Johns Hopkins Engineering

Immunoengineering

Allergy and Autoimmunity

Autoimmune Diseases

JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

Learning Objectives

- Explain the mechanisms of tolerance.
- Identify major cellular and protein components of the immune response to allergies and autoimmunity and their functions
- Analyze allergic and autoimmune disorders and clinical phenotypes associated with them
- Evaluate the mechanisms of the cause of autoimmune diseases and recent increase in allergies and autoimmunity
- Propose interventions to reduce the severity of allergic and autoimmune diseases

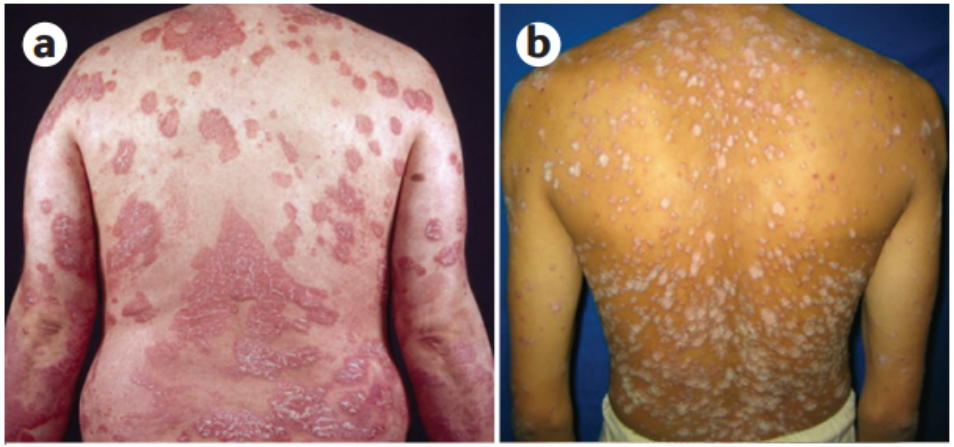
Examples

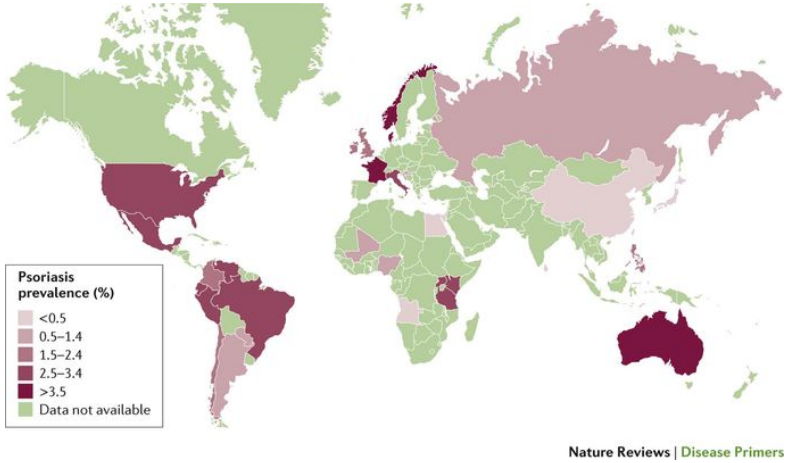
Disease	Disease mechanism	Consequence	Prevalence
Psoriasis	Autoreactive T cells against skin-associated antigens	Inflammation of skin with formation of scaly patches or plaques	1 in 50
Rheumatoid arthritis	Autoreactive T cells against antigens of joint synovium	Joint inflammation and destruction causing arthritis	1 in 100
Graves' disease	Autoantibodies against the thyroid-stimulating-hormone receptor	Hyperthyroidism: overproduction of thyroid hormones	1 in 100
Hashimoto's thyroiditis	Autoantibodies and autoreactive T cells against thyroid antigens	Destruction of thyroid tissue leading to hypothyroidism: underproduction of thyroid hormones	1 in 200
Systemic lupus erythematosus	Autoantibodies and autoreactive T cells against DNA, chromatin proteins, and ubiquitous ribonucleoprotein antigens	Glomerulonephritis, vasculitis, rash	1 in 200
Sjögren's syndrome	Autoantibodies and autoreactive T cells against ribonucleoprotein antigens	Lymphocyte infiltration of exocrine glands, leading to dry eyes and/or dry mouth; other organs may be involved, leading to systemic disease	1 in 300
Crohn's disease	Autoreactive T cells against intestinal flora antigens	Intestinal inflammation and scarring	1 in 500
Multiple sclerosis	Autoreactive T cells against brain antigens	Formation of sclerotic plaques in brain with destruction of myelin sheaths surrounding nerve cell axons, leading to muscle weakness, ataxia, and other symptoms	1 in 700
Type 1 diabetes (insulin-dependent diabetes mellitus, IDDM)	Autoreactive T cells against pancreatic islet cell antigens	Destruction of pancreatic islet β cells leading to nonproduction of insulin	1 in 800

