Intro to the Immune System

451Micro

PRESENTED BY

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There are 2 major lines of defense:

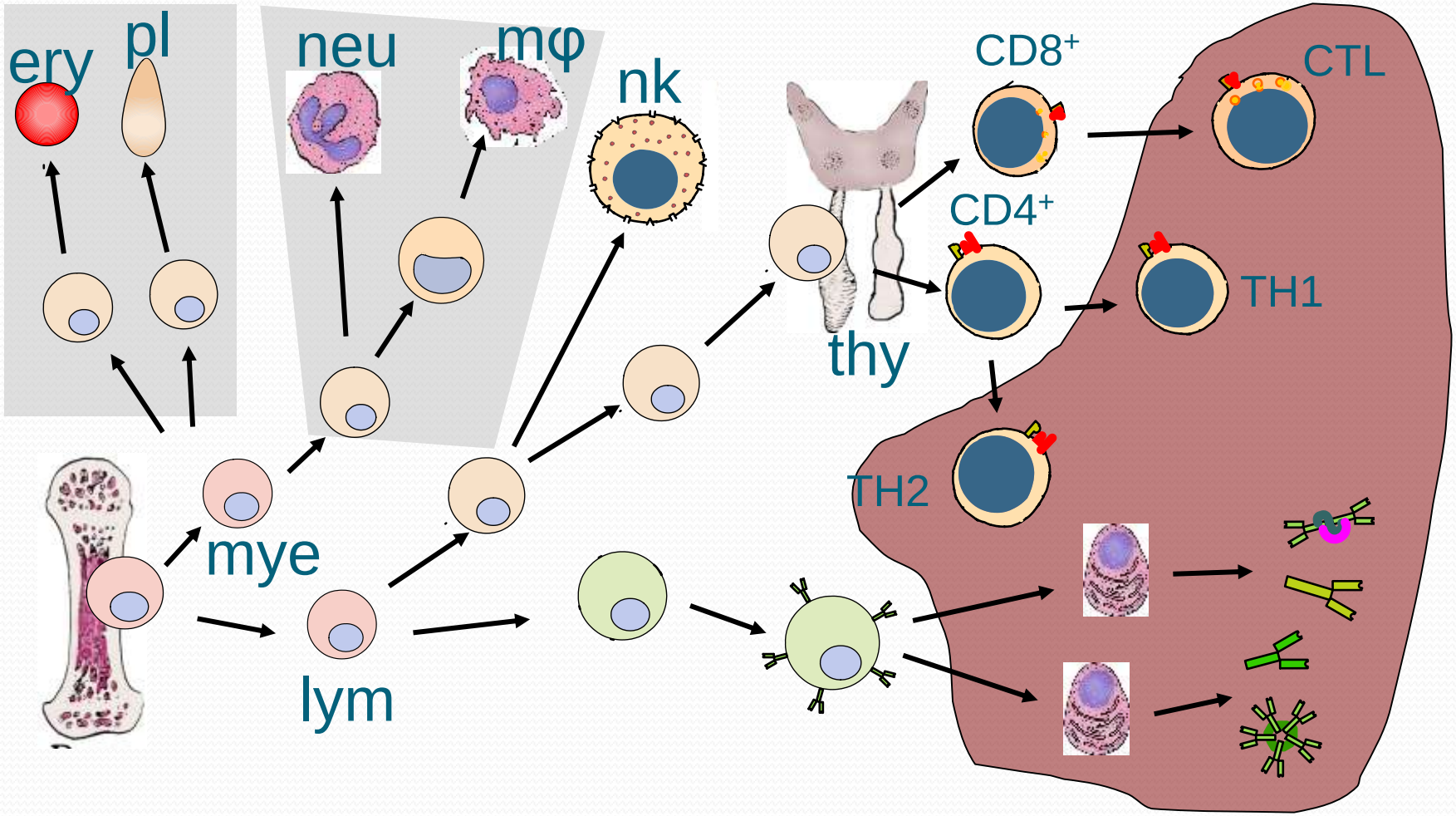
Non-specific (Innate Immunity)

