

The Rise of Multiple Sclerosis

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I recently read a paper by Michal Schwartz (Weizman Institute) (Multiple sclerosis as a by-product of the failure to sustain protective autoimmunity: a paradigm shift. *Neuroscientist*. 2002 Oct;8(5):405-13). The paper promotes the concept that autoimmune T cells have a protective role to play in their CNS. Such a concept provides the last piece of the puzzle for putting the rise of MS is a Darwinian perspective. As is well known, it has been long established that most people have naive T cells that are potentially reactive with myelin antigens. It always bothered me from an evolutionary perspective why such "forbidden clones" survived the Immunological Inquisition of the thymus. What I had not realized is that such autoimmune cells can help repair CNS tissue damage as discussed in the paper.

From an evolutionary point of view, such self reactive T cells must have served an important purpose when trauma was a big problem (i.e. most of human history). Thus autoimmunity can be "purposeful" and a positive trait in terms of natural selection. What the researchers miss is the key point that autoimmunity can also be "accidental". Such accidental autoimmunity occurs through molecular mimicry when autoimmune T cells are activated not because they are needed to help heal some damage but just because they cross-react with a foreign antigen from an infectious agent or food.

Of course from an evolutionary point of view, most individuals who accidentally activated autoimmune immune cells such that they caused problems were gradually negatively selected from the gene pool and the human genome became compatible with the foreign proteins of the Paleolithic environment (i.e. few pathogenic, accidental cross reactions). As an evolved, fail-safe system, vitamin D, which was always in high supply, upregulated regulatory (suppressive) immune cells which kept both purposeful and minor accidental autoimmune reactions in check and prevented them from doing more harm than good.

Autoimmune disease has arisen for two reasons:

1. The relatively recent introduction of innumerable, novel foreign proteins sourced from the foods of agriculture and from infectious agents that crossed over from domesticated animals. These cause many accidental activations of autoimmune T and B cells in genetically susceptible persons.
2. The large increase in accidental autoimmunity goes unchecked for many because the fail-safe vitamin D system fails to suppress such potentially problematic reactions due to a low availability of vitamin D. This short supply of vitamin D is of course mainly the result of human migration to high latitude, low sun areas.