Musculoskeletal Block

Immunology

Lecture 1

Mechanisms of Autoimmunity

In this document you will find some main points gathered from the 1st lecture..This document is NOT a replacement for the lecture..If you need additional information go back to the lecture or use a book as a reference so you understand everything correctly.

Hopefully all the information is correct and Hope you find them Useful.

Good Luck to everyone.

430 Immunology Team

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Immunology

Mechanisms of Autoimmunity

Some main points you can go through and revise from:

Definitions:

Autoimmunity → A condition that occurs when the immune system, mistakenly, attacks and destroys healthy body tissue.

Tolerance = Endurance → "Meaning that our Immune system bares with our own antigens and doesn't destroy them there for our own antigens can circle the body without action taken against them"

Self Antigens → Antigens that are naturally Present in our system. "Our own Antigens"

Non-Self Antigens → Foreign Antigens that may cause diseases and harm us. "Foreign Antigens"

Anergy → No energy "Cell becomes Powerless or Unresponsive"

Apoptosis → Programmed Cell Death

Sequestered → Hidden

Note:

*Normally, Our Immune System can tell the difference between self and non-Self antigens, meaning that it can tolerate (Not Attack) our own antigens.

There are 2 ways by which our Immune System DOES NOT attack our own antigens

These 2 ways are:

1- Deletion = Removal of B-Cells and T-Cells (Auto-reactive cells) which do not differentiate between Self and Non-Self Antigens.

2- Functional Inactivation = B-Cells and T-Cells Lose the power of Attacking our own Antigens.

Self Tolerance can be divided into 2 subdivisions:

1- Central Tolerance

2- Peripheral Tolerance

Central Tolerance:

***Central Tolerance →** Works to eliminate Auto reactive B-Cells In Bone Marrow and Auto reactive T-Cells in Thymus.

1- Happens in the Primary Lymphoid organs (Thymus and Bone Marrow)

2- Two types of cells are produced:

* Educated T-Cells (Cells which can tell the difference between self and Non-Self Antigens)

← Central Tolerance Continued:

* Auto-Reactive Cells (Cells which do not differentiate between self and Non-Self Antigens)

3- Educated T-Cells are allowed to go into Blood Stream (Because they are NOT going to attack your own antigens)

4-Auto-Reactive Cells are NOT allowed to go into Blood Stream (They are deleted before they do so)

Note:

Central Tolerance Does NOT remove ALL the auto reactive cells, There for we have Peripheral tolerance.

Peripheral Tolerance of T Lymphocytes :

1-Anergy:

*Anergy is the Opposite of Energy, Anergy means NO POWER (The cell becomes powerless)

Three Things are needed to Obtain Anergy:

*Antigen presentation on **MHC 1** or **MHC 2**
*__B7__(On antigen presenting Cell)
*__CTLA4__(on T-Cell) .. (Cytotoxic T-Lymphocyte Antigen 4) also known as **CD152**

-Normally, when a T-Cell attaches to the **MHC** on the antigen presenting cell and a B7 signal is sent the cell becomes activated.