and

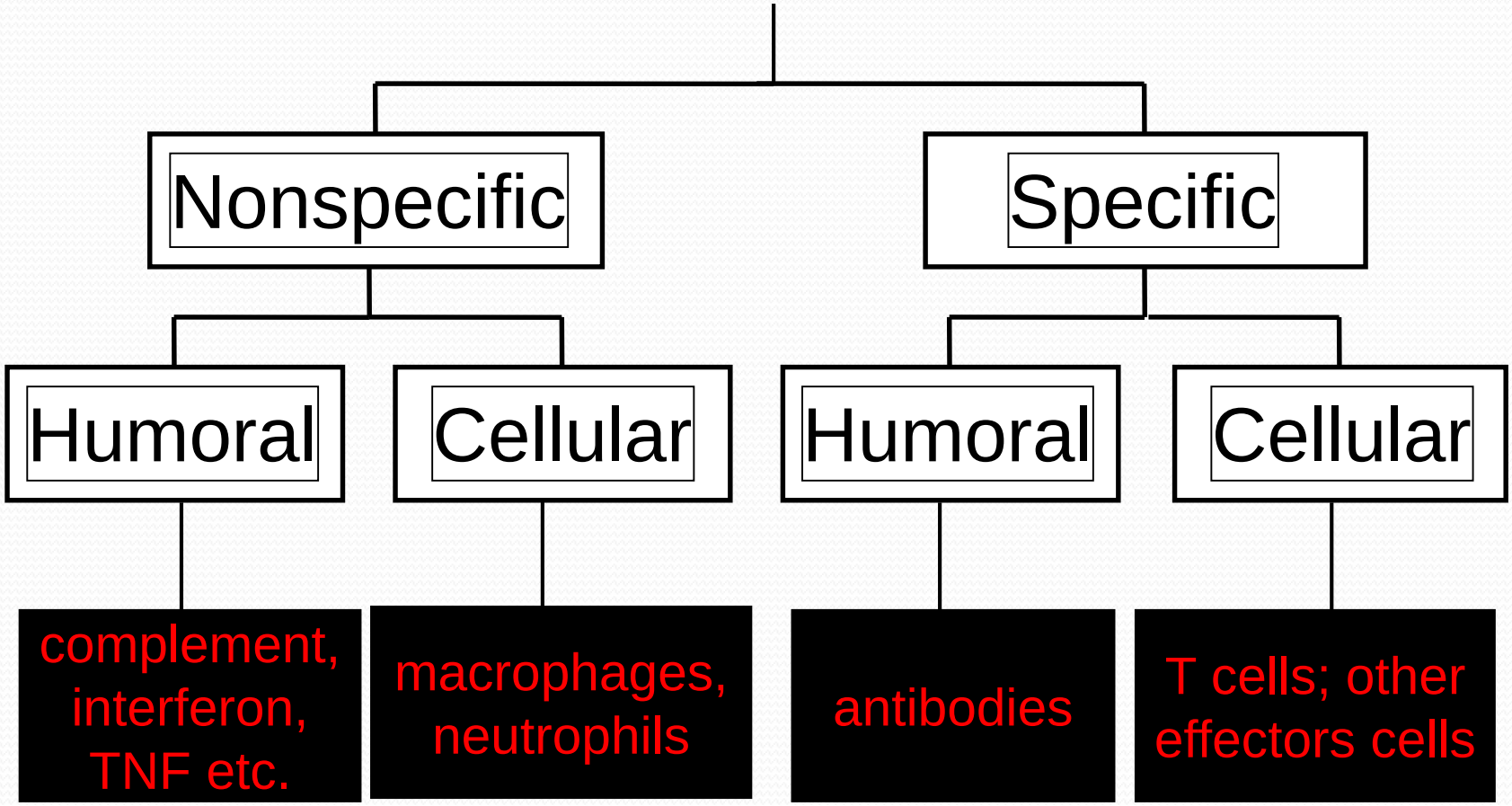
Specific (Adaptive Immunity)

Photo of macrophage cell

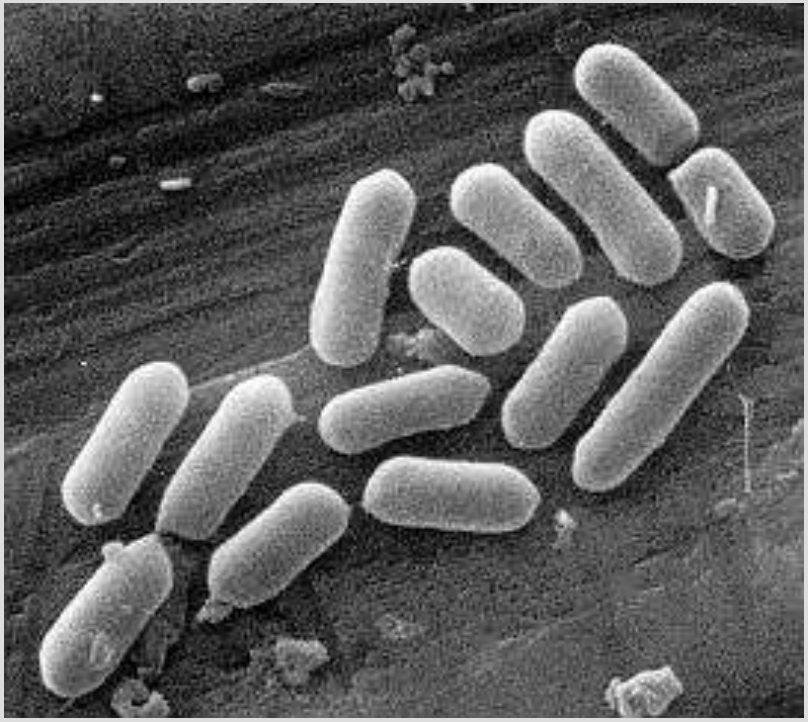
Development of the Immune System



Components of the Immune System



Innate (non-specific) Immunity



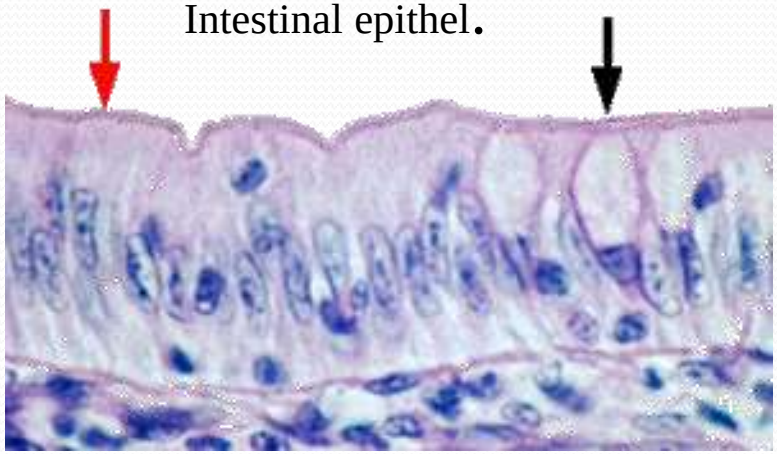
- <u>4 barriers to infection</u>:
  - Anatomic
  - Physiologic
  - Phagocytic
  - Inflammatory

