

IMMUNOLOGICAL TOLERANCE

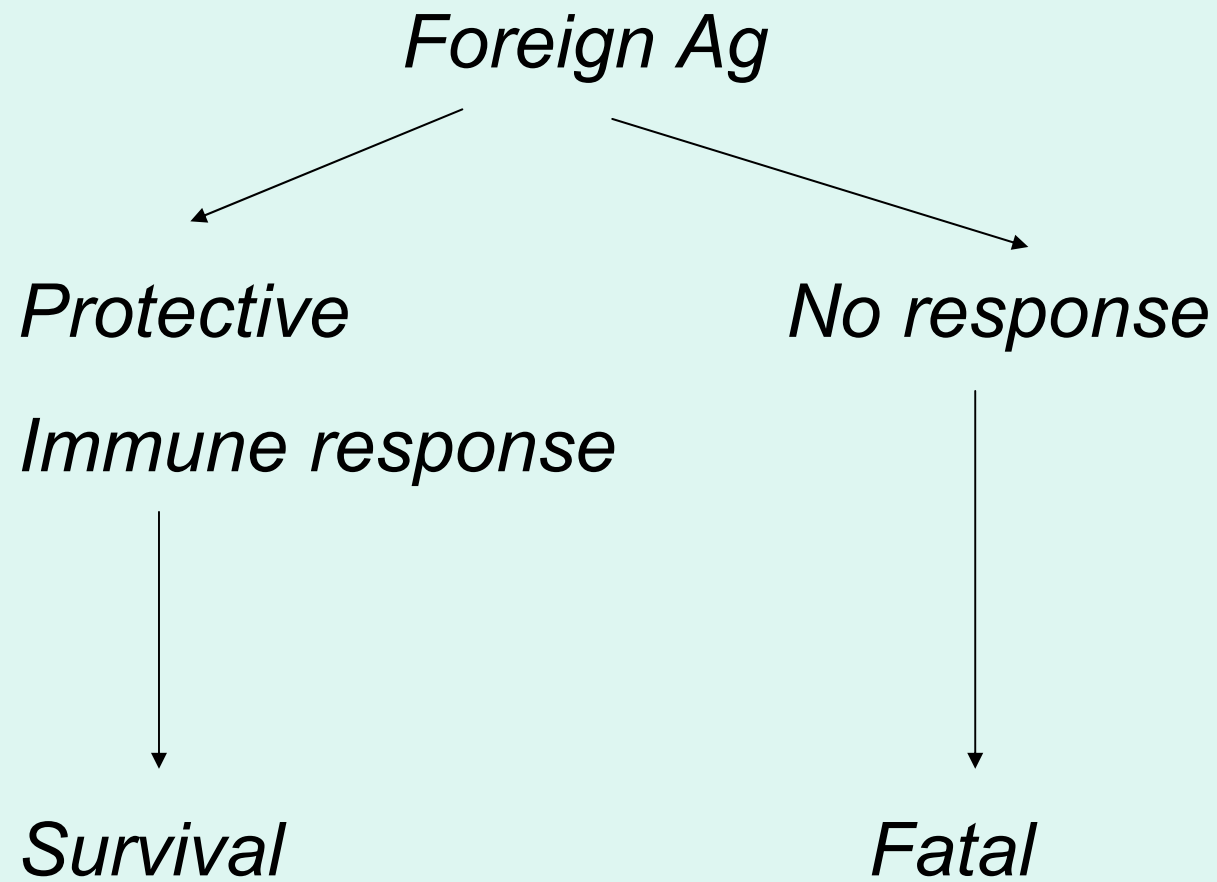
Definition

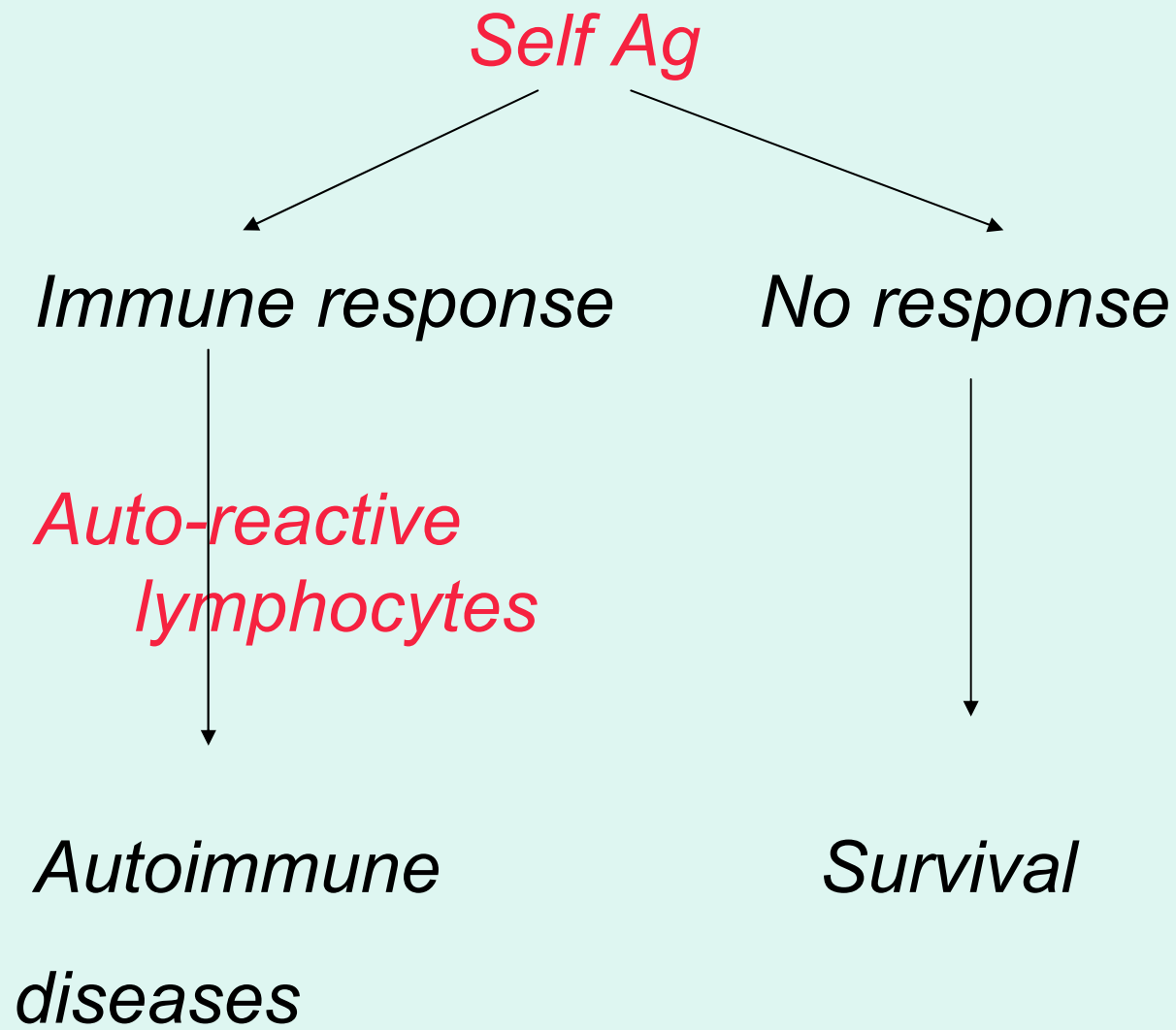
- Types of tolerance

Central Tolerance

Peripheral Tolerance

- T cell tolerance
- B cell tolerance
- Maintenance of tolerance





IMMUNOLOGICAL TOLERANCE

A state of specific immunological unresponsiveness to self Ag

Types of Tolerance

1. **Central Tolerance** carried out during fetal development in the **PRIMARY LYMPHOID ORGANS**

