

Autoimmunity

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Key points

- Autoimmunity involves a misdirection of the body's immune system against its own tissues, causing a large number of diseases.
- More than 80 autoimmune diseases have so far been identified: some affect only one tissue or organ, while others are 'systemic' (affecting multiple sites of the body).
- Hundreds of thousands of individuals in the UK are affected by autoimmunity.
- Most autoimmune diseases have very long-term effects on health, placing a large burden on the NHS and on national economies.
- Current treatment aims to minimise symptoms and is often not curative. It is imperative that immunological research receives adequate investment in order to better understand these conditions so that we can open up new therapeutic strategies.

of this damage the adrenal gland does not produce enough steroid hormones (primary adrenal insufficiency), resulting in symptoms which include fatigue, muscle weakness, and a loss of appetite. This can be fatal if not recognised and treated, but treatment is relatively simple.

- *Grave's disease* – affecting the thyroid, Grave's disease is one of the most common causes of hyperthyroidism. It results from the production of antibodies that mimic Thyroid Stimulating Hormone, which produces a false signal causing the thyroid gland to produce excessive thyroid hormone. Symptoms including insomnia, tremor, and hyperactivity.
- *Type 1 diabetes* – diabetes mellitus type 1 is a consequence of the autoimmune destruction of cells in the pancreas which produce insulin. Insulin is essential to control blood sugar levels and if left uncontrolled the disease can lead to serious complications, such as damage to the nerves, heart disease, and problems with the retina. Without adequate treatment type 1 diabetes would be fatal.
- *Crohn's disease* – a type of inflammatory bowel disease (IBD), Crohn's is a result of chronic inflammation of the lining of the gastrointestinal tract that can cause diarrhoea, abdominal pain, and fatigue.

Examples of systemic autoimmune diseases

- *Rheumatoid arthritis* – a chronic condition that causes painful stiffness and swelling in the joints. Rheumatoid arthritis is a result of the immune system attacking tissues in the joint lining, eventually leading to damage of the joint itself. Rheumatoid arthritis can also effect inflammation around other organs, such as the heart and lungs. It differs from osteoarthritis, which is generally caused by mechanical stresses on the joint.
- *Multiple sclerosis* – a chronic condition that can cause significant disability, multiple sclerosis is a disease in which the electrically insulating layers of the nerves are destroyed, thus affecting signalling between the brain and other parts of the body.
- *Lupus* – systemic lupus erythematosus is a complex condition affecting many parts of the body, including the skin, joints, heart, lungs and nervous system. It occurs as a result of a widespread systemic autoimmune reaction and results in symptoms including fatigue, joint pain, and rashes.
- *Scleroderma* – in scleroderma the immune system attacks the connective tissue under the skin, resulting in a thickening of these tissues. In more severe forms it can affect blood circulation and internal organs.

Treatment for autoimmune conditions typically involves managing the symptoms and controlling the autoimmune process whilst also attempting to maintain good immune function. Frontline therapies include corticosteroids and other immunosuppressant drugs, although these do not work in all patients are also associated with significant side effects due to immunosuppression. In those diseases affecting the function of particular organs or tissues remedial therapies may be required to counter the poor function of those tissues as a result of autoimmune damage. For example, type 1 diabetics require lifelong insulin replacement due to the body's inability to produce enough insulin following autoimmune destruction of cells in the pancreas. Similarly, with Addison's disease, patients require daily medication to replace lost production of steroid hormones.

How many people are affected by autoimmune diseases?

Autoimmune conditions are a significant cause of ill health in the UK. No figure exists for the total number of people affected by the 80 or

What is autoimmunity?

In healthy individuals the immune system constantly protects us from the native and foreign microorganisms – such as viruses, bacteria, and parasites – that might make us ill. However in some individuals this protection can be inappropriately misdirected against our own tissues and cells, giving rise to autoimmunity. Diseases that result from this phenomenon are known as autoimmune diseases.

Under normal circumstances specialised systems regulate the immune system to ensure host tissue is not attacked. A failure of immune regulation in autoimmunity means that antibodies (autoantibodies) and autoreactive immune cells attack the body's own tissues leading to autoimmune disease. How this happens varies from one condition to another, and ongoing research is aimed at understanding how the immune system goes wrong and how to correct the disorders. In some cases there is a hereditary component,¹ but environmental factors are also implicated; sometimes, autoimmunity may be triggered by infection,² a current example being the paralysis that may follow Zika virus infection.³ More research is urgently required to understand this better.

Autoimmune diseases

Autoimmune disorders are a broad spectrum of disease that can affect any part of the body. More than 80 have been identified, a considerable number with similar symptoms. Inflammation is the classic sign of autoimmunity although how this impacts on an individual is determined by which part of the body is affected. Autoimmune disorders can be placed into two general types: those that are localised to specific organs or tissues (such as thyroiditis) or those that are systemic and damage many organs or tissues (such as systemic lupus erythematosus).

