Autoimmune Technologies LLC

Applied Biomedical Science

SCIENCE AND FIBROMYALGIA

A Review of Recent Research for Fibromyalgia Awareness Day, May 12, 1999

In February of this year, an article in a scientific journal announced the discovery that a new immune system antibody had been found to be associated with many cases of fibromyalgia. This marked the first time that laboratory evidence of an immunological process involving fibromyalgia had ever been detected, and it is one of the most exciting developments in recent years concerning a disorder that may affect as many as 15% to 20% of adult women, and many men, in the United States.

What Is Fibromyalgia?

Fibromyalgia syndrome, or FM, is a chronic pain and fatigue disorder. Together with widespread pain and "tender points" in various areas of the body, signs and symptoms of FM include fatigue, sleep disorder, morning stiffness, headache, memory loss, disjointed thought processes, irritable bowel syndrome, and other symptoms. Millions of individuals, most of whom are women, in many countries throughout the world have been diagnosed with FM, and millions more have fibromyalgia-like symptoms that parallel but do not precisely meet the standards needed to be given a formal diagnosis of FM.

The direct medical costs of fibromyalgia in the United States alone have been estimated by one expert to be more than $16 billion per year. A large portion of this cost falls directly upon the patients.

The cause or causes of fibromyalgia are not currently known, but researchers have suggested that trauma, infection, and exposure to environmental factors may all trigger the development of this debilitating illness. Research has recently shown that there is a hereditary element in FM, and it is possible that susceptible individuals develop the disorder in response to one or more of these triggers.

In the United States, some 3% to 5% of adult women meet the strict diagnostic research criteria of the American College of Rheumatology for fibromyalgia, but as many as 15% to 20% of adult women may actually have fibromyalgia-like symptoms. For example, the strict diagnostic criteria for FM include tenderness to the touch in at least eleven of eighteen specific musculoskeletal points on the body, so tenderness in only ten of these points would mean that the patient did not meet the strict criteria for receiving a diagnosis of FM.

Why Are Antibodies Important?

Fibromyalgia has always been difficult to diagnose, in part because it involves many different symptoms and seems to have multiple causes. FM symptomatology includes pain that changes and migrates, a characteristic of pain that doesn't fit neatly into every medical textbook. And there has in the past been no confirming laboratory test for FM. For these and other reasons, not everyone in the health care system has felt that FM is a "real" disorder that involves a unique physiological process.

Many physicians practicing today think that fibromyalgia is a product of aging, the result of a psychological problem, or a part of some other process, and they do not believe that FM is a distinct disorder. Because of this, fibromyalgia patients frequently find they need to prove, to themselves or to others, that they do have a "real" disorder and that they are not just being whiners, malingerers, or slackers. This problem extends from the home and family into the workplace, and it often becomes an issue in disability insurance claims, where the absence of objective proof of illness can be a major barrier to claim settlement.

The discovery of the new antibodies in many FM patients is the first hard evidence that an immunological response is under way in these patients. FM patients can't "imagine" antibodies into existence, and the presence of the new antibodies does not correlate with the existence of other diseases, so the antibodies in the FM patients' blood serve as an objective laboratory marker for fibromyalgia and demonstrate that FM is a "real" disorder that involves a physiological disease process.

Together with the medical benefits that can be expected to result from this discovery, there may be other practical applications for FM patients. One attorney who is experienced in handling fibromyalgia disability cases believes that disability insurers will have to look at FM much differently from the way they have in the past. "Now that this laboratory test is available, the absence of objective evidence can no longer be routinely cited as a reason for disallowing a claim," he said.

What Are these Antibodies and What Do They Mean?

Researchers don't yet understand the disease process itself, but they can indeed detect the antibodies associated with it. Called anti-polymer antibodies, they were discovered several years ago by scientists studying silicone breast implant patients at Tulane University Medical Center in New Orleans. The scientists were surprised to find that blood samples from a large number of breast implant patients who were ill with fibromyalgia-like symptoms contained what seemed to be a new antibody. After carefully checking and rechecking their results they found that the antibody was in fact previously unknown, and they decided to call it an anti-polymer antibody. They named the test that detects the antibody the Anti-Polymer Antibody Assay, or APA Assay. They published their findings in *The Lancet* in 1997, and Tulane later obtained several patents on the APA Assay.