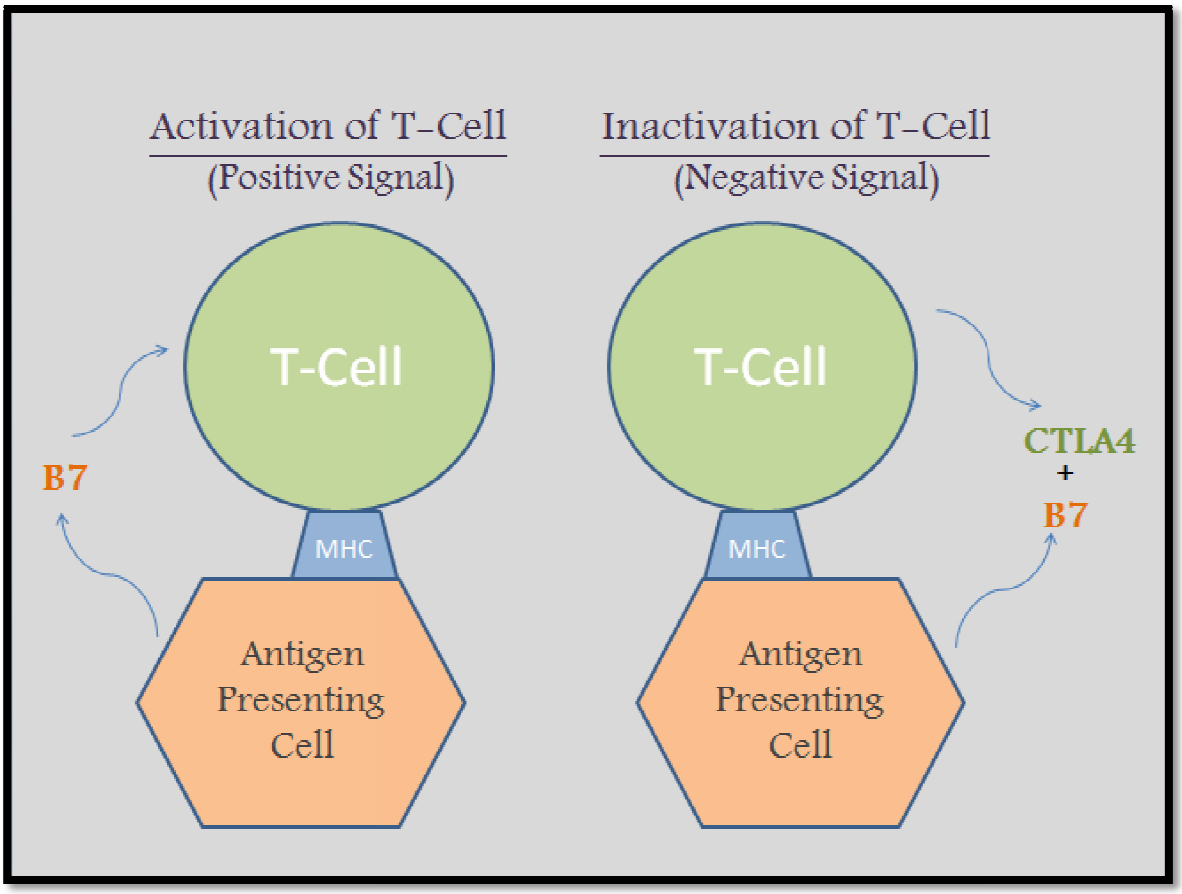
-In the case of an auto-reactive cell the B7 Binds to the **CTLA4** which sends out a Negative signal and that's how the cell becomes inactive. (So the body can protect itself from autoimmune diseases).

2- Apoptosis (Programmed Cell Death):

