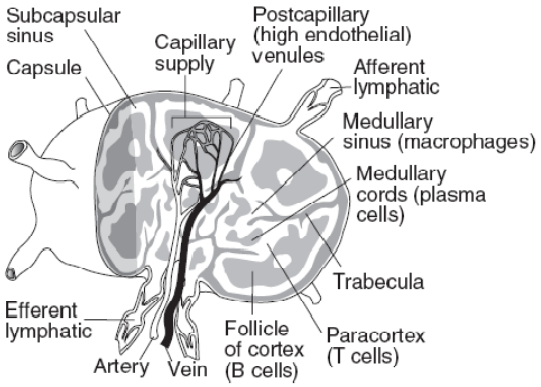
Lymph node

A 2° lymphoid organ that has many afferents, 1 or more efferents. Encapsulated, with trabeculae. Functions are nonspecific filtration by macrophages, storage and activation of B and T cells, antibody production.

Follicle

Site of B-cell localization and proliferation. In outer cortex. 1° follicles are dense and dormant. 2° follicles have pale central germinal centers and are active.



Medulla

Consists of medullary cords (closely packed lymphocytes and plasma cells) and medullary sinuses. Medullary sinuses communicate with efferent lymphatics and contain reticular cells and macrophages.

Paracortex

Houses T cells. Region of cortex between follicles and medulla. Contains high endothelial venules through which T and B cells enter from blood. In an extreme cellular immune response, paracortex becomes greatly enlarged. Not well developed in patients with DiGeorge syndrome.

Paracortex enlarges in an extreme cellular immune response (i.e., viral).

Lymph drainage

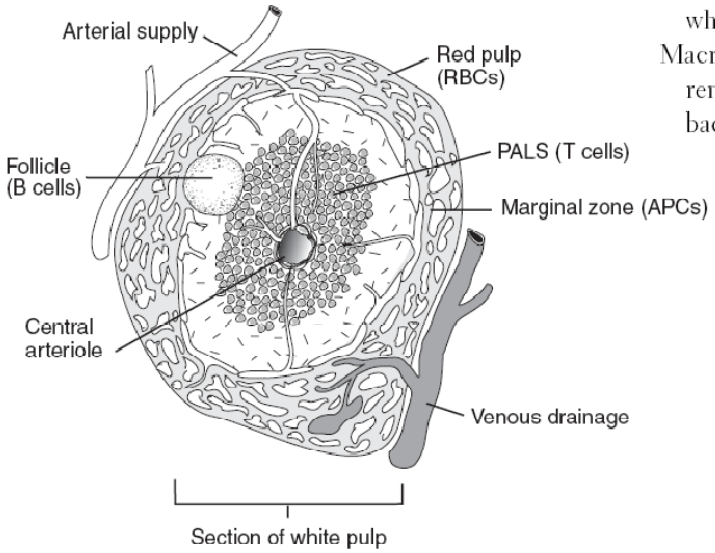
Area of body	1° lymph node drainage site
1. Upper limb, lateral breast	1. Axillary
2. Stomach	2. Celiac
3. Duodenum, jejunum	3. Superior mesenteric
4. Sigmoid colon	4. Colic → inferior mesenteric
5. Rectum (lower part), anal canal above pectinate line	5. Internal iliac
6. Anal canal below pectinate line	6. Superficial inguinal
7. Testes	7. Superficial and deep plexuses → para-aortic
8. Scrotum	8. Superficial inguinal
9. Thigh (superficial)	9. Superficial inguinal
10. Lateral side of dorsum of foot	10. Popliteal

Right lymphatic duct—drains right arm and right half of head.

Thoracic duct—drains everything else.

Sinusoids of spleen

Long, vascular channels in red pulp with fenestrated "barrel hoop" basement membrane. Macrophages found nearby.



T cells are found in the periarterial lymphatic sheath (PALS) and in the red pulp of the spleen. B cells are found in follicles within the white pulp of the spleen.
Macrophages in the spleen remove encapsulated bacteria.