Tulane licensed the APA Assay to Autoimmune Technologies LLC, a small New Orleans biomedical research and development company. Autoimmune Technologies continued to do research into anti-polymer antibodies and began a study of FM patients who did not have breast implants or other implants of any kind. The researchers found that a large percentage of FM patients had these antibodies and found that the presence of anti-polymer antibodies correlated with the severity of the patients' FM symptoms. The antibodies were found in only small numbers of patients with other diseases, such as lupus, who did not also have FM. As a result, these researchers found that the APA Assay served as a blood test for fibromyalgia. Their work was published in the February 1999 issue of *The Journal of Rheumatology*.

The researchers also found that anti-polymer antibodies were not present in all FM patients. This finding supports the concept that there may be multiple triggers of fibromyalgia, and the researchers surmise that anti-polymer antibodies are associated with one particular trigger of FM. They are now conducting additional research to test that theory as well as to further explain the disease process.

If You Don't Have the Antibodies, Does that Mean You Don't Have FM?

No, not having the antibodies doesn't mean that a patient doesn't have fibromyalgia. In the published studies, anti-polymer antibodies were found in fewer than 70% of patients with the most severe FM symptoms and in about 50% of patients who had ever received a diagnosis of fibromyalgia.

There is a saying that medical testing is like prospecting for gold: finding something proves that it is there, but not finding something doesn't prove that it isn't there. Not finding anti-polymer antibodies might mean that a patient is not currently producing the antibodies, or it might mean that the patient's symptoms are associated with an FM trigger that is not related to the antibodies, or it might mean something else. It does NOT mean that the patient does not have FM.

Another example of this is the test for rheumatoid arthritis that looks for a protein called Rheumatoid Factor, or RF, which is associated with that disorder. About 20% of rheumatoid arthritis patients test negative for RF, but the negative test results do not mean that those patients don't have rheumatoid arthritis.

Research in the United States

The APA Assay detects the presence of anti-polymer antibodies, and Autoimmune Technologies is now designing the research protocols to use in asking the U.S. Food and Drug Administration to approve diagnostic use of that information. The company is continuing its work to define the disease process associated with anti-polymer antibodies and to demonstrate which FM trigger may be associated with the antibodies. The company has also initiated studies to determine whether certain drugs are working better in patients who test positive on the APA Assay than on patients who do not.

Research in Europe

After the publication of the article in *The Lancet* in 1997, scientists in The Netherlands approached Autoimmune Technologies and expressed an interest in conducting research there using the APA Assay. Dutch scientists subsequently found the APA Assay to be reproducible and useful for evaluating the presence of anti-polymer antibodies in human serum, and the APA Assay was introduced into the National Institute of Public Health and the Environment, or RIVM, in 1998. Antibody research using the APA Assay is now under way in The Netherlands.

Is the Test Available Yet?

At present, any physician in the U.S. or any other country may order the APA Assay from Autoimmune Technologies to determine if a patient's blood contains anti-polymer antibodies, although it remains the responsibility of the physician ordering the APA Assay to decide how to make use of the results of the test in his or her investigation into the patient's condition. In the United States, a combination of U.S. Food and Drug Administration regulations and patent laws prohibit any other labs from conducting the APA Assay until it has been put into a portable kit format and the diagnostic value of the kit and the information that the APA Assay conveys about anti-polymer antibodies has been approved by the FDA. Such a test kit is now being developed by Autoimmune Technologies. In most European and other countries the physicians make their own determinations of the diagnostic values of such tests, and the test kit will be made available in those countries as soon as it is ready.

Information on the Web

The National Fibromyalgia Awareness Campaign maintains a Web site at **http://members.xoom.com/nfac/home.htm** that provides a good starting point for exploring the many excellent fibromyalgia sites and related medical sites on the Internet. The Web address of Autoimmune Technologies is **www.autoimmune.com**.

To Fibromyalgia Patients

The scientists and physicians involved in this research all hope that their work will eventually lead to better treatments for, and ultimately to a cure for, fibromyalgia. Today, on Fibromyalgia Awareness Day, they offer their thoughts to all of the patients who are living with FM and wish them well.

For further information, please visit www.autoimmune.com.

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