Figure 15.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Psoriasis

Disease	Disease mechanism	Consequence	Prevalence
Psoriasis	Autoreactive T cells against skin-associated antigens	Inflammation of skin with formation of scaly patches or plaques	1 in 50

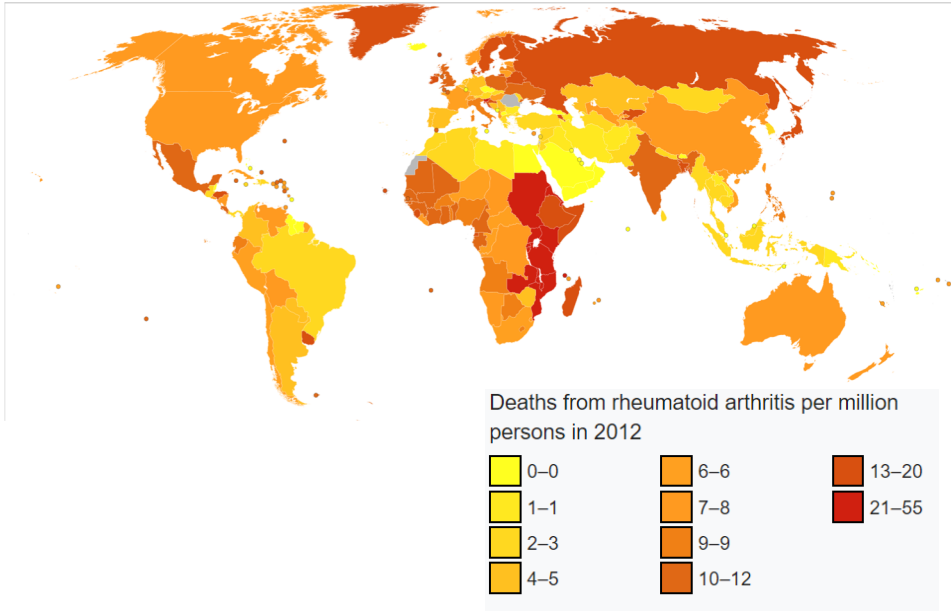




J.E. Greb et al., Psoriasis, *Nature Reviews Disease Primers 2* (2016) 16082

Rheumatoid Arthritis

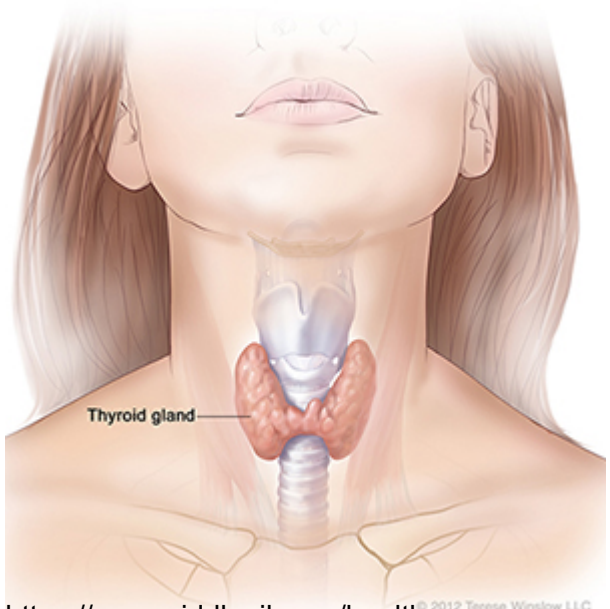
Rheumatoid arthritis	**Autoreactive T cells against antigens of joint synovium**	**Joint inflammation and destruction causing arthritis**	**1 in 100**