Thymus

Site of T-cell differentiation and maturation. Encapsulated. From epithelium of 3rd branchial pouches. Lymphocytes of mesenchymal origin. Cortex is dense with immature T cells; medulla is pale with mature T cells and epithelial reticular cells and contains Hassall's corpuscles. Positive (MHC restriction) and negative selection (nonreactive to self) occur at the corticomedullary junction.

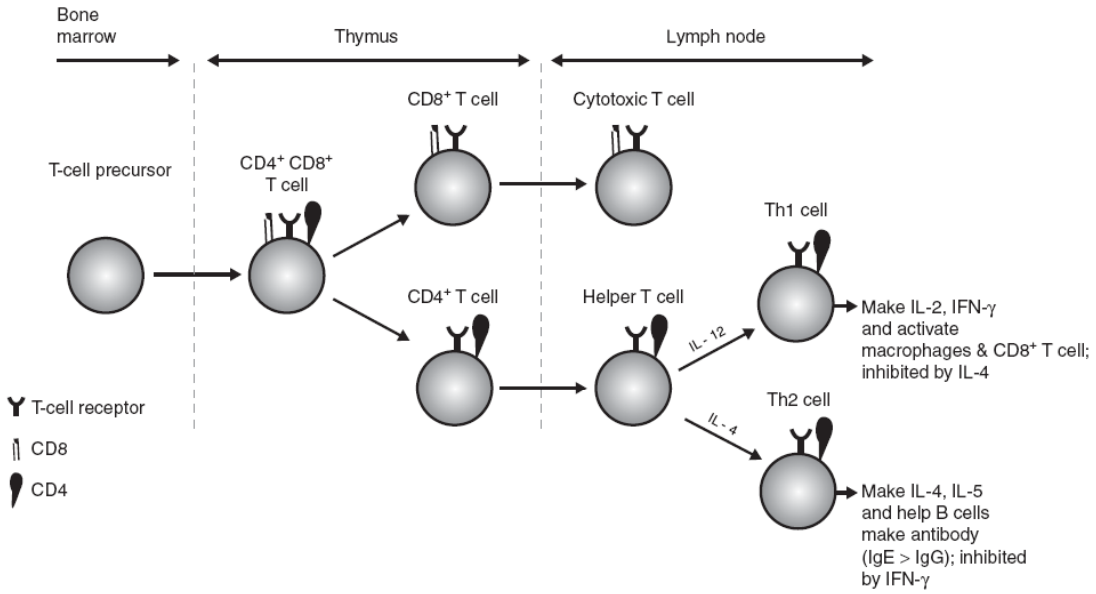
T cells = Thymus.
B cells = **B**one marrow.

Innate vs. adaptive immunity

Innate—receptors that recognize pathogens are germline encoded. Response to pathogens is fast and nonspecific. No memory. Consists of neutrophils, macrophages, dendritic cells, and complement.

Adaptive—receptors that recognize pathogens undergo VDJ recombination during lymphocyte development. Response is slow on first exposure, but memory response is faster and more robust. Consists of T cells, B cells, and circulating antibody.

Differentiation of T cells



MHC I and II

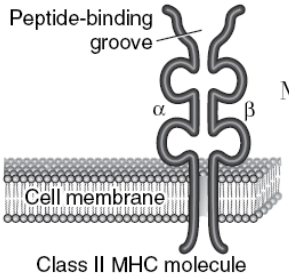
MHC = major histocompatibility complex, encoded by **H**uman **L**eukocyte **A**ntigen (HLA) genes.

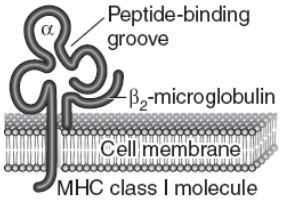
MHC I = HLA-A, HLA-B, HLA-C.
- Expressed on almost all nucleated cells.
- Antigen is loaded in RER of mostly intracellular peptides.
- Mediates viral immunity.
- Pairs with β_2-microglobulin.

MHC II = HLA-DR, HLA-DP, HLA-DQ.
- Expressed only on antigen-presenting cells (APCs).
- Antigen is loaded in an acidified endosome.

MHC I—HLA I letter (A, B, C).

MHC II—HLA II letters (DR, DP, DQ).