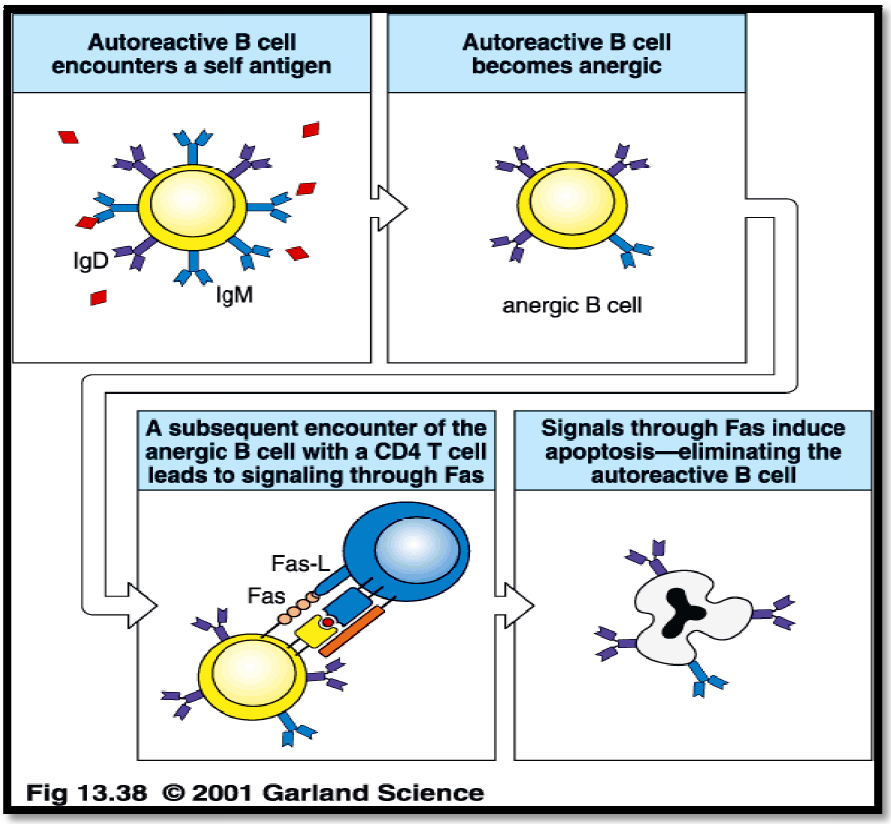
Apoptosis can occur in 2 ways

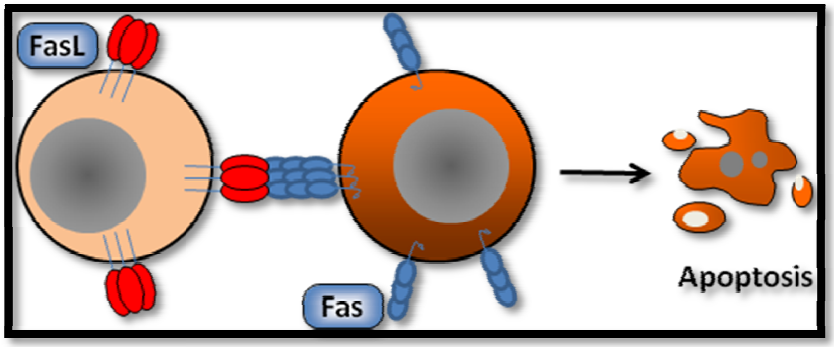
*Fas/FasL Apoptosis (**FasR = Fas Receptor →** (is present on the T-Cell), **(Fas-L =Fas Legend(CD95L)→** is present one the Antigen presenting cell)..When they bind to each other they induce apoptosis.

*Expression of pro-apoptotic proteins.



Pictures Showing Fas/FasL Apoptosis





Note:

*Clonal ignorance → in which host immune responses are directed to ignore self-antigens.

The Auto-reactive cell does not cross the Blood barrier and there for does not reach slef antigens.

Failure of Immune Tolerance (Development of Autoimmunity)

1. Release or exposure of sequestered antigens:

-Some self antigens cannot be seen by the developing Immune system because they are hidden in certain tissues

-Therefore the Immune system does not develop tolerance against them.

-And that's why T-Cells are activated against those antigens if they are released (Like in Myocardial Infarction)

Examples of Sequestered Antigens: *(Very Important)*

*Myelin basic protein (MBP), associated with MS (Multiple sclerosis)

*Sperm-associated antigens in some individuals following vasectomy

*Lens and corneal proteins of the eye following infection or trauma

*Heart muscle antigens following myocardial infarction

Just to help you understand ..Vasectomy→ is a surgical procedure in which the vasa deferentia of a man are severed, and sometimes tied or sealed. (This is how the antigens might be released)

2.Cross-reacting Antigens (Molecular Mimicry):

*** Mimicry..(Mimic)=similar to or (Acts like)**

-Some viral and Bacterial Antigens have the same components as our self antigens

- This phenomenon, known as molecular mimicry, occurs in a wide variety of organisms. ← *(Important)*

- Molecular mimicry can cause auto immune diseases

3. Inappropriate Expression of Class II MHC Molecules:

- **Class II MHC** ordinarily expressed on antigen presenting cells, such as macrophages, dendritic cells and B cells *(Important)*

- The appearance of **MHC** on Non-antigen presenting cells causes activation of T-Cells

-Those activated T-Cells Then Attack our Autoantigens

*An autoantigen is usually a normal protein or complex of proteins (and sometimes DNA or RNA)