https://en.wikipedia.org/wiki/Rheumatoid_arthritis

Grave's Disease

Graves' disease	**Autoantibodies against the thyroid-stimulating-hormone receptor**	**Hyperthyroidism: overproduction of thyroid hormones**	**1 in 100**

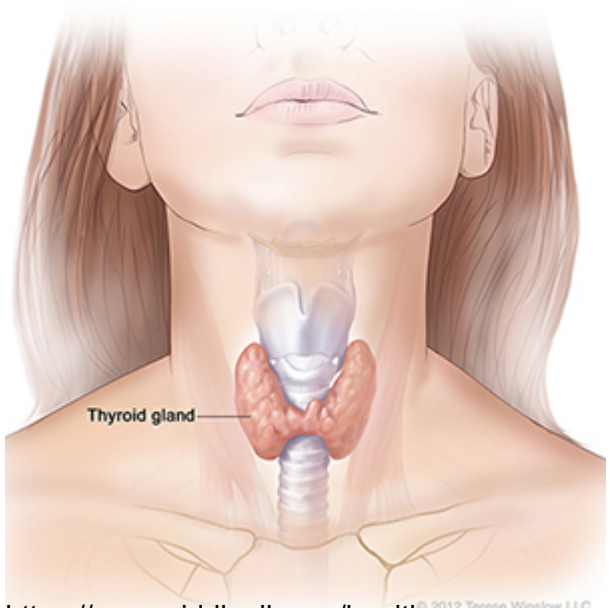


https://www.niddk.nih.gov/health-information/endocrine-diseases/graves-disease

(Menconi, Francesca, Claudio Marcocci, and Michele Marinò. "Diagnosis and classification of Graves' disease." *Autoimmunity reviews* 13.4 (2014): 398-402.)

Hashimoto’s Thyroiditis

Hashimoto's thyroiditis	**Autoantibodies and autoreactive T cells against thyroid antigens**	**Destruction of thyroid tissue leading to hypothyroidism: underproduction of thyroid hormones**	**1 in 200**

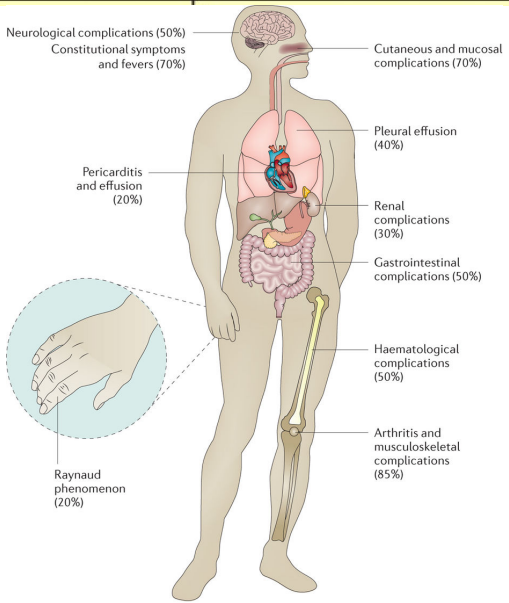


https://www.niddk.nih.gov/health-information/endocrine-diseases/graves-disease

https://www.niddk.nih.gov/health-information/endocrine-diseases/hashimotos-disease

Systemic lupus erythematosus

Systemic lupus erythematosus	**Autoantibodies and autoreactive T cells against DNA, chromatin proteins, and ubiquitous ribonucleoprotein antigens**	**Glomerulonephritis, vasculitis, rash**	**1 in 200**



Kaul et al., Systemic lupus erythematosus, *Nature Reviews Disease Primers 2* (2016) 16039