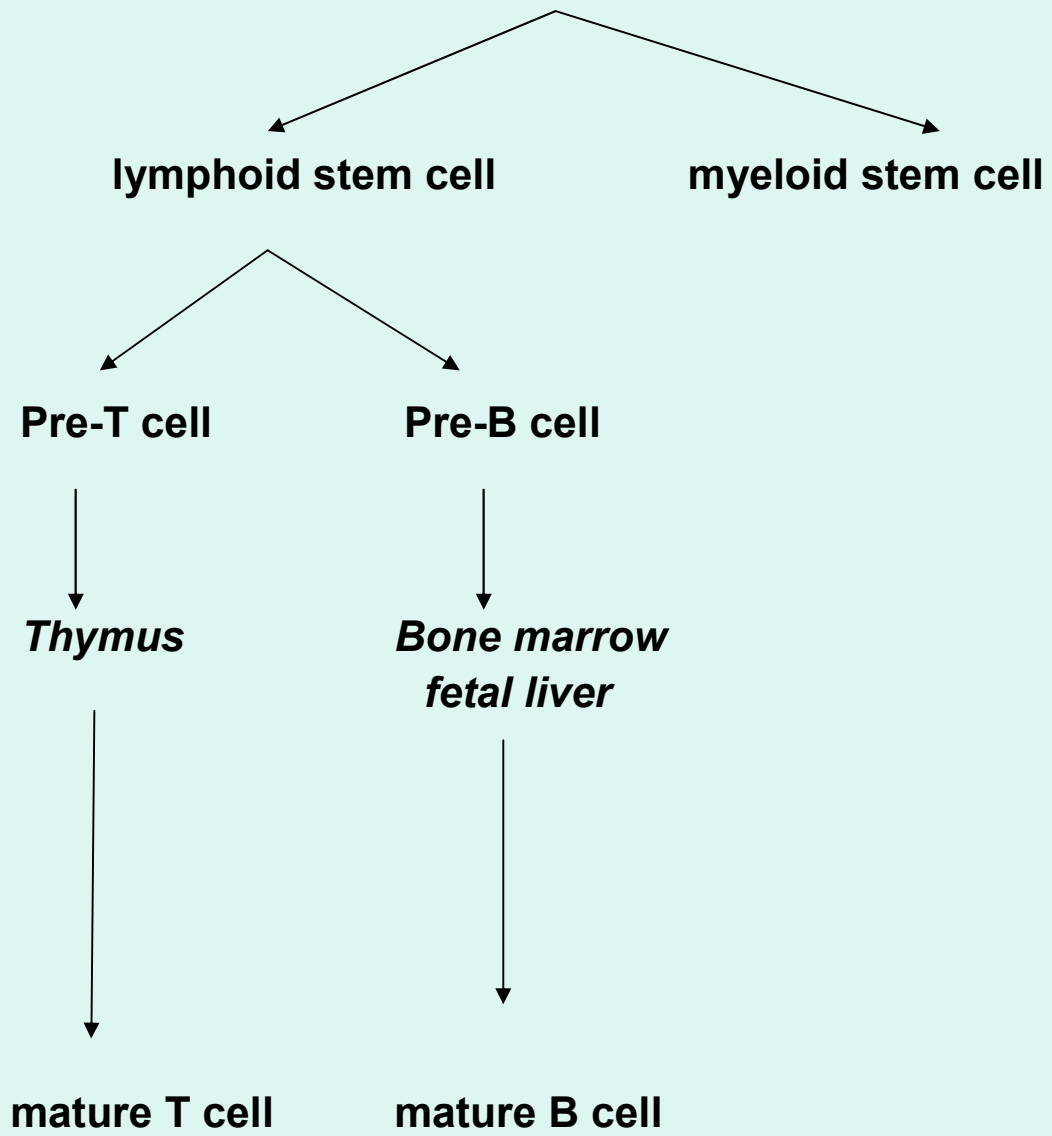
i. Thymus for T cells

ii. Bone marrow & fetal liver for B cells

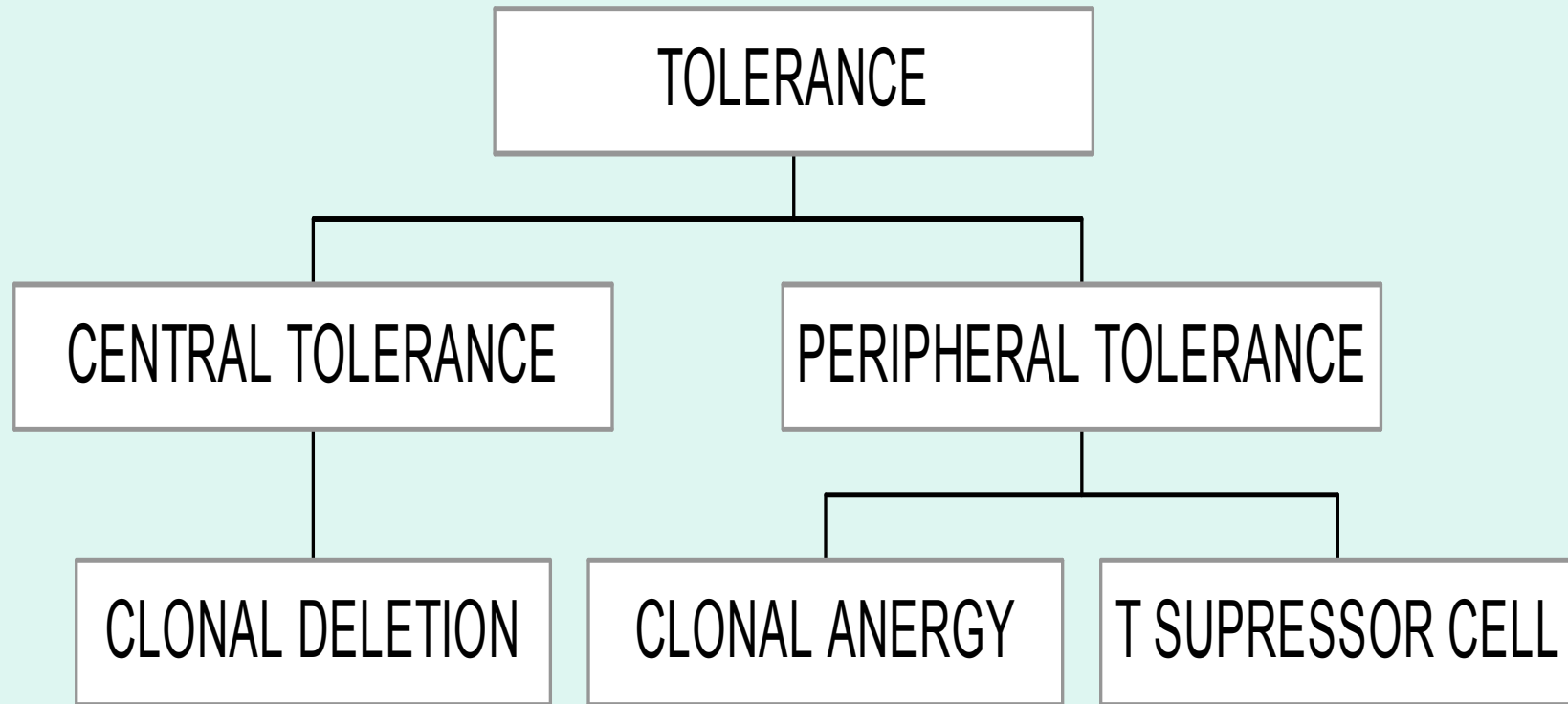
2. **Peripheral Tolerance,**

operates in the **SECONDARY LYMPHOID ORGANS**, in the periphery after birth

HAEMATOPOIESIS
