

Autoimmune diseases

In autoimmune diseases, the activity of the immune system is directed against the patient's own body. A typical feature is the appearance of "autoantibodies". In contrast to normal antibodies which are directed against infectious agents (bacteria or viruses) that have invaded the body, autoantibodies are directed against the body's cells and can disturb their function.

How are autoantibodies formed?

There are always fragments of destroyed or no longer functional cells in human blood. Normally they are recognised by the immune system as endogenous substances and are removed from the blood stream. Unlike foreign invading bacterial or viral pathogens, they are tolerated and do not provoke an immune reaction.

For reasons that are as yet unknown, endogenous substances (cell residues, fragments) can nevertheless trigger an immune reaction. These substances are called autoantigens. They are treated by the immune system as if they were foreign pathogens, and antibodies are formed against them.

Our immune system makes use of the same mechanisms for this purpose as for the usual production of antibodies. B and T cells as well as macrophages bind the autoantigens on their surface and come into contact with each other. Direct cell-to-cell contact and the messenger substances released then stimulate the B cells to produce autoantibodies.

What effect do autoantibodies have in the blood?

Autoantibodies reach various organs via the blood stream. There they can occupy binding sites on organ cells or blood vessels. In this way they prevent e.g. hormones, growth factors and other substances important for the maintenance of cell function from reaching their proper destination.

If the quantity of circulating autoantibodies is particularly large, they activate macrophages or T cells which then fatally destroy healthy tissue as well. In extreme cases, the functionality of cells and tissues can be impaired to such an extent that organ failure may actually occur.

Examples of effects on organ functions are:

- Autoantibodies form complexes, form depositions on the walls of blood vessels and block small and medium-sized blood vessels. This leads to a deficient oxygen supply and to reduced elimination of toxins and metabolites.
The consequences are e.g. disturbed kidney function, damage to the nervous and muscle systems or to the skin.
- Autoantibodies bind to nerve cells and thus prevent the transmission of impulses from the nerve cell to the muscle. The consequence is that muscular contraction fails to occur, and the locomotor system is impaired in its function.
- Autoantibodies can massively inhibit the function of healthy cells, with the result that they are eliminated by macrophages on account of their absence of activity. By this means entire tissue structures can be destroyed. Disorders of this sort can affect all organs.

When is a disease an autoimmune disease?

The autoimmune diseases are divided into diseases which affect only one organ, and diseases which extend to several organs and the vascular system (systemic autoimmune diseases).

Autoimmune diseases can take an acute or chronic course.

In **acute diseases** a sudden rise in the concentration of autoantibodies and uncontrolled inflammatory activity are responsible for the symptoms that occur. Acute autoimmune diseases are confined to one organ (e.g. the blood and system of blood vessels, the peripheral nervous system).

Chronic autoimmune diseases are characterised by persisting disorders of the immune system. They can affect a single organ or several organs at the same time. A typical feature is the formation of T and B cell clones (an accumulation of cells of the same type) directed against the patient's own body. These cell clones then bind autoantigens and autoantibodies almost exclusively and thus they cease to be available for immune defence against foreign pathogens.

The organ-specific autoimmune diseases include:

Diseases of the blood:	Immune thrombocytopenia (ITP), autoimmune haemolytic anaemia (AIHA), autoimmune neutropenia (AIN)
Diseases of the nervous system:	Guillain-Barré Syndrome, chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy, multiple sclerosis
Neuromuscular diseases:	Myasthenia gravis, dermatomyositis / polymyositis, inclusion body myositis
Diseases of the intestines:	Ulcerative colitis, Crohn's disease
Skin diseases:	Pemphigus vulgaris/foiaceus, bullous pemphigoid, epidermolysis bullosa acquisita (EBA), psoriasis, livedoid vasculitis

Systemic autoimmune diseases (with multiple organ involvement) are:

Kawasaki Syndrome, systemic lupus erythematosus, Sjögren's syndrome, Still's Syndrome, Felty's Syndrome, rheumatoid arthritis, reactive arthritis, systemic scleroderma, Wegener's granulomatosis

The treatment of autoimmune diseases

The objective of the treatment of autoimmune diseases is to reduce rapidly the undesirable inflammatory activity. It should also prevent the formation of new autoantibodies. This is achieved by influencing cellular activity.

The therapeutic agents available are drugs which inhibit the activity of immune cells (=immunosuppressants such as corticosteroids and cytostatics), control the activity of immune cells (=immunomodulators such as intravenous immunoglobulins) and blood replacement procedures (plasma-pheresis, immunoadsorption).

Immunosuppressants relatively rapidly and very effectively arrest the activity of the cells that produce inflammatory substances or autoantibodies. However, they can also impair the normal production of antibodies, i.e. those directed against pathogens, and disturb the multiplication and regeneration of cells. This must be born in mind particularly when immunosuppressant therapy is required over a prolonged period on account of the severity of the disease.

The immunomodulators as they are known, which include the **immunoglobulins**, also influence the activity of cells. But their action tends to be fairly moderate. They reduce cell activity gradually but do not arrest it completely. The immune response to foreign pathogens is preserved.

In acute, rapidly progressing or severe autoimmune diseases due to inflammation, immunoglobulins are given in high doses and then usually result in clinical improvement within a few days. The diseases for which immunoglobulins are recommended as first-line therapy include immune thrombocytopenia (ITP, a disease of platelets), Guillain-Barré syndrome (GBS, a neurological disease) and Kawasaki syndrome (a vascular disease in children).

In chronic autoimmune diseases, intravenous immunoglobulins are administered as an adjuvant to immunosuppressant therapies (for example corticosteroids). They assist the regeneration of destroyed tissue, bind inflammatory substances and ensure their more rapid destruction. In addition they help to maintain the patient's defence against infection.

Methods of treatment such as **plasmapheresis or immunoadsorption** serve to remove autoantibodies, immune complexes and inflammatory substances quickly from the blood. However, they have no direct effect on the immune cells whose function has been disturbed.

The decision to choose one of these possible therapies depends on the severity of the disease (organ involvement, functional impairment) and on the speed with which the disease is progressing. If prolonged treatment is necessary, as it often is in cases of chronic autoimmune diseases, different therapies are combined.