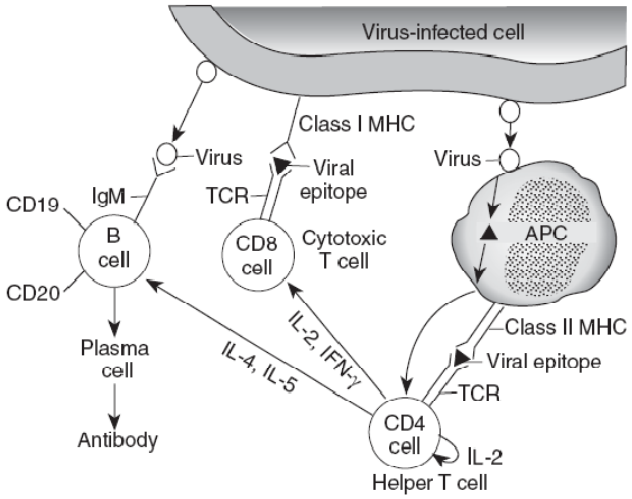


Major function of B and T cells

B cells	T cells
Make antibody	$CD4^+$ T cells help B cells make antibody and produce γ-interferon, which activates macrophages
IgG antibodies opsonize bacteria, viruses	Kill virus-infected cells directly ($CD8^+$ T cells)
Allergy (type I hypersensitivity): IgE	Delayed cell-mediated hypersensitivity (type IV)
Cytotoxic (type II) and immune complex (type III) hypersensitivity: IgG	
Antibodies cause organ rejection (hyperacute)	Organ (allograft) rejection (acute and chronic)

T-cell glycoproteins

Helper T cells have CD4, which binds to MHC II on APCs. Cytotoxic T cells have CD8, which binds to MHC I on virus-infected cells.



Product of CD and MHC = 8 (CD4 × MHC **II** = 8 = CD8 × MHC **I**).

CD3 complex—cluster of polypeptides associated with a T-cell receptor. Important in signal transduction.

APCs:

1. Macrophage
2. B cell
3. Dendritic cell

T-cell activation

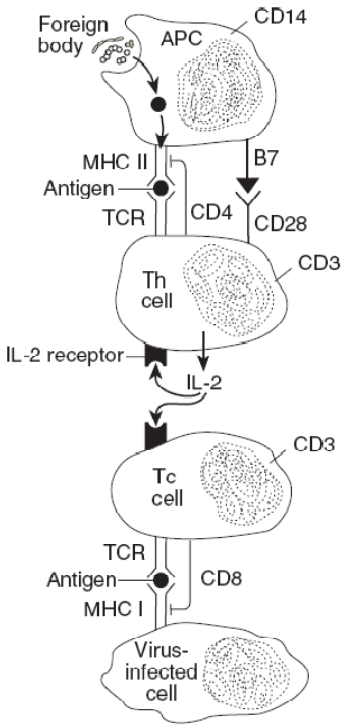
2 signals are required for T-cell activation—signal 1 and signal 2.

Th activation:

1. Foreign body is phagocytosed by APC
2. Foreign antigen is presented on MHC II and recognized by TCR on Th cell (signal 1)
3. "Costimulatory signal" is given by interaction of B7 and CD28 (signal 2)
4. Th cell activated to produce cytokines

Tc activation:

1. Endogenously synthesized (viral or self) proteins are presented on MHC I and recognized by TCR on Tc cell (signal 1)
2. IL-2 from Th cell activates Tc cell to kill virus-infected cell (signal 2)