Stem cell



ROUTES TO TOLERANCE



ROUTES TO T CELL TOLERANCE

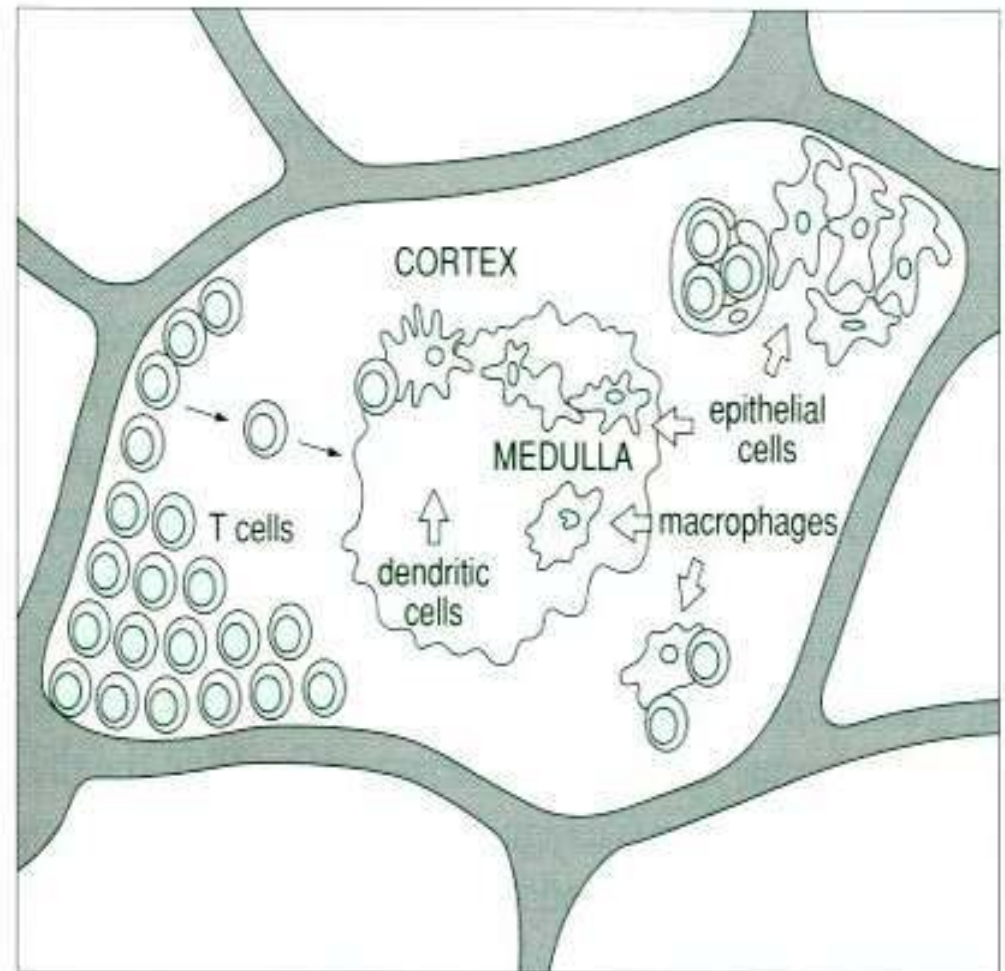
I. **CENTRAL TOLERANCE**

CLONAL DELETION

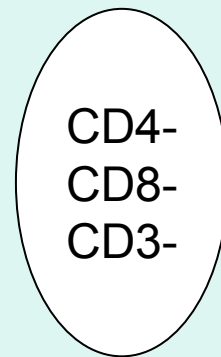
Takes place following LYMPHOPOIESIS in a specialized organ, the **thymus**.