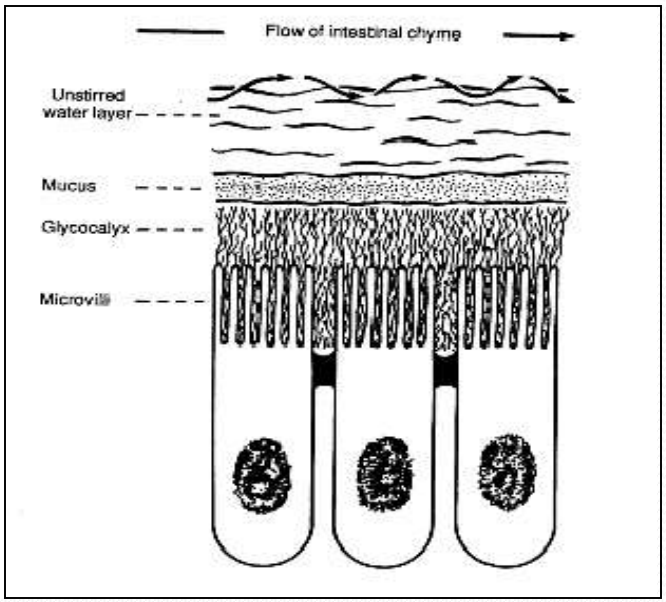
  •1st line of defense

  •includes chemicals, structure of skin/other epithelia, and mechanisms as well as cells – mainly neutrophils and macrophage

Most MO's are quickly cleared within a few days by <u>innate immunity</u> – **before** adaptive immunities are activated

Innate barriers to infections…





1) **Anatomic**

skin -> epidermis w/ keratin

mucus memb. ->inner surfaces

2) **Physiological**

temperature, pH, soluble subst.

3) **Phagocytes**

blood monocytes, tissue MØ, and neutrophils

4) **Inflammatory response**

triggered by wound/foreign particle

5 Cardinal signs reflect 3 major events of inflam response:

-vasodilation

- >capillary permeability

-influx of phagocytes

The Inflammation Process

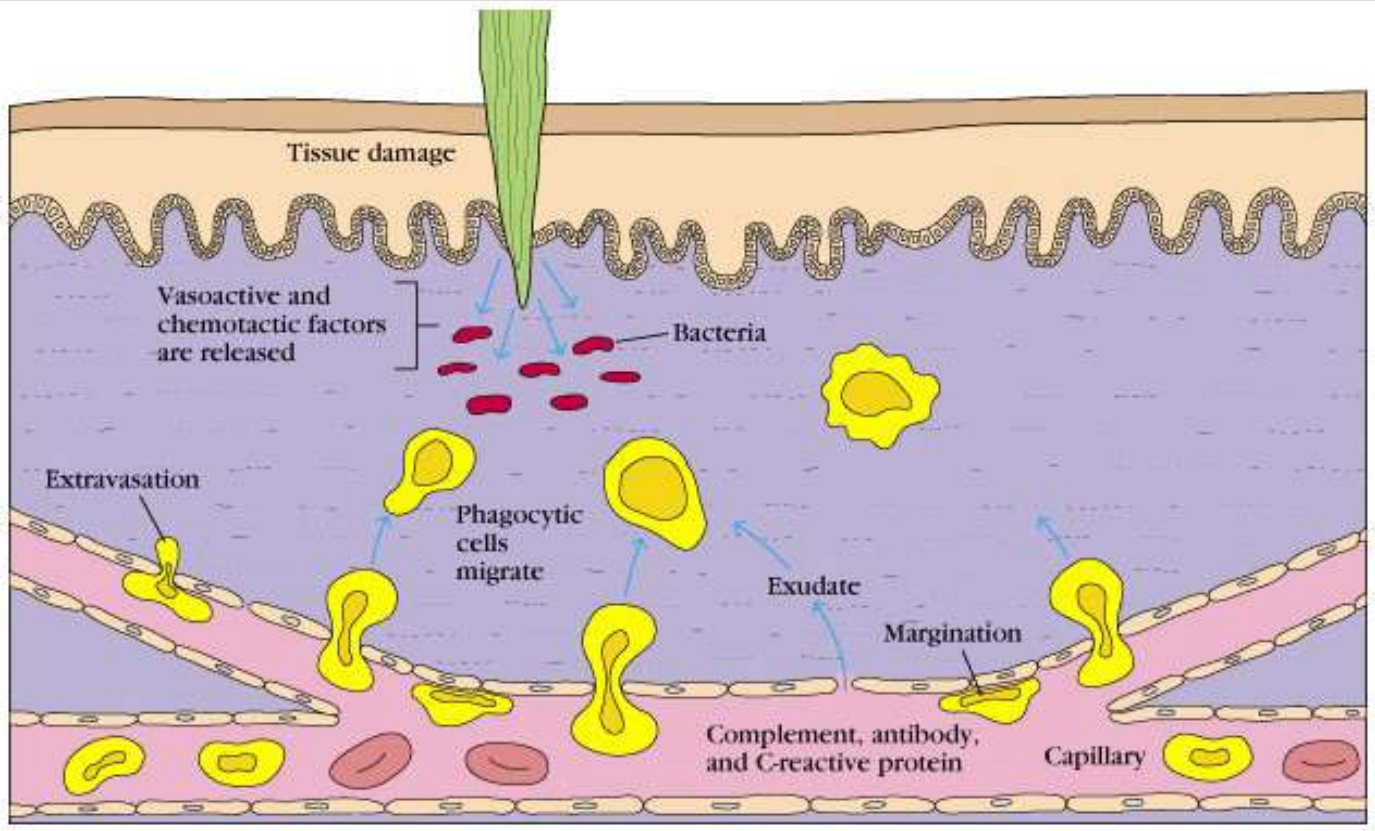
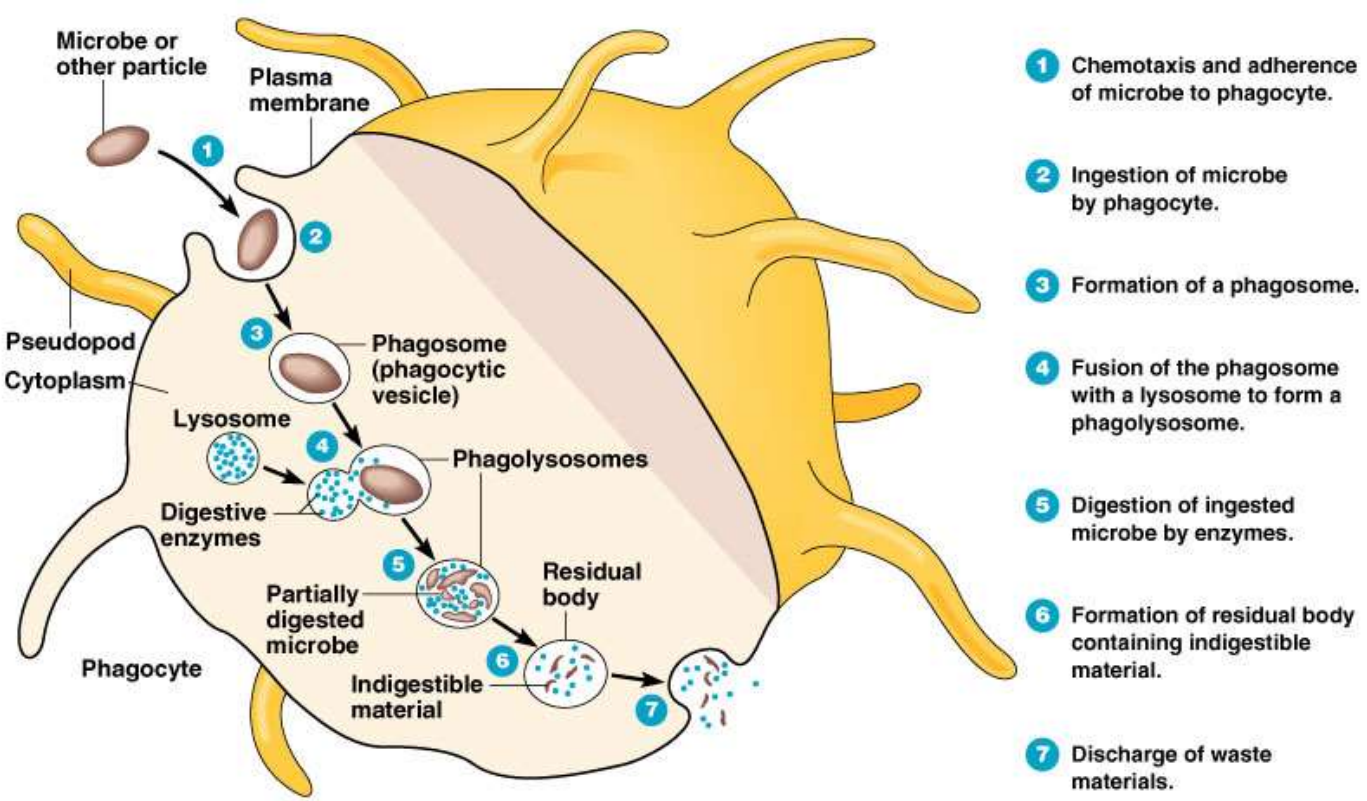