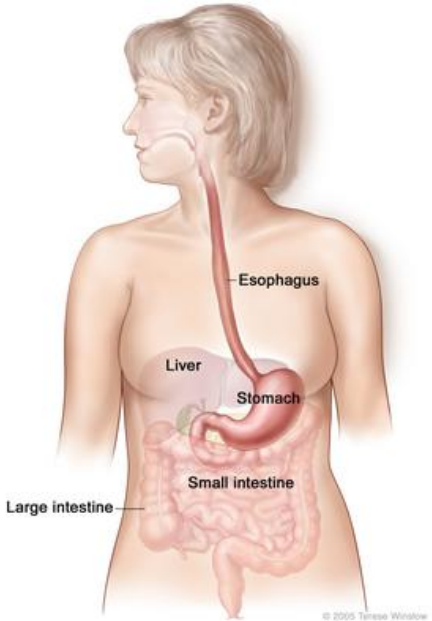
Sjogren's syndrome

Sjögren's syndrome	Autoantibodies and autoreactive T cells against ribonucleoprotein antigens	Lymphocyte infiltration of exocrine glands, leading to dry eyes and/or dry mouth; other organs may be involved, leading to systemic disease	1 in 300

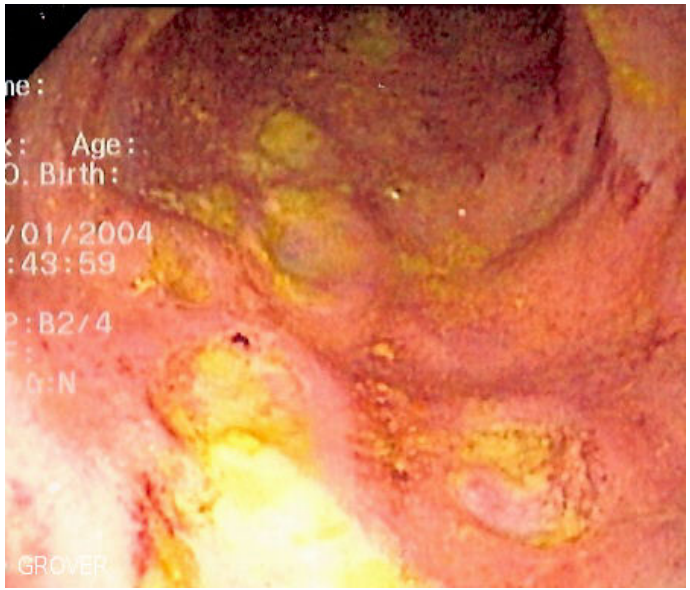
Brito-Zeron et al., Sjögren syndrome, *Nature Reviews Disease Primers 3* (2016) 16047

Chron's Disease

Crohn's disease	**Autoreactive T cells against intestinal flora antigens**	**Intestinal inflammation and scarring**	**1 in 500**



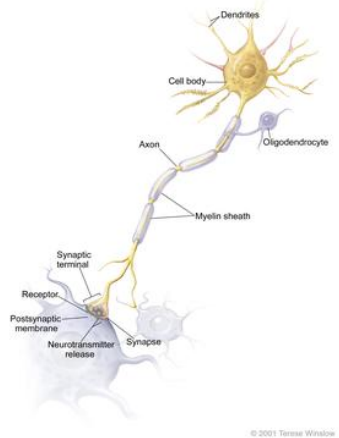
https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0022855/



https://en.wikipedia.org/wiki/Crohn%27s_disease#/media/File:CD_colitis.jpg

Multiple Sclerosis

Multiple sclerosis	**Autoreactive T cells against brain antigens**	**Formation of sclerotic plaques in brain with destruction of myelin sheaths surrounding nerve cell axons, leading to muscle weakness, ataxia, and other symptoms**	**1 in 700**