- The thymus is composed of several lobes, each of which has cortical and medullary regions:

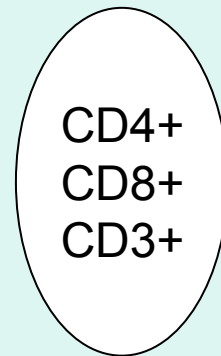
- The **cortex** contains **immature thymocytes** in close contact with **thymic epithelial cells**.
- **Medullary areas** contain **more mature thymocytes, epithelial cells, and dendritic cells and macrophages**



Arrival in the Thymus

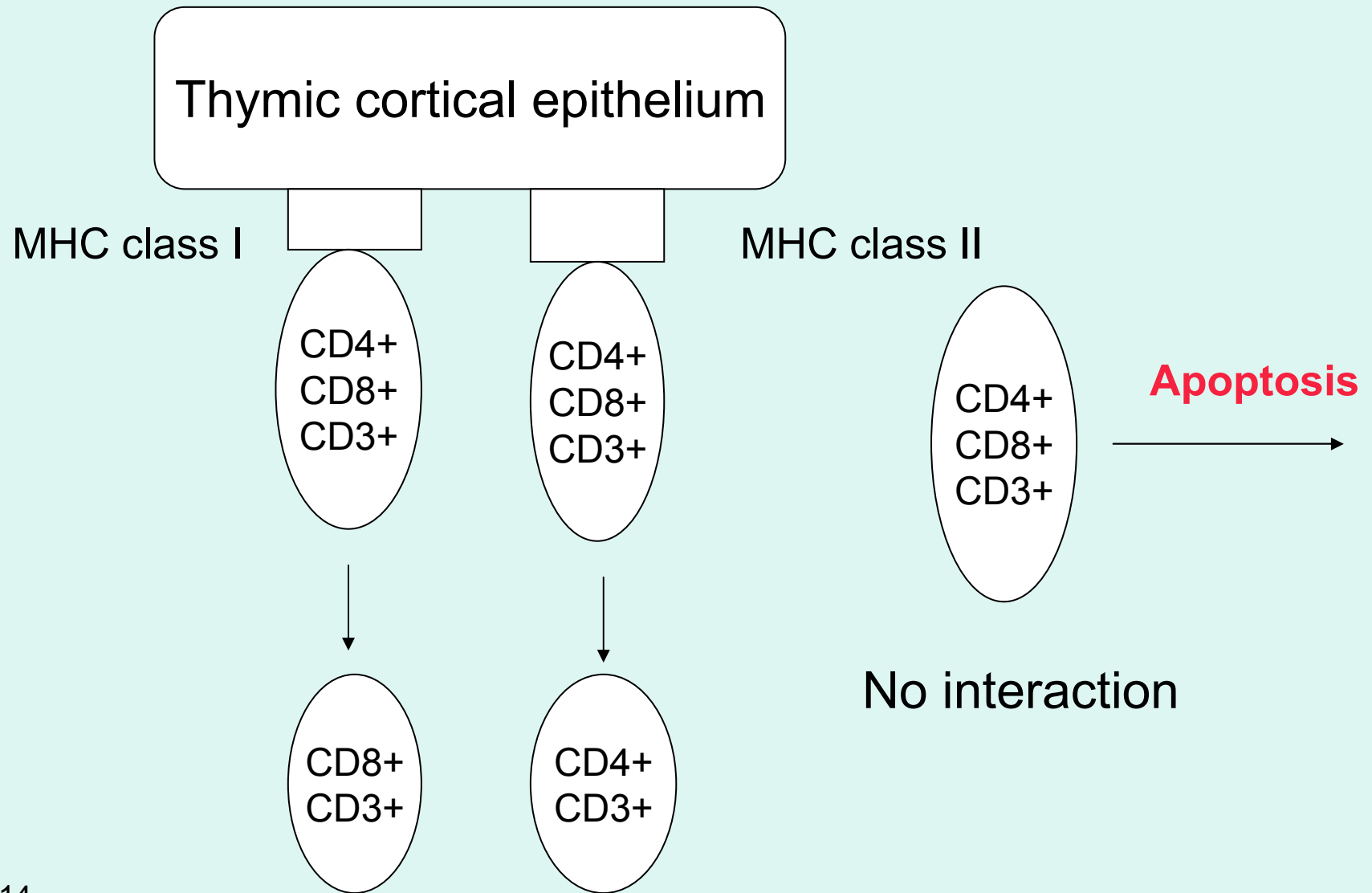


Early thymocytes
Double Negative

