

Introduction to Autoimmune Disease

by Dr. Adele Visser

Introduction

In essence, autoimmune disease occurs as a result of the loss of immunological tolerance, leading to an immune response against self-molecules. The underlying causes are poorly understood, however certain environmental and genetic factors have been identified. Women account for more than 75% of cases and current data suggest the role of sex hormones in the inception of this class of disorders.

Overview of Autoimmune Disease

Autoimmune disease occurs due to reactivity to self-antigens, which may be specific to organs to more systemic antigens (Figure 1).

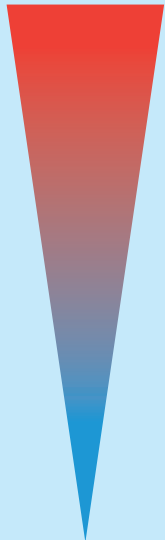
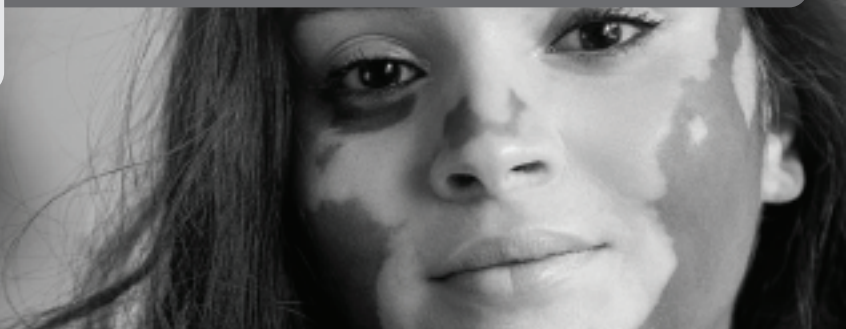
Disease	Auto-antigen	Organ Specific
Hashimoto's thyroiditis	... Thyroglobulin	
Thyrotoxicosis	... Thyroid-stimulating hormone	
Pernicious anaemia	... H ⁺ /K ⁺ -ATPase	
Autoimmune atrophic gastritis	... Intrinsic factor	
Addison disease	... 21-hydroxylase	
Insulin-dependent diabetes mellitus	... Glutamic acid decarboxylase 65	
Goodpasture syndrome	... Type IV collagen	
Myasthenia gravis	... Acetylcholine receptor	
Male infertility (some cases)	... Epididymal glycoprotein FA-1	
Sympathetic ophthalmia	... Interphotoreceptor retinol binding protein	
Multiple sclerosis	... Myelin basic protein	
Autoimmune haemolytic anaemia	... X antigen, glycophorin	
Ulcerative colitis	... Catalase, α-enolase	
Rheumatoid arthritis	... Rheumatoid factor	
Scleroderma	... Topoisomerase 1, laminins	
Systemic lupus erythematosus	... DNA nucleotides and histones, Sm-RNP	
		Non-organ Specific

Figure 1. Range of autoimmune diseases with their associated auto-antigens and target repertoire (adapted from reference 1).



Mechanisms of Autoimmune Disease

Auto-reactive immune cells (specifically T and B lymphocytes) are found in healthy individuals and are typically regulated by the actions of immune tolerance. A disruption in this balance manifests as autoimmune disease. Various mechanisms have been described.

It is typically used in the setting of:

I. Release of Isolated Auto-antigens

Certain antigens are found in protected or cryptic sites, where they are not exposed to the immune system as such. Various reactive T-cells are not deleted during thymic training but are not exposed to the antigen itself.

However, upon cellular damage through trauma or viral infection, these antigens may become exposed, triggering an autoimmune response and consequently disease. Diabetes mellitus following infection by Coxsackie B viruses serve as an example.

II. Chemical Alteration of Self-peptides

As in the previous mechanism, self-reacting T-cells may be present but not activated. Another stimulus may increase the secretion of IFN- γ which upregulates the antigen-presenting MHC molecules, enhancing the chances of autoreactivity.

A further example is the induction of a hapten-induced autoimmune response where drugs lead to the development of a self-reactive immune state. The drug molecule binds to a self-antigen, which leads to sufficient alteration to allow for immune stimulation.

III. Molecular Mimicry

Fragments from various infectious agents may show sufficient similarity to self-antigens and thereby induce an immune reaction to both. The membrane proteins from the group B *Streptococci* show similarity to cardiac myosin and may consequently lead to rheumatic fever. Similar associations have been made with *Yersinia enterocolitica* and Grave's disease.

IV. Polyclonal Activators

Again, microbial antigens have been implicated in the activation T-cells which bind to both MCH class II molecules on B-cells, and directly to B-cells themselves. This super-activation leads to the formation of a large repertoire of antibodies, some of which may be self-reactive.

V. Genetic Factors

Genetic association is more frequently seen in organ-specific autoimmune disease. Despite this, concordance rates between identical twins are relatively low, owing to the varied identity of the TCR and Ig genes' formation due to recombination and somatic hypermutation processes. However, associations are noted with certain MCH haplotypes and may also be found in T-cell Receptor haplotypes.

Conclusion

The highly complicated nature of the human immune system makes a simplistic explanation to autoimmune disease highly improbable. Not only is the disease pathogenesis highly variable, but so also the clinical manifestations and laboratory findings associated there-with. With this in mind, it would be prudent to always employ a multi-disciplinary approach where the clinical features stand central to decision making.

References

1. Smit DA, Germolec DR. 1999. Introduction to Immunology and Autoimmunity. *Environmental Health Perspectives*. 107(5): 661-665
2. Hodson R, 2021. Autoimmune disease. *Nature*. 595, S45 doi: <https://doi.org/10.1038/d41586-021-01833-y>

JDJ Pathology Laboratories

☎ 031 201 4647

📞 067 826 7473

📠 031 201 4910

✉ clientservices@jdjd.co.za

✉ accounts@jdjd.co.za

🌐 www.jdjd.co.za