The Gender Bias of Autoimmune Diseases

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The Immune System & Autoimmune Diseases

The immune system is the part of the body that is responsible for protecting the body against foreign invaders.(1)

The bodies first line of defense are physical and chemical barriers such as skin, mucosal membranes and stomach acid. If organisms do manage to enter, the body has 2 possible responses, the innate, which is preformed, always prepared but is non-specific and the adaptive response which takes time but provides a more potent and specific response (also provides memory). (1)

The adaptive response is composed of both a cell mediated (mainly T-cells) and a humoral (mainly B-cells) immune response. (1)

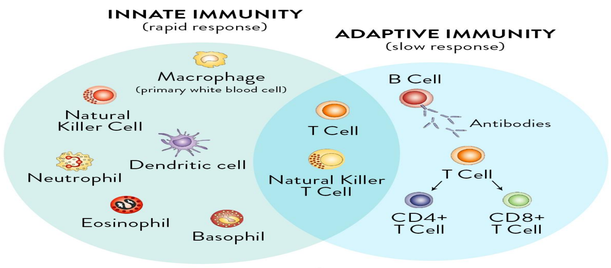

Figure 1.1(7)

Tolerance can be seen as a specific immunological unresponsiveness to the bodies self antigen, problems in this process may lead to loss of tolerance and the development of an immune response to self antigens. This is the method by which autoimmune diseases develop. The most important step is the activation of self reactive helper (CD_4) T cells. (1)

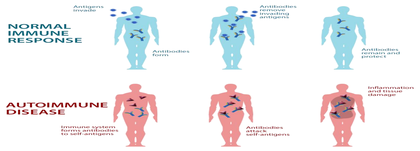

Figure 1.2(8)

The Prevalence Of Autoimmune Diseases In Females

In general it is clear that autoimmune diseases are more common in females.(1) (2)Overall Around 90% of all autoimmune diseases occur in females. (2)

It is however important to note that numbers taken from different geographical locations show variable results, although the conclusion is the same this shows that other environmental factors must be taken into consideration.(2)

Figure 2.1(9)

Autoimmune Disease	Female (%)	Prevalence (per 10^5)
Neurological system		
Multiple sclerosis	64	58.3
Narcolepsy	39	30.6
Endocrine system		
Addison's disease	63	14
Diabetes mellitus, type 1	45	480
Graves' disease	88	629
Hashimoto's autoimmune thyroiditis	95	791.7
Gastrointestinal system		
Autoimmune hepatitis type 1	78	16.9
Coeliac disease	57	750
Crohn's disease	41	25
Pernicious anemia/atrophic gastritis	67	150.9
Primary biliary cirrhosis	89	14.6
Ulcerative colitis	65	30
Haemopoetic system		
Antiphospholipid syndrome	74	21.5
Immune thrombocytopenic purpura	70	72
Musculoskeletal system		
Rheumatoid arthritis	75	860
Cardiovascular system		
Kawasaki disease	40	10
Rheumatic fever	50	250
Temporal arteritis	85	30
Cutaneous/mucous membranes		
Alopecia areata	50	150
Dermatitis herpetiformis	36	11.2
Vitiligo	52	400.2
Systemic		
Scleroderma	92	24
Sjögren's syndrome	94	14.4
Systemic lupus erythematosus	88	32

Figure 2.2(2)

Genetic Differences Between Males & Females

While males carry an X and a Y chromosome females carry 2 X chromosomes. To prevent over expression of the X chromosome one of them becomes inactivated and becomes what is known as a Barr body. This structure is however missing in males. The fact that males have only one X chromosome also explains why males are more severely affected by X linked genetic diseases, as all cells of the male body would harbor the mutated X chromosome. (3) (4)

Figure 3.1(10)

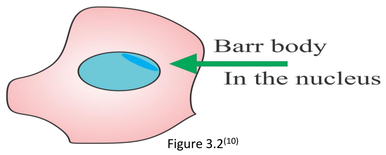

Figure 3.2(10)

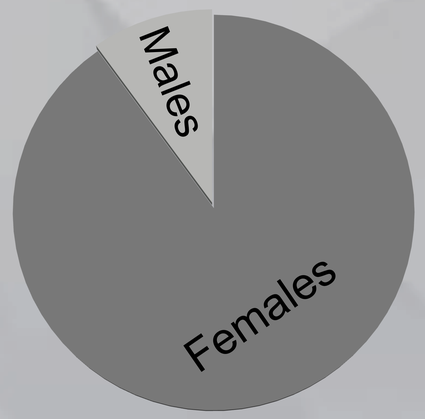

Figure 4

Hormonal Differences Between Males & Females

The class of sex hormone found in males are the androgens (mainly testosterone and dihydrotestosterone). These are responsible for the development of male characteristics.(5)

In females the 2 main hormones are estrogen and progesterone which are responsible for the development of female sex organs, and female characteristics, they are both also involved in pregnancy and the menstrual cycle.(5)

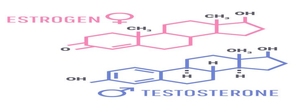

Figure 5(11)

Immunological Difference

It is now well known that immune cells carry receptors for estrogen (ER), progesterone (PR) and androgens (AR). Very little is known about the PR and the AR, but both testosterone and progesterone are known to be anti-inflammatory. More is known on the ER and they have even been classified into 2 types, an alpha and beta receptor. However the exact function of estrogen on the immune system is yet to be determined, but studies have shown that it increases both the humoral and cell mediated immune response. (2)(3)

Figure 6.1

It is a well established fact that the female immune system is stronger than that of the male. The X chromosome was found to carry genes that play an important role in our immune response. So having 2 of copies of that chromosome allows for a more diverse & effective immune response.(3)(6)

The X chromosome however was found to play an important role in the higher incidence of autoimmune diseases in females. So we can see it acting as a double-edged sword providing a stronger defense system that may end up attacking itself. (3)

Figure 6.2(12)

Conclusion

It is clear that females are at a higher risk to develop autoimmune diseases, and many possible factors have been identified however more work should be done on the rates of developing a disease and the severity of its symptoms in relation to time to obtain a better understanding of the effects of hormones on the immune system for example during pregnancy and after menopause.

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