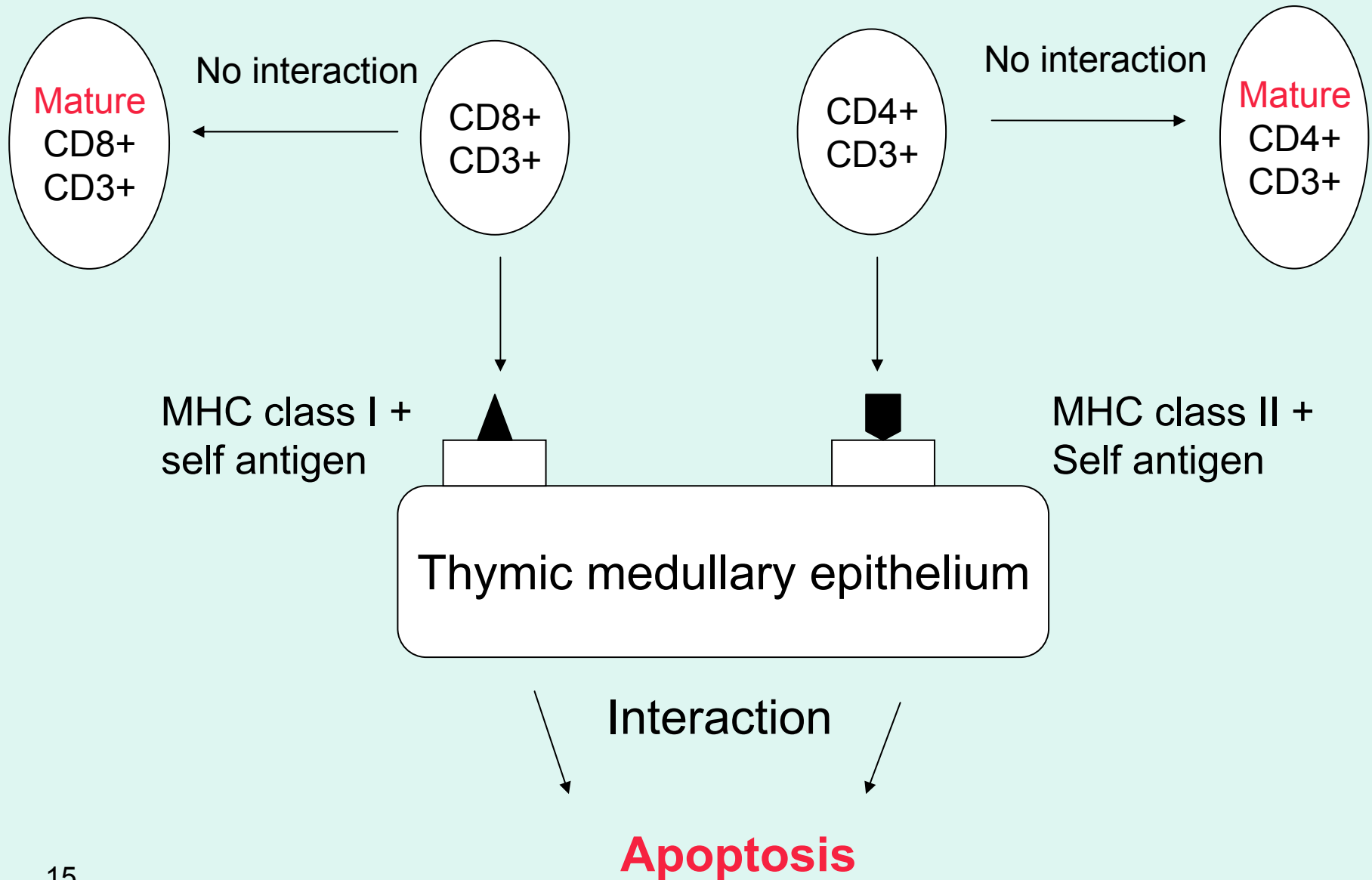


Double Positive

Positive Selection in the thymic cortex



Negative Selection in the thymic medulla



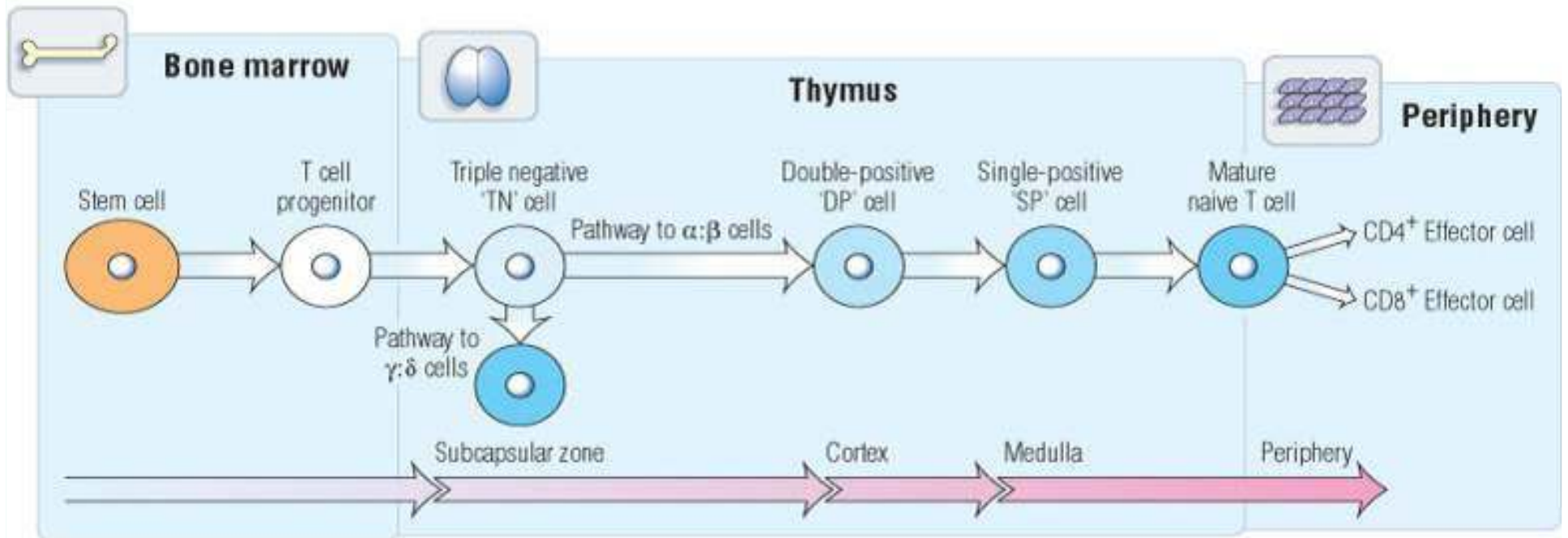
- **Thymic development of T cells results in:**
 - 1) Production of T cell receptors for antigen (TCR)
 - 2) Lymphocytes begin to express CD3, CD4, and CD8
 - 3) Selection of T cells that can interact effectively with self-MHC- **Positive selection**