-And therefore causes autoimmune diseases

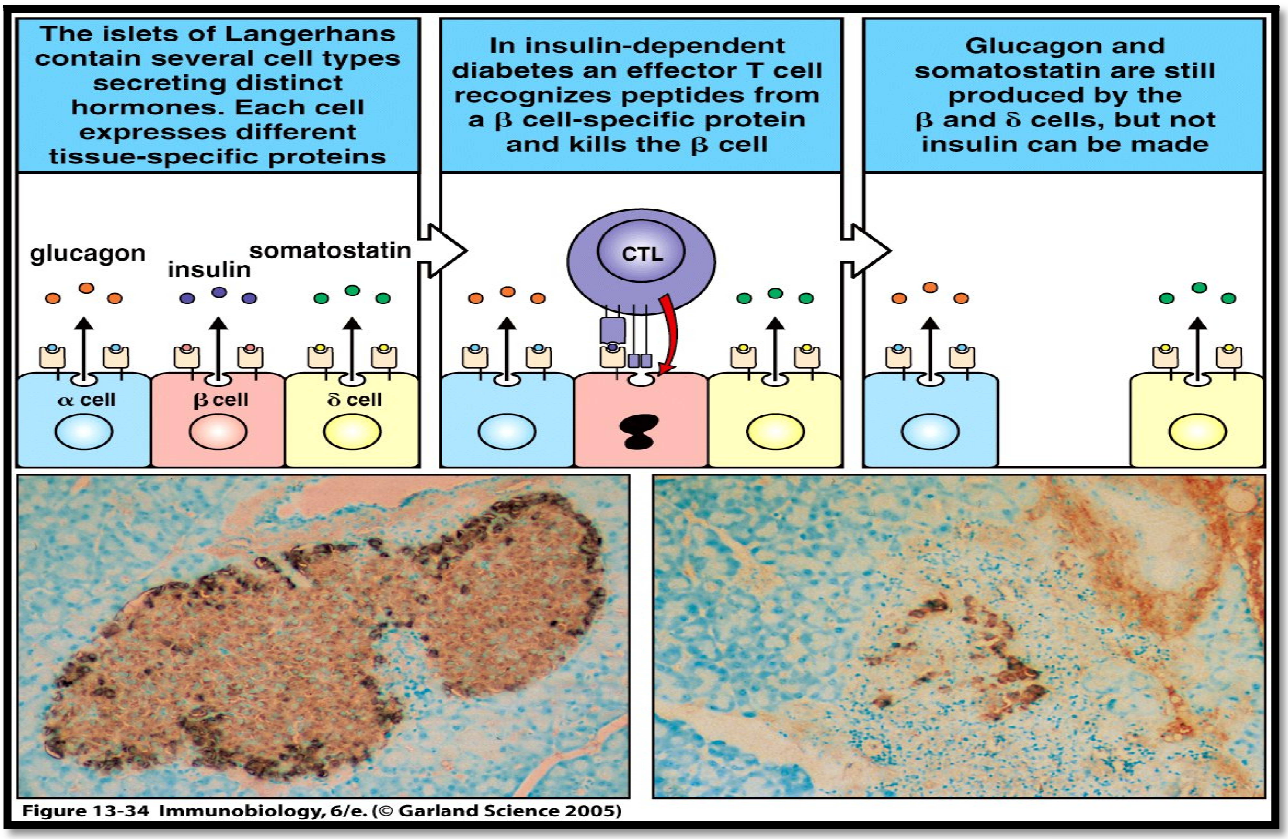
- This may occur due to the local production of **IFN-γ,** which is known to increase class II MHC expression on a variety of cells ← *(Important)*

- The inducer of **IFN-γ** under these circumstances could be a viral infection.

An Example of the appearance of **MHC** on Non-antigen presenting cells → Diabetes Type 1

Brief Explanation on How Diabetes Type 1 Happens:

1-MHC is expressed on Insulin Producing cells
2-These Cells are attacked and destroyed by the immune system
3-The subsequent lack of insulin leads to increased blood and urine glucose = Diabetes