Fig 1-4 Kuby 5e



(a) Phases of phagocytosis

Adaptive Immunity

Displays four (4) attributes:

1) antibody specificity – distinguishes minute differences in molecular structure to determine non-self antigens.

2) diversity – the immune system can produce a hugely diverse set of recognition molecules which allows us to recognize literally billions of molecular shapes

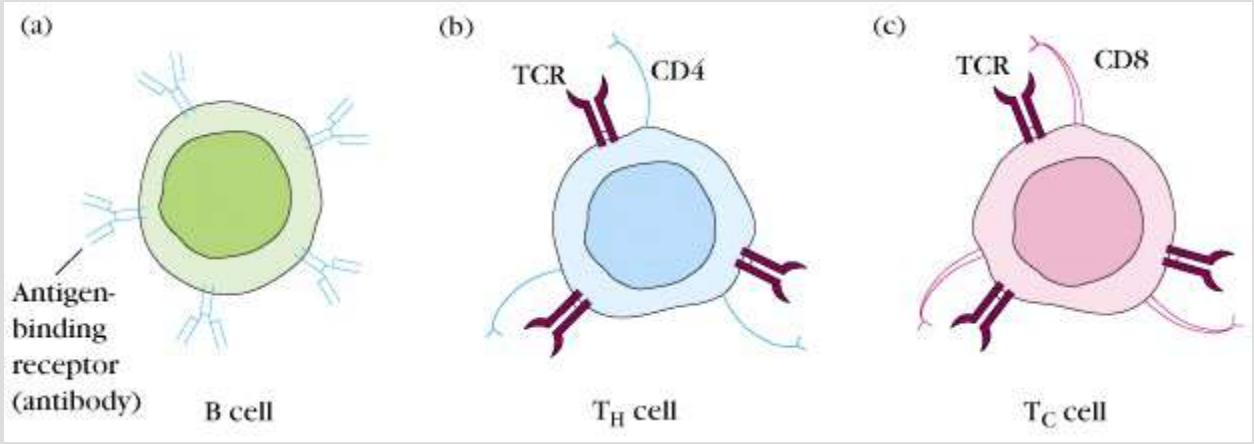
3) memory – once it has responded to an antigen, the system maintains a memory of that Ag

4) **self-nonself recognition** –the system typically responds only to foreign molecules

***adaptive IR is not independent of innate IR – they're connected**

Adaptive Immunity requires 2 major groups of cells:

a. B and T Lymphocytes (B or T cells)

