

# Multiple Sclerosis

Lindsay Nicholson, University of Bristol, UK

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**Multiple sclerosis (MS)** is a human disease that affects the nervous system. The most common pattern of disease is intermittent attacks affecting sight, mobility or sensation followed by gradual recovery. Over time the attacks can lead to permanent disability. The most widely accepted explanation for MS is that the immune system orchestrates repeated episodes of inflammation within the brain, because its normal ability to distinguish healthy tissue from infected tissue has failed. With modern imaging techniques such as **magnetic resonance imaging (MRI)**, these events within the brain can be visualised. As the disease progresses inflammation cause scars, which are associated with loss of insulation on the nerve and with secondary loss of nerve cells. These are recognised at post mortem as 'sclerosis'.

As discussed (See: **Autoimmunity: introduction**), genetic, environmental and stochastic elements all contribute to the development of disease, and while treatment for MS has advanced rapidly in recent years, with the powerful new drugs in development showing a great deal of efficacy in slowing the rate of MS attacks, these drugs also have rare but extremely serious side effects, and further advancements in treatment are needed.

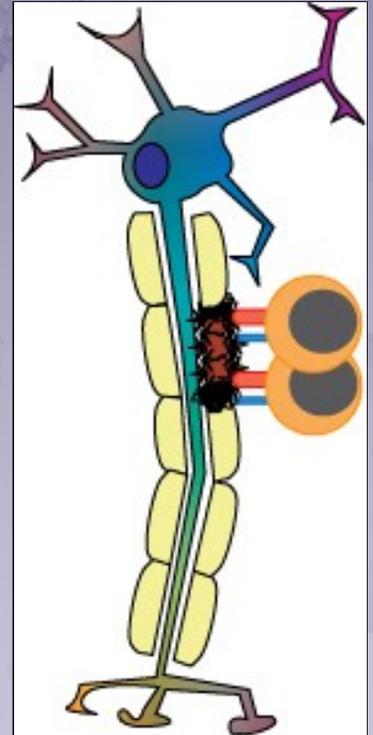
So what are the pressing questions about the immunology of MS that researchers need to answer? Some core concerns are: why does normal immune regulation fail, why does the disease remit and relapse, and how can we move treatment towards the goal of selectively shutting down the anti-self response while preserving the immune system's ability to deal with infection?

Most people agree that MS is triggered by an external event, and this is certainly the case in animal models that are used to study this condition. However, it is unlikely that acute infection with a single microorganism provides a unique initiation point. And it is important to recognise that animal models show that autoimmunity can be spontaneous and sometimes becomes commoner where rates of infection are low rather than high. It is extremely challenging to devise ways of studying this trigger in humans and most of our understanding of this process comes from animal models.

Relapses and remission are likely to be related to activation of cell traffic into the central nervous system triggered by perturbation of the immune response. They do correlate, in animal models, with a spreading of the immune response to different brain proteins but this may simply reflect ongoing inflammation. Other models show that periodic behaviour can arise spontaneously, when the target of the immune response cannot be eliminated. It is also possible that relapses are triggered more easily than the first attack and so happen more often.

Because new drug treatments have rare but extremely serious side effects, we need to learn how to predict those patients with the worst prognosis and offer them these treatments early, while holding them back when progression is expected to be slow. This is another ambitious goal that the research of the future will address.

Finally selective immune therapy remains an important focus and a real possibility. Using vaccination to teach the immune system to 'remember' an infection before it is encountered, is one of the great triumphs of clinical immunology and public health of the 20th century. What the treatment of autoimmunity requires in the 21st century is teaching the immune system to forget.



**Figure 1.** In multiple sclerosis, loss of insulation on the nerve and secondary loss of nerve cells arises in the context of inflammation driven by immune cells that target proteins in the brain.