get better. But there are other medications which could be tried.”

Since there may be deficiencies, have you found that by giving vitamins, the neuropathy may go away?

“There have been some scattered reports of patients with celiac disease with neuropathies and other neurological problems, and it was always attributed to malnutrition because these patients have a problem with absorption. But, in fact, when this was looked at, it couldn't be documented. B12 levels were normal, and other vitamins were normal in most cases. Occasionally, you would have malnutrition of that sort that could explain the neuropathy. People would say it's probably malnutrition anyway – we just didn't know what to measure. But here, I think we're finding it's probably not malnutrition frequently. In fact, there are papers that took a group of people with celiac disease and neuropathy and gave them extra vitamin supplements, and they didn't really get better.”

How aware are neurologists about celiac disease?

“If you look at textbooks on neuropathy, you don't see celiac disease mentioned. However, there is a Neuropathy Association which really only began recently. They have about 50,000 members, and they publish a newsletter. We published an abstract of our findings at an annual neurology meeting, and these findings were included in the Neuropathy Association's newsletter. So our findings went to these 50,000 members, including 15,000 neurologists. The newsletter has been bombarded with letters saying, ‘I had my neurologist test me for celiac disease and I have it – that's terrific, and I'm hopeful again, etc, etc.’ I've had physicians call me because of what they read in the newsletter as well. And this has just been in the last month. So it's beginning to percolate. It's going to be one of these things where the patient is going to take the newsletter to their physician and show them. It doesn't always work, but sometimes it does.”