Important cytokines

IL-1	Secreted by macrophages. Causes acute inflammation. Induces chemokine production to recruit leukocytes; activates endothelium to express adhesion molecules. An endogenous pyrogen.	IL-2: stimulates T cells. IL-3: stimulates bone marrow. IL-4: stimulates IgE production. IL-5: stimulates IgA production.
IL-2	Secreted by Th cells. Stimulates growth of helper and cytotoxic T cells.	
IL-3	Secreted by activated T cells. Supports the growth and differentiation of bone marrow stem cells. Has a function similar to GM-CSF.	
IL-4	Secreted by Th2 cells. Promotes growth of B cells. Enhances class switching to IgE and IgG.	
IL-5	Secreted by Th2 cells. Promotes differentiation of B cells. Enhances class switching to IgA. Stimulates production and activation of eosinophils.	
IL-6	Secreted by Th cells and macrophages. Stimulates production of acute-phase reactants and immunoglobulins.	
IL-8	Secreted by macrophages. Major chemotactic factor for neutrophils.	"Clean up on **aisle** 8." Neutrophils are recruited by **IL**-8 to clear infections.
IL-10	Secreted by regulatory T cells. Inhibits actions of activated T cells.	
IL-12	Secreted by B cells and macrophages. Activates NK and Th1 cells.	
γ-interferon	Secreted by Th1 cells. Stimulates macrophages.	
TNF	Secreted by macrophages. Mediates septic shock. Causes leukocyte recruitment, vascular leak.	

Cell surface proteins

Helper T cells	CD4, TCR, CD3, CD28, CD40L.
Cytotoxic T cells	CD8, TCR, CD3.
B cells	IgM, B7, CD19, CD20, CD21, CD40, MHC II.
Macrophages	MHC II, B7, CD40, CD14. Receptors for Fc and C3b.
NK cells	Receptors for MHC I, CD16, CD56.
All cells except mature red cells	MHC I.

Immune deficiencies

1. **↓ production of:**

B cells—**B**ruton's agammaglobulinemia	X-linked recessive defect in a tyrosine kinase gene associated with low levels of all classes of immunoglobulins. ↓ number of B cells. Associated with recurrent **B**acterial infections after 6 months of age, when levels of maternal IgG antibody decline. Occurs in **B**oys (X-linked).
T cells—Thymic aplasia (DiGeorge syndrome)	Thymus and parathyroids fail to develop owing to failure of development of the 3rd and 4th pharyngeal pouches. Presents with **T**etany owing to hypocalcemia. Recurrent viral and fungal infections due to T-cell deficiency. Congenital defects of heart and great vessels. 22q11 deletion.
B and T cells—severe combined immunodeficiency (SCID)	Defect in early stem-cell differentiation. Presents with recurrent viral, bacterial, fungal, and protozoal infections. May have multiple causes (e.g., failure to synthesize MHC II antigens, defective IL-2 receptors, or adenosine deaminase deficiency).

2. **↓ activation of:**

T cells—IL-12 receptor deficiency	Presents with disseminated mycobacterial infections due to ↓ Th1 response.
B cells—hyper-IgM syndrome	Defect in CD40 ligand on CD4 T helper cells leads to inability to class switch. Presents early in life with severe pyogenic infections. High levels of IgM; very low levels of IgG, IgA, and IgE.
B cells—Wiskott-Aldrich syndrome	X-linked defect in the ability to mount an IgM response to capsular polysaccharides of bacteria. Associated with elevated IgA levels (**A**ldrich = ↑ Ig**A**), normal IgE levels, and low IgM levels. Triad of symptoms includes recurrent pyogenic **I**nfections, thrombocytopenic **P**urpura, **E**czema (**WIPE**).
Macrophages—Job's syndrome	Failure of IFN-γ production by helper T cells. Neutrophils fail to respond to chemotactic stimuli. Presents with coarse **F**acies, cold (noninflamed) staphylococcal **A**bscesses, retained primary **T**eeth, ↑ Ig**E**, and **D**ermatologic problems (eczema) (**FATED**).

3. **Phagocytic cell deficiency:**

Leukocyte adhesion deficiency syndrome (type 1)	Defect in LFA-1 integrin proteins on phagocytes. Presents early with recurrent bacterial infections, absent pus formation, and delayed separation of umbilicus.
Chédiak-Higashi disease	Autosomal recessive. Defect in microtubular function and lysosomal emptying of phagocytic cells. Presents with recurrent pyogenic infections by staphylococci and streptococci, partial albinism, and peripheral neuropathy.
Chronic granulomatous disease	Defect in phagocytosis of neutrophils owing to lack of NADPH oxidase activity or similar enzymes. Presents with marked susceptibility to opportunistic infections with bacteria, especially *S. aureus*, *E. coli*, and *Aspergillus*. Diagnosis confirmed with negative nitroblue tetrazolium dye reduction test.