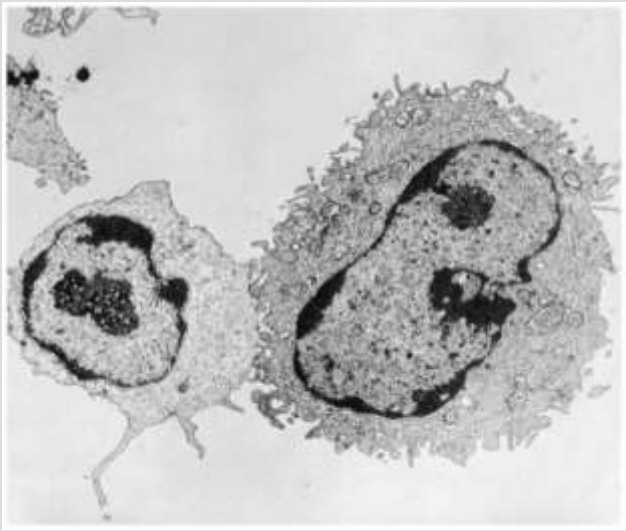


b. Antigen presenting cells (APC's)

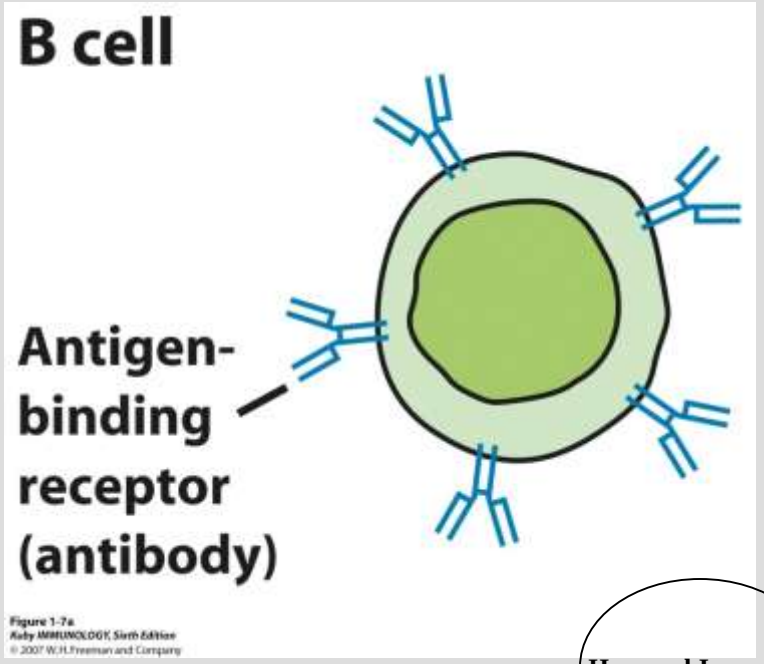
-macrophage (MØ)

-dendritic cells (DC)

-B cells



B Lymphocytes:



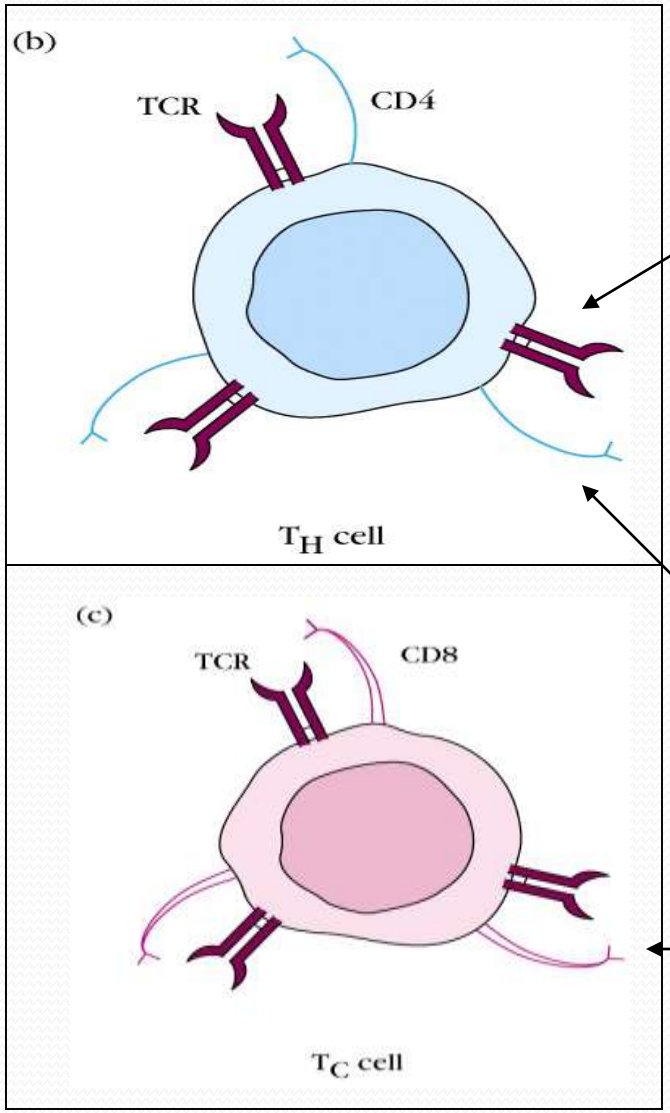
- Form and mature in bone marrow
- Exhibit antibody receptors on membrane
- Once naïve B cells bind Ag, they divide rapidly to produce:
  - Plasma cells (effector B cells)
  - Memory cells

Humoral Immunity →

Plasma cells are secretory; live only a few days (produce > 2,000 molecules of Ig/sec)