4) Elimination of self-reactive cells that are stimulated by MHC + self Ag- **Negative selection**

5) Mature T cells ready to go to the periphery are TCR/CD3+, and either CD4 or CD8 positive

CLONAL DELETION

Physical deletion/elimination of T cells that have **receptors specific for self antigens** from the peripheral repertoire



Self-reactive T cells



Escape to the periphery

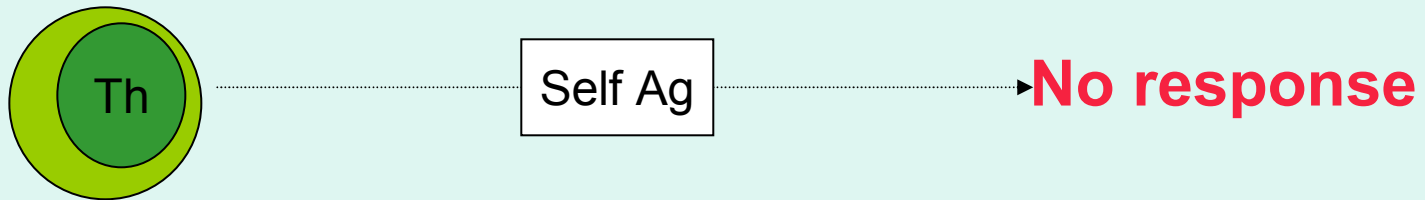


Controlled by **Anergy**

II. PERIPHERAL TOLERANCE

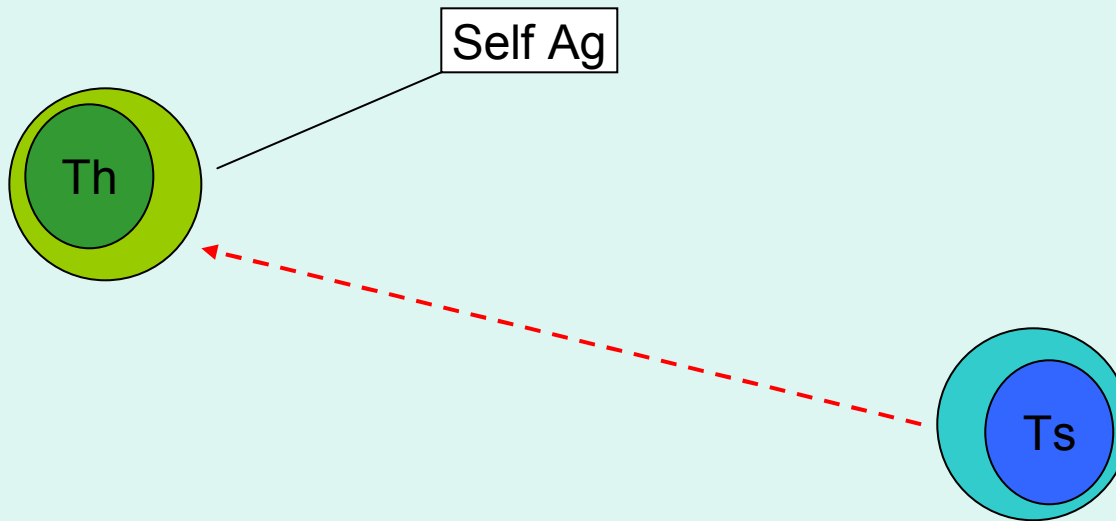
•CLONAL ANERGY

Down regulation of the mechanism of response



•INHIBITION OF T CELLS

Continuous inhibition of cellular activity by suppressor cells, Ts (via IL-10, TGF- β)