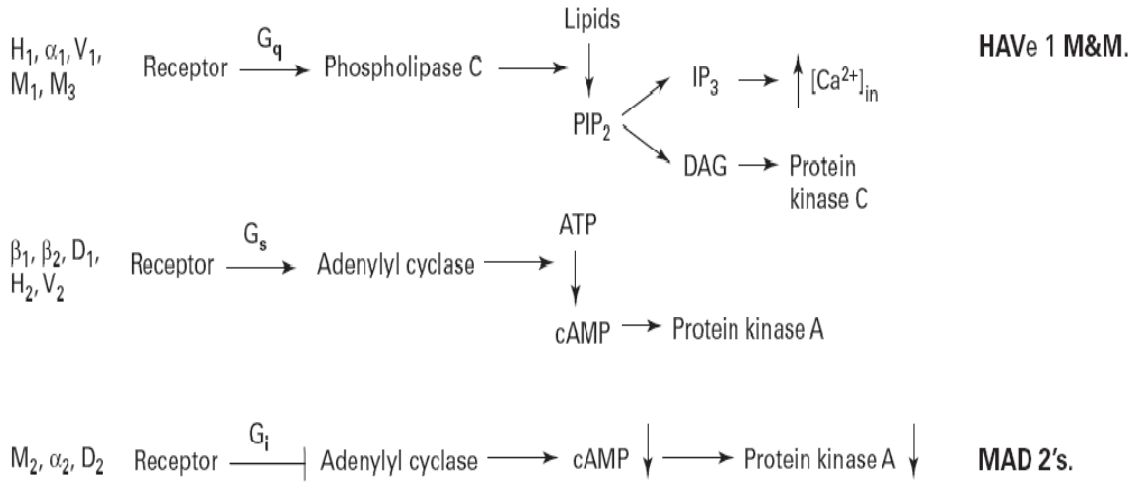
4. **Idiopathic dysfunction of:**

T cells—chronic mucocutaneous candidiasis	T-cell dysfunction specifically against *Candida albicans*. Presents with skin and mucous membrane *Candida* infections.
B cells—selective immunoglobulin deficiency	Deficiency in a specific class of immunoglobulins—possibly due to a defect in isotype switching. Selective IgA deficiency is the most common selective immunoglobulin deficiency. Presents with sinus and lung infections; milk allergies and diarrhea are common.
B cells—ataxia-telangiectasia	Defect in DNA repair enzymes with associated IgA deficiency. Presents with cerebellar problems (ataxia) and spider angiomas (telangiectasia).
B cells—common variable immunodeficiency	Normal numbers of circulating B cells, ↓ plasma cells (defect in B-cell maturation), ↓ Ig, can be acquired in 20s–30s.

G-protein-linked 2nd messengers

Receptor	G-protein class	Major functions
α_1	q	↑ vascular smooth muscle contraction
α_2	i	↓ sympathetic outflow, ↓ insulin release
β_1	s	↑ heart rate, ↑ contractility, ↑ renin release, ↑ lipolysis, maintains aqueous humor formation
β_2	s	Vasodilation, bronchodilation, ↑ heart rate, ↑ contractility, ↑ lipolysis, ↑ glucagon release
M_1	q	CNS, enteric nervous system
M_2	i	↓ heart rate and contractility
M_3	q	↑ exocrine gland secretions, ↑ gut peristalsis, ↑ bladder contraction
D_1	s	Relaxes renal vascular smooth muscle
D_2	i	Modulates transmitter release, especially in brain
H_1	q	↑ nasal and bronchial mucus production, contraction of bronchioles, pruritus, and pain
H_2	s	↑ gastric acid secretion
V_1	q	↑ vascular smooth muscle contraction
V_2	s	↑ H_2O permeability and reabsorption in the collecting tubules of the kidney

"**Q**iss (kiss) and **qiq** (kick) till you're **siq** (sick) of **sqs** (sex)."



HAVe 1 **M&M**.

MAD 2's.