4. Polyclonal B-Cell Activation

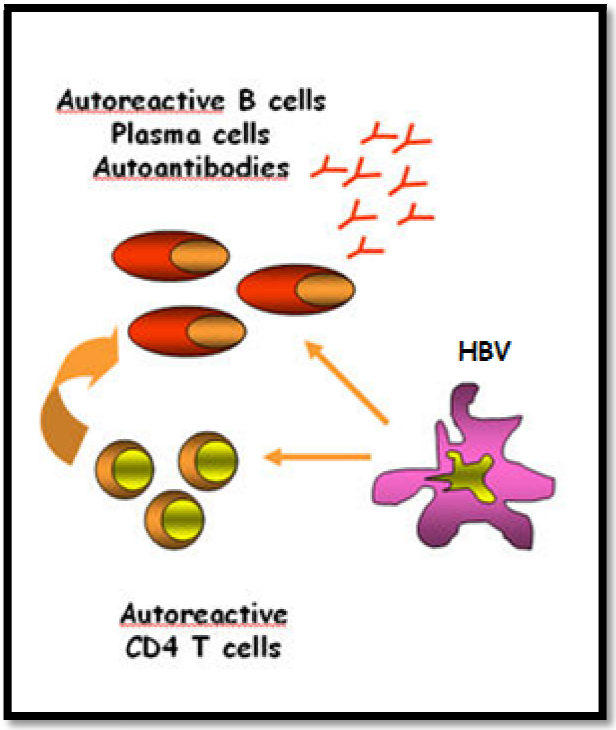
*This happens when certain Viruses or Bacteria attack and activate non-specific B-Cells

Examples of these viruses & Bacterias:

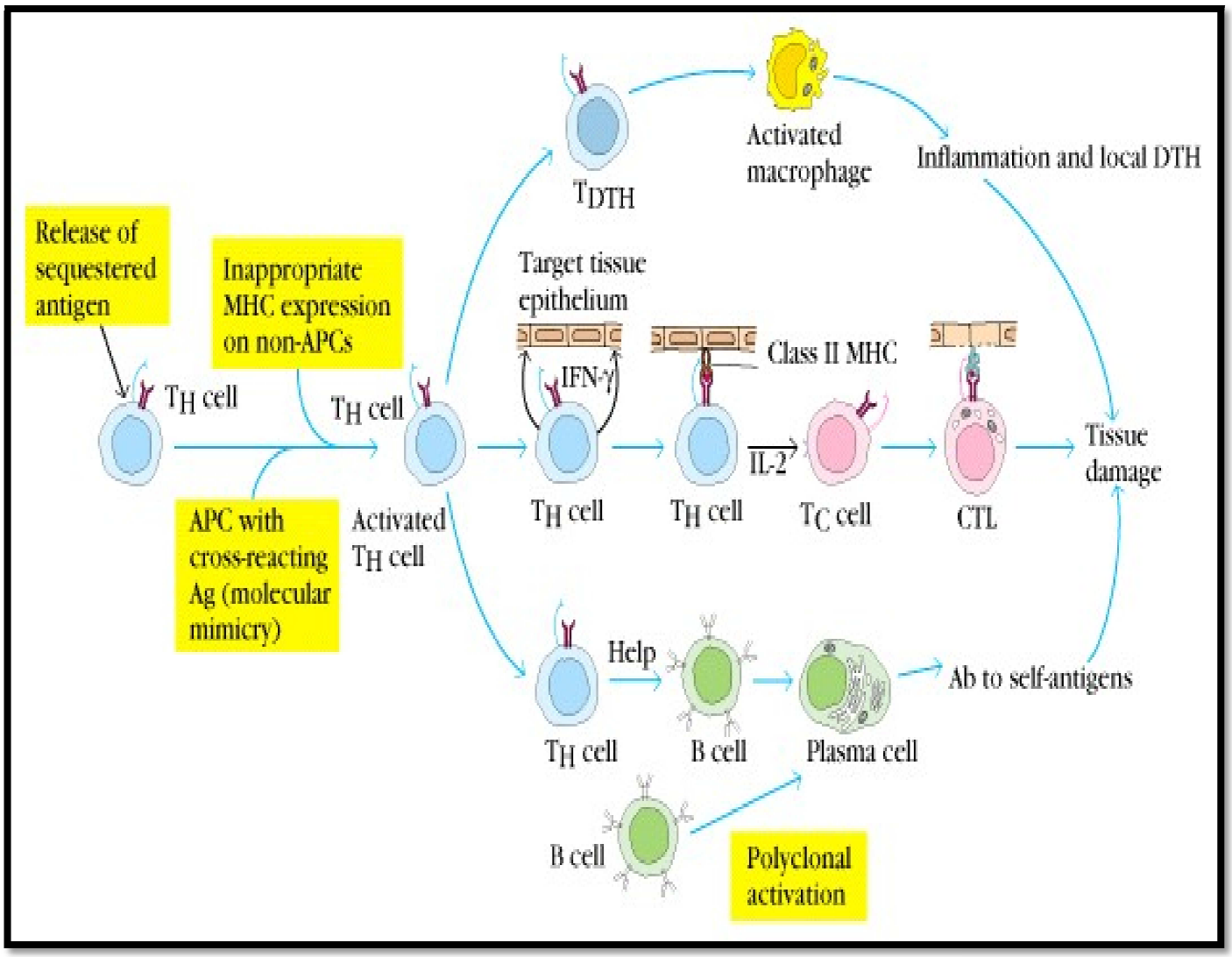
*Certain gram negative bacteria
*Herpes simplex virus
*Cytomegalovirus
*Epstein Barr Virus
*Human immunodeficiency virus (HIV)

