

FIBROMYALGIA RESEARCH REVIEW

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IS THERE A ROLE FOR THE IMMUNE SYSTEM IN FIBROMYALGIA?

The human immune system consists of a number of organs and cells that enable the body to resist infection. However, it has been suggested that dysfunction of the immune system plays an important role in fibromyalgia syndrome (FMS). This month we report on three recent research papers that support the view that the immune system of FMS patients is compromised.

ALTERED CYTOKINE AND CHEMOKINE LEVELS PROVIDE EVIDENCE FOR AN IMMUNOLOGICAL BASIS OF FIBROMYALGIA.

Two recent studies conducted in the USA and Germany have both provided evidence in support of a role for the immune system in FMS. Both groups analysed the levels of cytokines or chemokines in the blood of FMS patients. Cytokines and chemokines are biochemicals released by the cells of the immune system and exert powerful responses, including inflammation or cell migration, which permit the immune system to respond to infection. The American researchers found elevated levels of two inflammatory chemokines (known as MCP-1 and eotaxin) in the blood of 92 FMS patients, when compared with 77 healthy control patients. MCP-1 (monocyte chemoattractant protein) is found in the joints of people with rheumatoid arthritis, where it may serve to attract other inflammatory immune system cells and thus perpetuate inflammation in the joints.

Inflammation is the process by which the body reacts to injury, irritation or infection. Cells of the immune system are directed to the site of injury or infection, resulting in redness, warmth, swelling and pain. The goal of inflammation is to contain an infection in a small-tissue space, however chronic inflammation in the absence of an injury or infection can result in chronic pain. However the role of inflammation in fibromyalgia, if any, is unclear. Perhaps more relevant to FMS is the fact that MCP-1 reduces the ability of muscles to take up glucose in response to insulin. Therefore the authors of this study suggest that enhanced MCP-1 production in FMS patients may lead to abnormalities in muscle energy metabolism and muscle tissue oxygenation.

Similarly, a group of German researchers recently found elevated levels of a number of proinflammatory cytokines in the blood of 20 FMS patients. They concluded that although these proinflammatory cytokines are involved in FMS, they do not directly provoke pain. Proinflammatory cytokine levels were associated with increased pain intensity, however a 6 month multidisciplinary pain treatment plan succeeded in significantly reducing the both pain intensity and levels of these cytokines in FMS patients. Therefore while the precise role of cytokines and the inflammation they provoke in FMS patients is currently unknown, it appears that therapy can successfully restore their normal balance.

"High plasma levels of MCP-1 and eotaxin provide evidence for an immunological basis of fibromyalgia." 2008. Zhang Z, Cherryholmes G, Mao A, Marek C, Longmate J, Kalos M, St. Amand RP, Shively JE. *Experimental Biology and Medicine*.

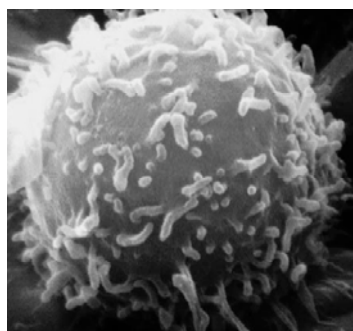
Division of Immunology, Beckman Research Institute of the City of Hope, 1450 E. Duarte Road, Duarte, CA 91010, USA.

"Circulating cytokine levels compared to pain in patients with fibromyalgia - a prospective longitudinal study over 6 months." 2008. Wang H, Moser M, Schiltenswolf M, Buchner M. *Journal of Rheumatology*.

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AN IMBALANCE OF LYMPHOCYTE CELLS IN STRESSED CHRONIC PAIN PATIENTS.

Complex regional pain syndrome (CRPS) and fibromyalgia syndrome (FMS) are both chronic pain syndromes that are often preceded by extremely stressful experiences or major adverse life events. Despite the known connection between the nervous and immune systems, it is not known how stress affects the balance of lymphocytes. Lymphocytes are white blood cells found in the bone marrow, thymus, spleen and lymph nodes. Lymphocytes (see picture below) make up a major part of the immune system and can be subdivided into two main types - B lymphocytes, which produce antibodies, and T lymphocytes. T lymphocytes can be further classified as "cytotoxic" T lymphocytes (also known as CD8+ cells), or "helper" T lymphocytes (also known as CD4+ cells), which release a number of biochemicals (cytokines) that act on other cells of the immune system. CD8+ and CD4+ cells can be distinguished biochemically by the different proteins that decorate the cell surface.



Given the proposed dysfunction of the immune system in FMS, a group of researchers from Germany proposed to investigate the levels of T lymphocyte cells in CRPS and FMS patients, and relate these findings to emotional stress. The researchers recruited 15 patients with chronic regional pain syndrome and 22 patients with FMS and discovered that the number of cytotoxic CD8+ lymphocytes was significantly reduced in both CRPS and FMS patients. Interestingly, acute human stress is known to induce a decrease in the number of CD8+ lymphocytes, therefore it is possible that the prolonged, chronic stress experienced by sufferers of both these syndromes leads to a decrease in CD8+ T cell numbers. CD8+ lymphocytes play an important role in the recognition and destruction of viral or tumour cells, and a reduction in their numbers may lead to an increased susceptibility to infection. Further studies are thus required in order to determine whether the immunological changes found in both CRPS and FMS patients play a role in these illnesses, or whether they are a consequence of the stress response.

"Lymphocyte subsets and the role of Th1/Th2 balance in stressed chronic pain patients." 2007. Kaufmann I, Eisner C, Richter P, Beyer A, Chouker A, Schnellig G, Thiel M. *Neuroimmunomodulation* 14:272-280.

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