Memory cells have longer life span than naïve B cells

T Lymphocytes



- Formed in bone marrow; migrate to and mature in Thymus gland
- Exhibit unique T-cell Antigen receptors (**TCR**'s) on surface
- **TCR**'s can only recognize Ag with associated with MHC glycoproteins
  - **MHC I** – found on nearly all nucleated cells
  - **MHC II** – found only on APC's

Once T cell binds to Ag, it triggers cell division to form both memory T cells and effector T cells

There are 2 populations of T cells characterized by the type of **CD glycoprotein** found on surface:

T_H – exhibits **CD4**

T_C – exhibits **CD8**

The Antigen presentation scenario:

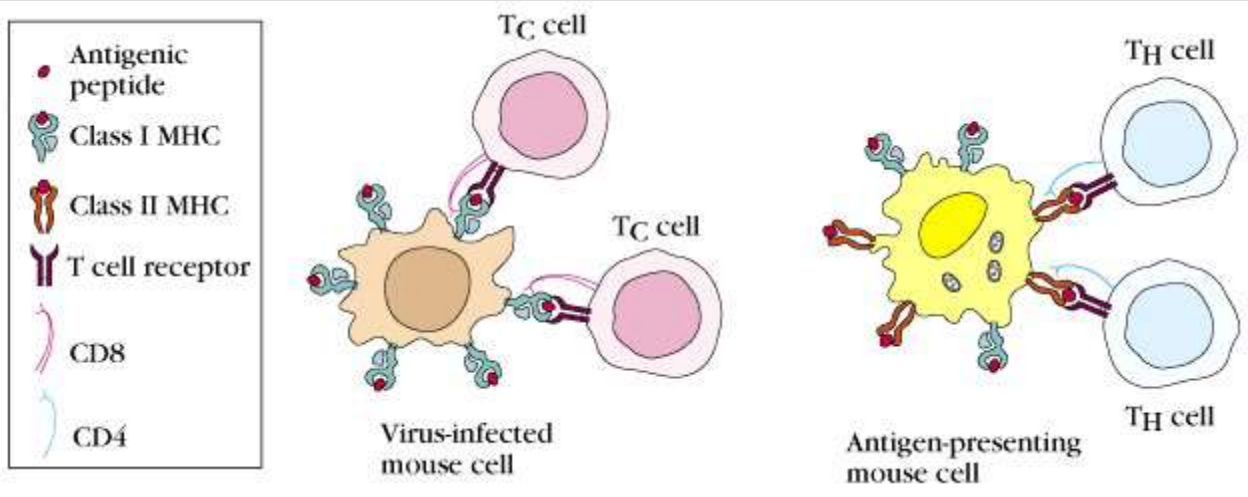


Fig 1-8 Kuby, 4e

Different patterns of cytokines determines types of IR:

-if T_C cell recognizes an Ag/MHC I complex, it divides and differentiates to become CTL

if T_H cell recognizes Ag/MHC II complex, it divides and stimulates B cells, T_C cells, and MØ

Humoral vs Cell-mediated Immune Response:

Humoral IR: occurs when Ag becomes coated with Ab which brings about the elimination of the foreign body

-cross-link several Ag's to form clumps -> more easily phago'd

-bind complement proteins

-neutralize toxins, viruses, and bacteria from binding target cells

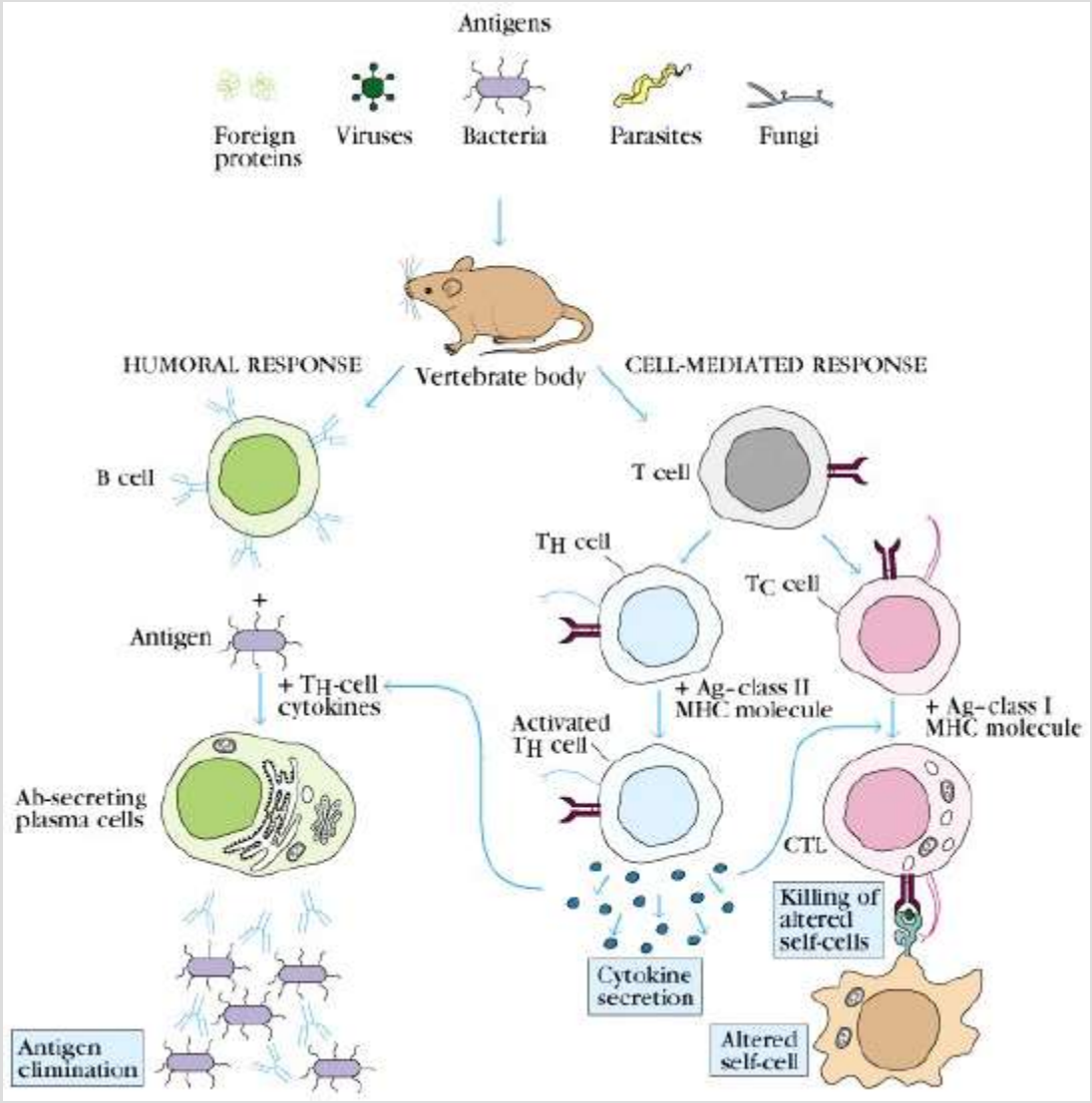
Cell-Mediated IR: occurs when effector T cells are activated

