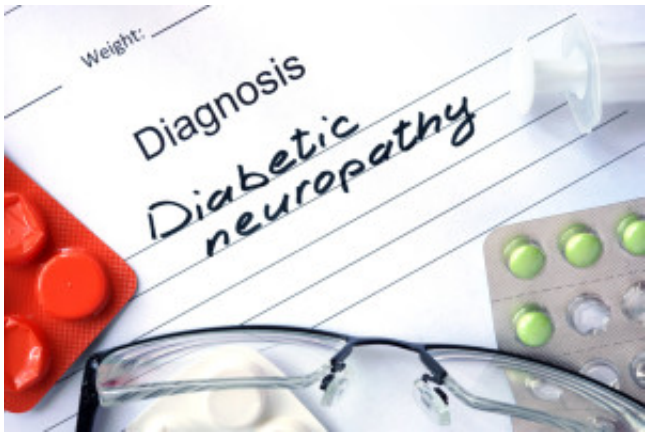
Diabetic peripheral neuropathy



Diabetic peripheral neuropathy is nerve damage caused by diabetes. Population-based studies have suggested more than half of patients with either type I or type II diabetes will develop neuropathy, and as much as 30% of those manifestations are symptomatic. Approximately 10–20% may experience pain or loss of sensation that require treatment. Up to 50% of patients, however, may experience no symptoms and therefore can only be detected by neurological investigations.

Loss of sensation and other problems associated with nerve damage make a patient prone to developing skin ulcers (open sores) that can become infected and may not heal. This serious complication of diabetes can lead to loss of a foot, a leg, or even a life.

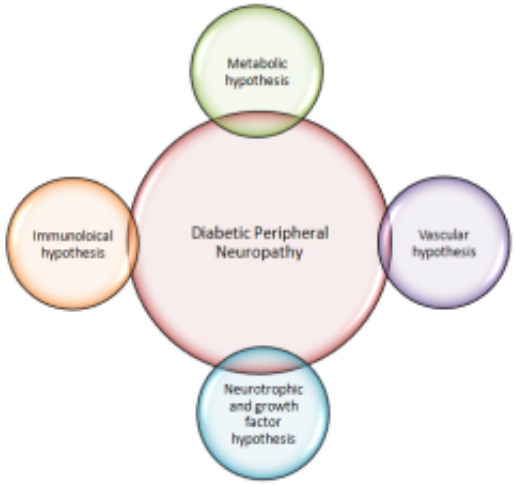
Three different groups of nerves can be affected by diabetic neuropathy:

> *Sensory* nerves, which enable people to feel pain, temperature, and other sensations
> *Motor* nerves, which control the muscles and give them their strength and tone
> *Autonomic* nerves, which allow the body to perform certain involuntary functions, such as sweating.

Defining a precise cause for diabetic peripheral neuropathy which affects sensory nerves is difficult. Numerous theories have been previously proposed individually, but the exact cause remains uncertain. Nerve damage is likely due to a combination of factors: metabolic factors, such as high blood glucose, long duration of diabetes, abnormal blood fat levels and inflammatory reaction and possibly neurovascular factors, leading to damage to the blood vessels that carry oxygen and nutrients to nerves.

Autoimmunity, which is defined as a misdirected immune response that develops when the body attacks its own cells, has been identified in a significant number of neuropathies that are not associated with diabetes. The presence of antibodies in patients with recent onset type 1 diabetes has been associated with increased glucose levels in the blood and reduced peripheral nerve

function, suggesting a common mechanism for neuronal damage. Patients with high antibodies were shown to have reduced motor nerve conduction velocities in the nerves tested, high thermal threshold detection for hot and cold, and decreased autonomic function.



We have investigated, for the first time, the presence of anti-nuclear antibodies in the blood serum of patients with diabetic peripheral neuropathy after exclusion of other causes. One of the most remarkable findings was that highly significant differences between the percentages of positive and negative autoimmune antibodies (ANA) was witnessed in patients with peripheral neuropathy when compared to control, proposing the possibility of an autoimmune factor involvement in the development of the disease.

In summary, the understanding of the development of diabetes has changed in the last few years, with immunological pathways playing pivotal roles in the development and progression of diabetes complications. These new findings lead to a consideration of new therapeutic approaches. Inflammation and autoimmunity in the setting of diabetes is nowadays a matter of great interest. It is possible that in the coming years the hope of new therapeutic strategies based on immunological properties with beneficial actions on diabetes complications may be converted to real clinical treatments.

The role of inflammation and autoimmunity in diabetes complications is starting to unfold. Metabolic and vascular pathways damage the neuronal unit and this may cause antigenic leakage with resulting activation of the immune system. Autoimmunity in diabetic neuropathy has always been questioned. The ultimate proof of the relevance of circulating antibodies to neuronal structures will rest with identification of the specific antigen and reversal of diabetic neuropathies with neutralization of the antibody to the antigen.

Publication

Diabetic peripheral neuropathy, is it an autoimmune disease?
Janahi NM, Santos D, Blyth C, Bakhiet M, Ellis M
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