-These viruses induce the proliferation of numerous clones of B cells to secrete **IgM** in the absence of a requirement for **CD4 T cell** help (B-Cells Secrete them when we don't need them)
- Polyclonal activation leads to the activation of self-reactive B cells and autoantibody production

- Patients with infectious mononucleosis (caused by EBV) and AIDS (HIV) have a variety of auto-antibodies



Summary of proposed mechanisms of autoimmunity



5. Hormonal Factors

*About 90% of autoimmune diseases occur in women – cause not known

-In animal models estrogen can induce B cells to enhance formation of anti-DNA antibodies

-SLE either appears or exacerbates during pregnancy

*Hormones are at their Peak in a Female when she is Pregnant.

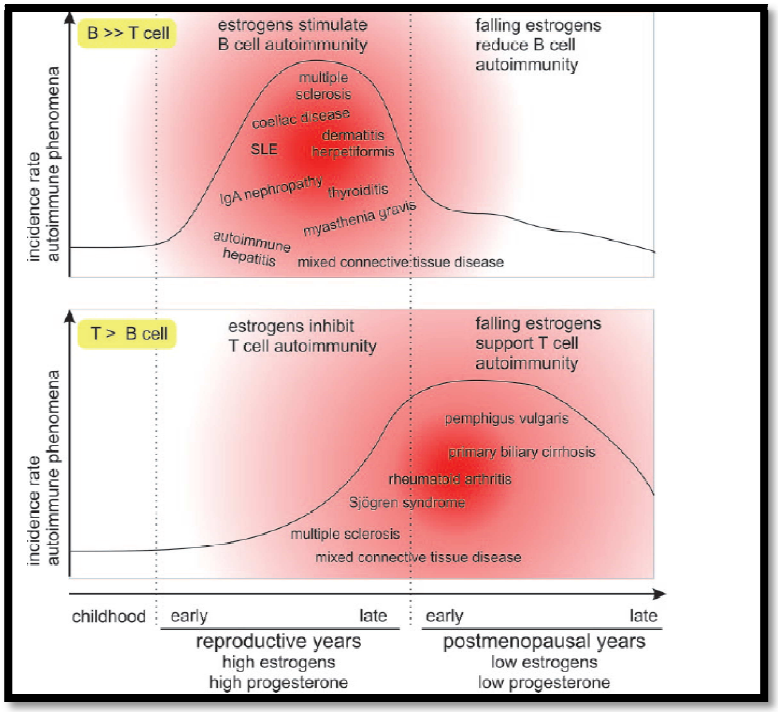


Diagram Shows That:

Women During Reproductive Years > Autoimmune Disease is Caused Mainly by B-Cells (Antibody Mediated Autoimmune diseases)

Women During Menopausal Years > Autoimmune Disease is Caused Mainly By T-Cells (Cell Mediated Autoimmune diseases)

6. Drug- Induced Lupus Erythematosus

Lupus erythematosus like syndrome develops inpatients receiving a variety of drugs such as

*Hydralazine (used for hypertension)
*Procainamide
*Isoniazid
*Penicillin

-Many are associated with the development of ANAs
-Renal and CNS involvement is uncommon
-Anti-histone antibodies are frequently present

- Some drugs .. If taken for a Long Time .. Can Cause Autoimmune diseases By Production of antibodies against self Antigens → Can Cause ANA (Antinuclear Antibody) Which is Abnormal in a Healthy Individual
- SLE = Systemic Lupus Erythematosus > Butterfly Rash