-activated T_H cells → activate phagocytic cells

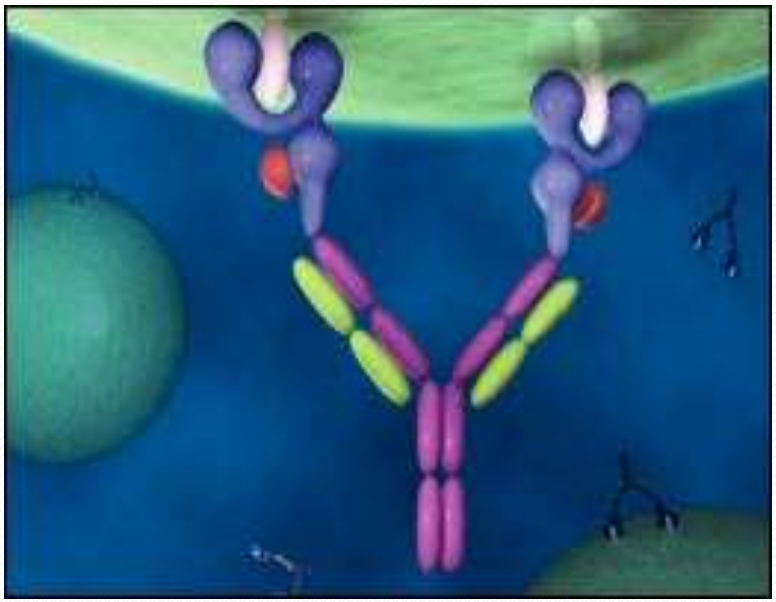
activate B cells to produce Ab

-activated T_C cells → kill altered self cells (viral infected and tumor cells)

Fig 1-7, Kuby, 4e



Next, a bit about antigens (Ag's)…



Ag recognition

Stems from recognition of distinct sites called **epitope** or **antigenic determinant**

- **B cells** can recog. Ag alone and many of them!
- **T cells** ONLY when assoc with MHC molecules (on APC or altered self cells)

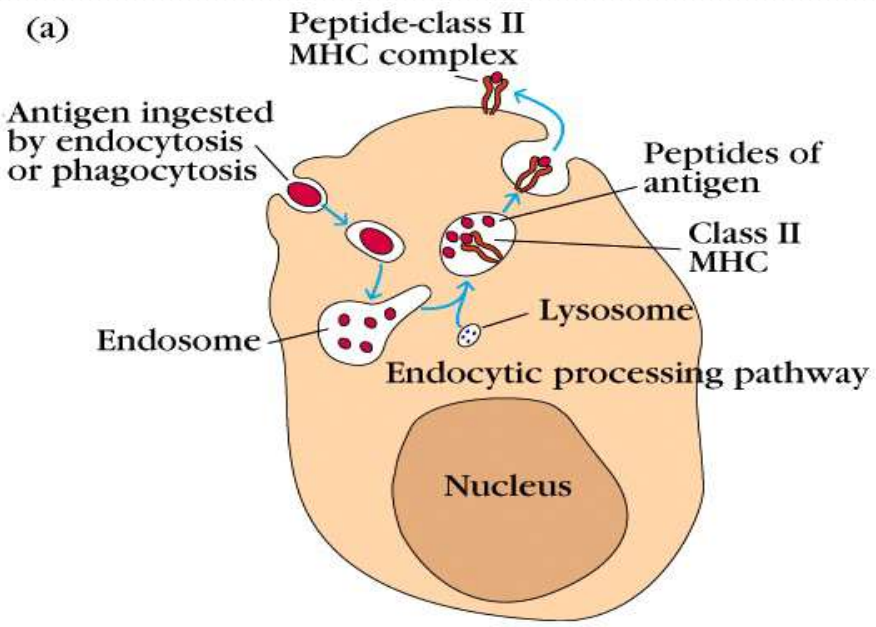
**Maturation of B & T cells creates enormous receptor diversity for binding foreign Ag

MHC molecules bind Antigenic peptides after Ag processing

- Relation of Ag with MHC I or II appears to be determined by the **route in which Ag enters the cell**

  - **Exogenous Ag** is found OUTSIDE host cells and enters via phagocytosis in APC's ONLY!