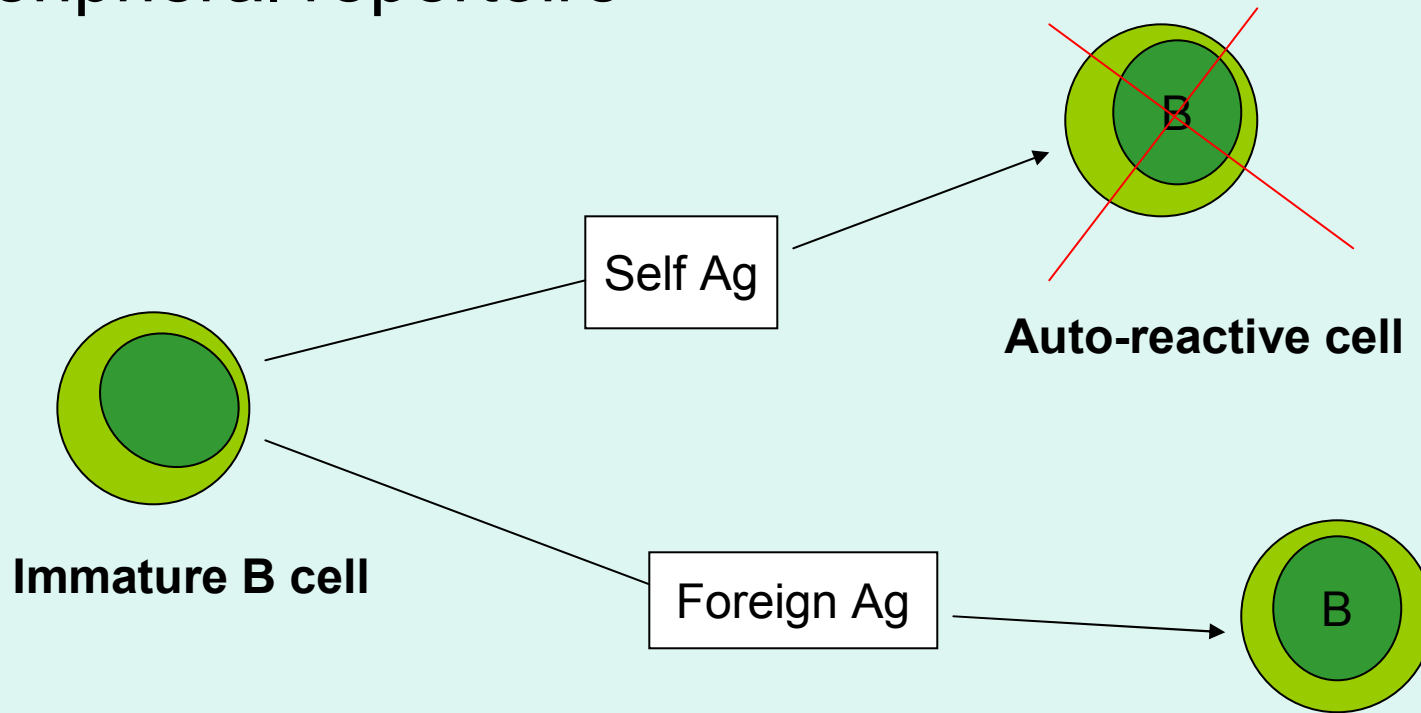


Routes to B cell Tolerance

Central Tolerance

Clonal Deletion

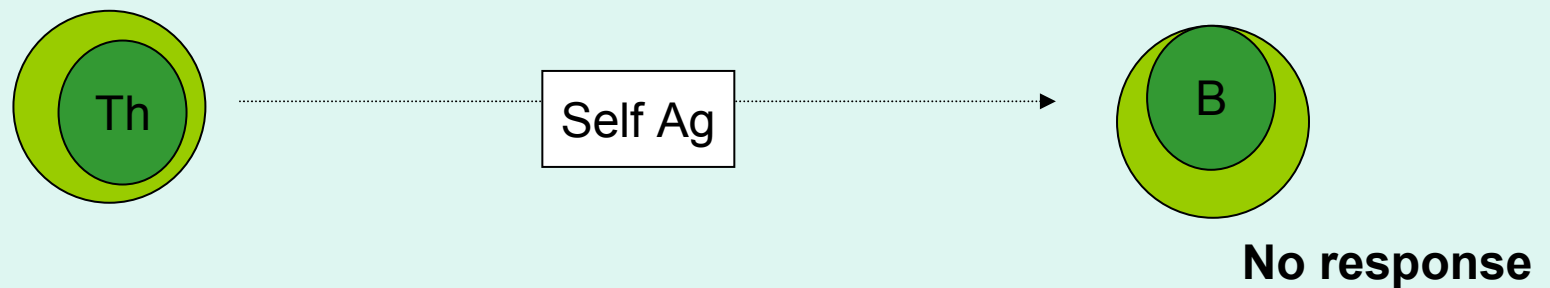
Physical deletion/elimination of B cells from the peripheral repertoire



Peripheral Tolerance

1. Direct- Clonal Anergy

Down regulation of the mechanism of response



2. Indirect- No Help from Th



HOW IS SELF-TOLERANCE MAINTAINED?

- **Clonal Deletion or Anergy** - Autoreactive lymphocytes are deleted or are non-functional
- **Sequestration of Autoantigens** – Self-Ag are isolated/hidden from immune system
- **Lack of Processing or Presentation** – Self-Ag are not processed or presented
- **Suppression** - Ts cells suppress autoimmune responses.