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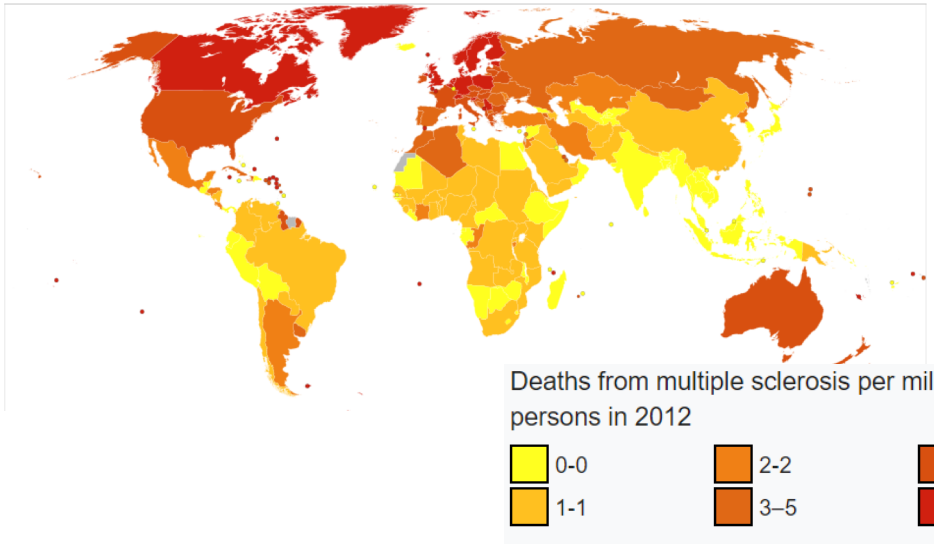
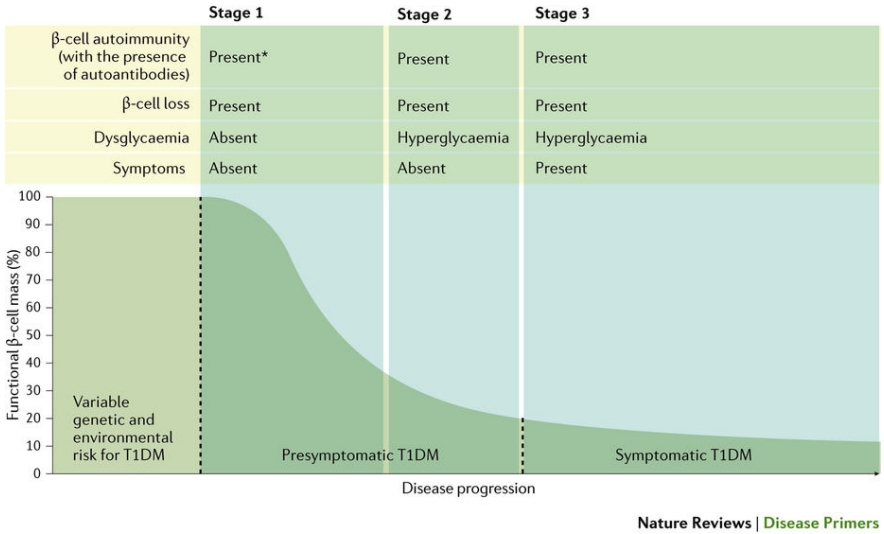


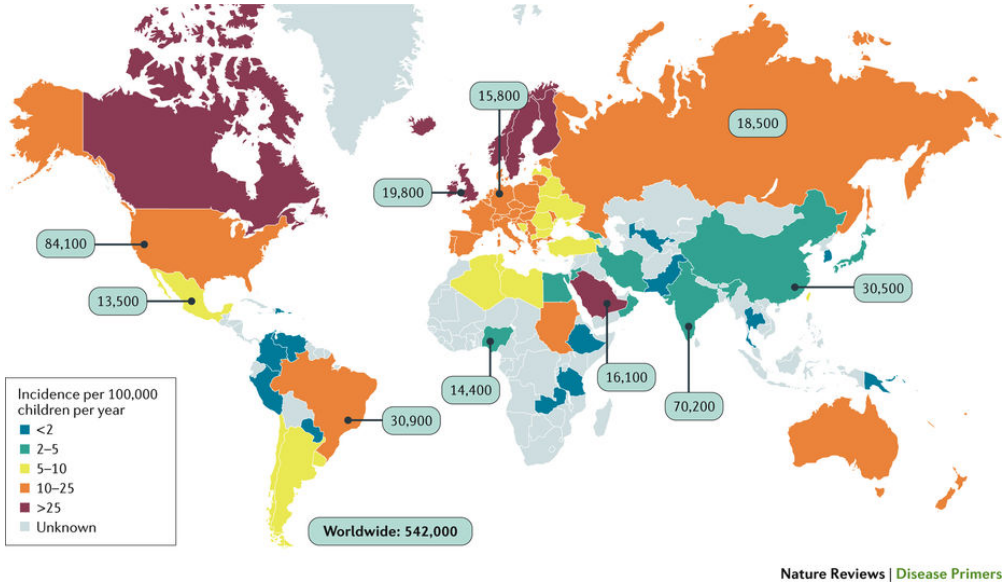
https://en.wikipedia.org/wiki/Multiple_sclerosis#/media/File:Multiple_sclerosis_world_map-Deaths_per_million_persons-WHO2012.svg