Examples of localised autoimmune diseases

- *Addison's disease* – this disease results from damage to the outer layer of the adrenal gland (the adrenal cortex), of which autoimmunity is the most common cause. As a result

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more identified autoimmune disorders, although estimates do exist for specific diseases:

- According to Diabetes UK there are around 400,000 people in the UK with type 1 diabetes and this rate is growing at a rate of 3% per annum.⁴
- Rheumatoid arthritis affects roughly 700,000 people in the UK, according to the British Society for Rheumatology.⁵
- At least 115,000 people in the UK live with Crohn's disease.⁶
- A 2014 study estimated a UK-wide figure of 127,000 for prevalence of MS with the number of people affected by the condition growing at a rate of 2.4% per year.⁷
- As estimated 8,400 people in the UK have Addison's disease.⁸
- Lupus is thought to affect up to 50,000 people in the UK.⁹

Due to the chronic nature of these conditions – and often associated complications – a significant cost-burden is associated with their treatment. For example, the direct cost to the UK of treating type 1 diabetes was estimated to be £1bn in 2010/11, while the indirect cost (for example through loss of productivity due to illness) was put at £0.9bn.¹⁰ These figures are expected to increase to £1.8bn and £2.4bn respectively by 2035/36.¹⁰ Other conditions are similarly associated with high cost-burdens for both the NHS and society. Multiple sclerosis, for example, is estimated to cost the UK £2.3bn annually,¹¹ while a report from the National Rheumatoid Arthritis Society suggests NHS expenditure on treating rheumatoid arthritis totalled £700m in 2010, with an additional cost to the national economy of £8bn.¹²

The importance of supporting autoimmune research

Autoimmune disorders are poorly understood. Although we are able to recognise the underlying mechanisms for many conditions, the precise nature of why autoimmunity arises is unknown. Moreover, existing therapeutic approaches are limited in their benefits and only seek to minimise symptoms and restore lost function of damaged organs and tissues; there are no established cures. For many patients an autoimmune disease can be a life-changing diagnosis, and yet in addition to the primary diagnosis their condition is likely to also be associated with a number of other chronic comorbidities. These disorders are therefore associated with significant clinical burden and a high cost both for the NHS and the wider economy. For these reasons, investment in autoimmune research is vital.

By better understanding the immune pathways that can lead to impaired immunity and the subsequent development of autoimmune conditions we can hope to open up new therapeutic approaches. In recent decades new modalities of treatment have been derived from monoclonal antibodies such as Humira, infliximab, and rituximab. These drugs are an example of how novel therapies can be derived from an improved understanding of how the immune system attacks our own tissues. Unfortunately, such treatments are not universally effective, must be continued indefinitely, and remain extremely expensive. In the future however, new research will hope to uncover ways of preventing or completely resolving autoimmune diseases. For example, ongoing efforts to produce a vaccine against type 1 diabetes which prevents destruction of pancreatic beta cells by the immune system has shown promise in early trials.¹³ Such an intervention could form the basis of a potential cure, but the technology is still some way off and the success of early trials must be validated through longer term studies. Additional promise lies in the prospect of our ever increasing understanding of genetics and how this might influence not only an individual's susceptibility to these conditions but also their sensitivity to different therapeutic strategies.

Immunological research is the key that might one day unlock the breakthrough which resolves autoimmune disease; ending suffering for hundreds of thousands in the UK and millions worldwide. However, inflammatory and immune research only makes up a small proportion of publicly funded scientific research in the UK. For example, the Department of Health's National Institute for Health Research (NIHR) allocated £40.5m of a total £740.7m of its total spend in 2014/15 to research categorised as "inflammatory and the immune".¹⁴ This pales in comparison to the £134.7m spent on cancer research. Similarly, the Medical Research Council funded just £34.2m of immune research, of a total figure of more than £600m over the same period. Research approaches should of course be multi-disciplinary, but the immune system is a key and fundamental component in the progression of many diseases, and especially autoimmune conditions. We feel these funding allocations do not necessarily reflect this importance.

¹Kurko, J et al (2013). Genetics of Rheumatoid Arthritis – A comprehensive review.

²Root-Bernstein, R & Fairweather, D (2014). Complexities in the relationship between infection and autoimmunity.

³Cao-Lormeau V-M, Blkake A, Mons S, et al. (2016) Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study.

⁴Diabetes UK (2015). Facts and Stats.

⁵British Society for Rheumatology (2013). Simple Tasks. Rheumatic conditions in the UK: The problem. The impact. The answers.

⁶Crohn's and Colitis UK (2013). Crohn's disease.

⁷Mackenzie, IS et al. (2014). Incidence and prevalence of multiple sclerosis in the UK 1990-2010: a descriptive study in the General Practice Research Database.

⁸NHS Choices (2015). Addison's disease.

⁹HSCIC (2009/10). Health Episodes Statistics.

¹⁰Hex, N et al (2012). Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs.

¹¹Fineberg, NA (2013). The size, burden and cost of disorders of the brain in the UK.

¹²National Rheumatoid Arthritis Society (2010). The economic burden of rheumatoid arthritis.

¹³NHS Choices (2013). Vaccine against type 1 diabetes 'shows promise'.

¹⁴Answer to PQ 22997 (2016)