Type 1 Diabetes

Type 1 diabetes (insulin-dependent diabetes mellitus, IDDM)	**Autoreactive T cells against pancreatic islet cell antigens**	**Destruction of pancreatic islet β cells leading to nonproduction of insulin**	**1 in 800**

Figure 15.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)





Katsarou, A. et al. Type 1 diabetes mellitus. *Nat. Rev. Dis. Primers 3*, 17016 (2017)

Summary

- Unknown mechanisms
- Severe symptoms
- Sex/Genetic linkages
- Therapies for general immunosuppression
- Rise of some of the diseases in developing world
- Organ versus systemic disease

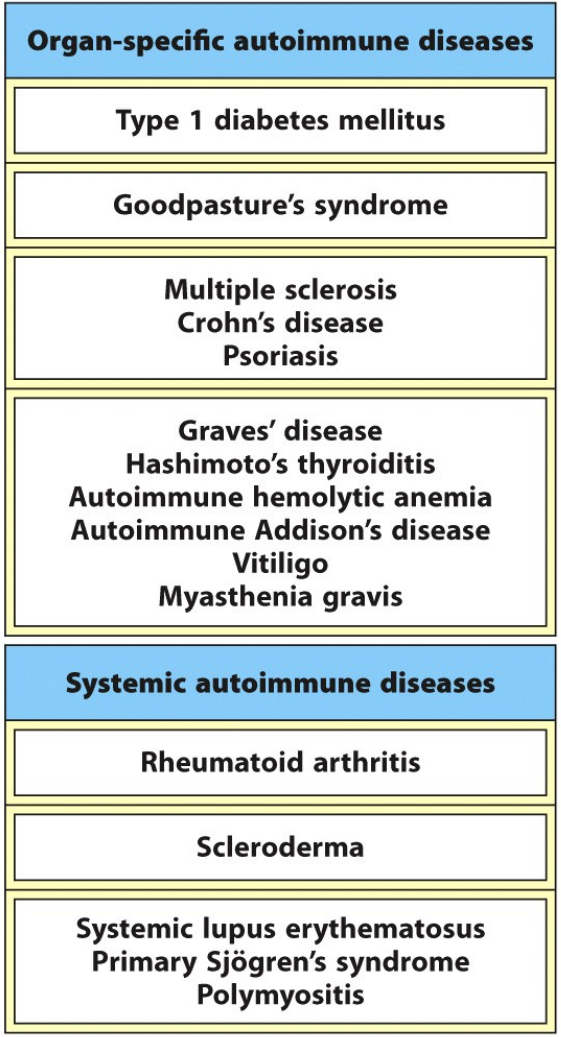


Figure 15.11 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Summary

Autoimmune diseases involve all aspects of the immune response			
Disease	**T cells**	**B cells**	**Antibody**
Systemic lupus erythematosus	Pathogenic Help for antibody	Present antigen to T cells	Pathogenic
Type 1 diabetes	Pathogenic	Present antigen to T cells	Present, but role unclear
Myasthenia gravis	Help for antibody	Antibody secretion	Pathogenic
Multiple sclerosis	Pathogenic	Present antigen to T cells	Present, but role unclear

Figure 15.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)