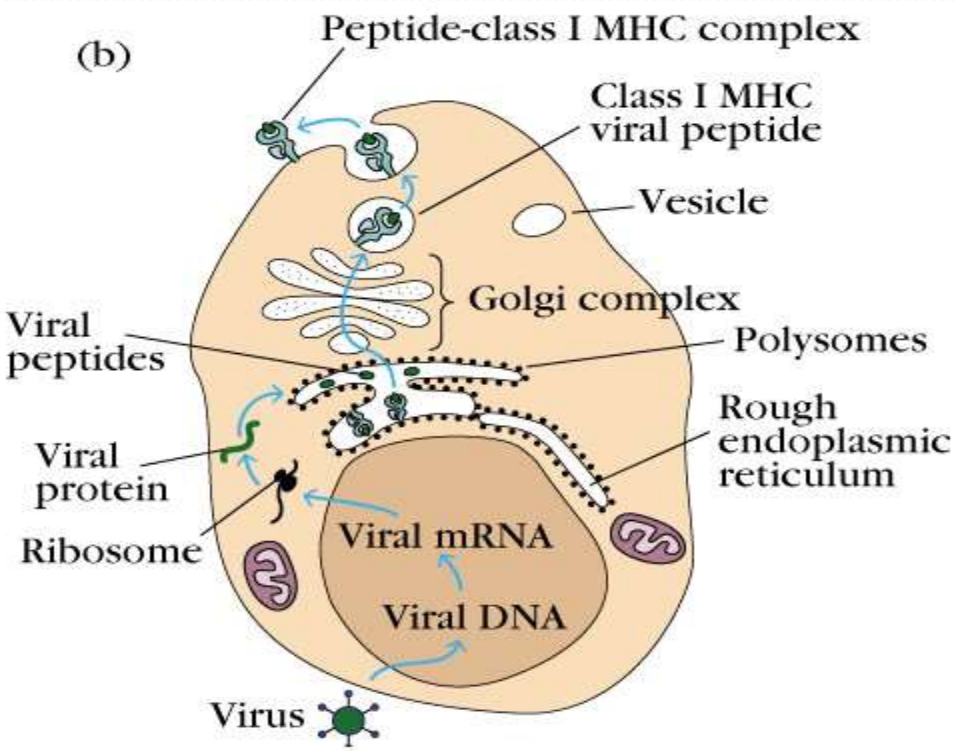
  - then APC digests Ag into peptide fragments, combines fragments with MHC Class II within the cell and transports MHC II/ Ag peptides to surface of cell → for presentation to **CD4 T cells** (these T cells are MHC II restricted)



Route of entry of Ag's (cont'd):

- **Endogenous Ag** is produced WITHIN the host cell
  (i.e. viral proteins of virally-infected cells or altered proteins produced by tumor cells)

The endogenous peptide fragments are combined to MHC I within the ER, transported to the cell surface → presented to **CD8 T cells** (CD8 T cells are MHC Class I restricted)



Mature (immunocompetent) humans contain a wide variety of Ag-reactive clones of B & T lymphocytes…

•B/T specificity developed **PRIOR** to contact with Ag in bone marrow or thymus

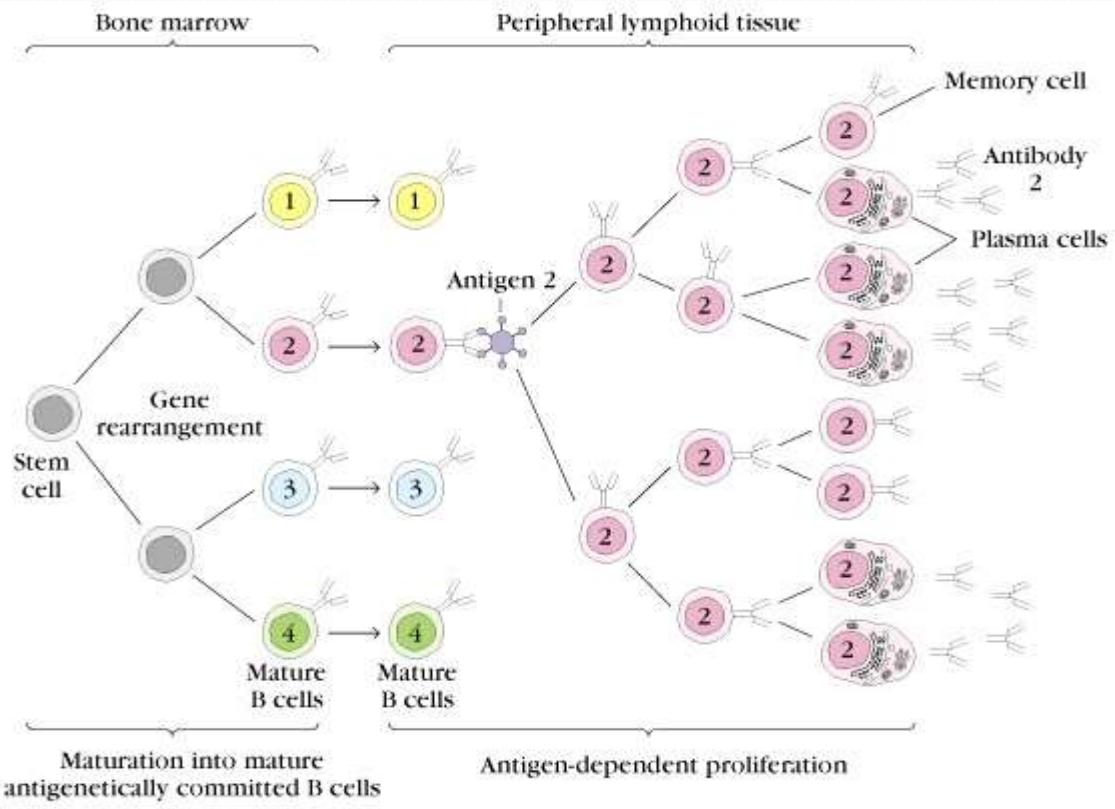
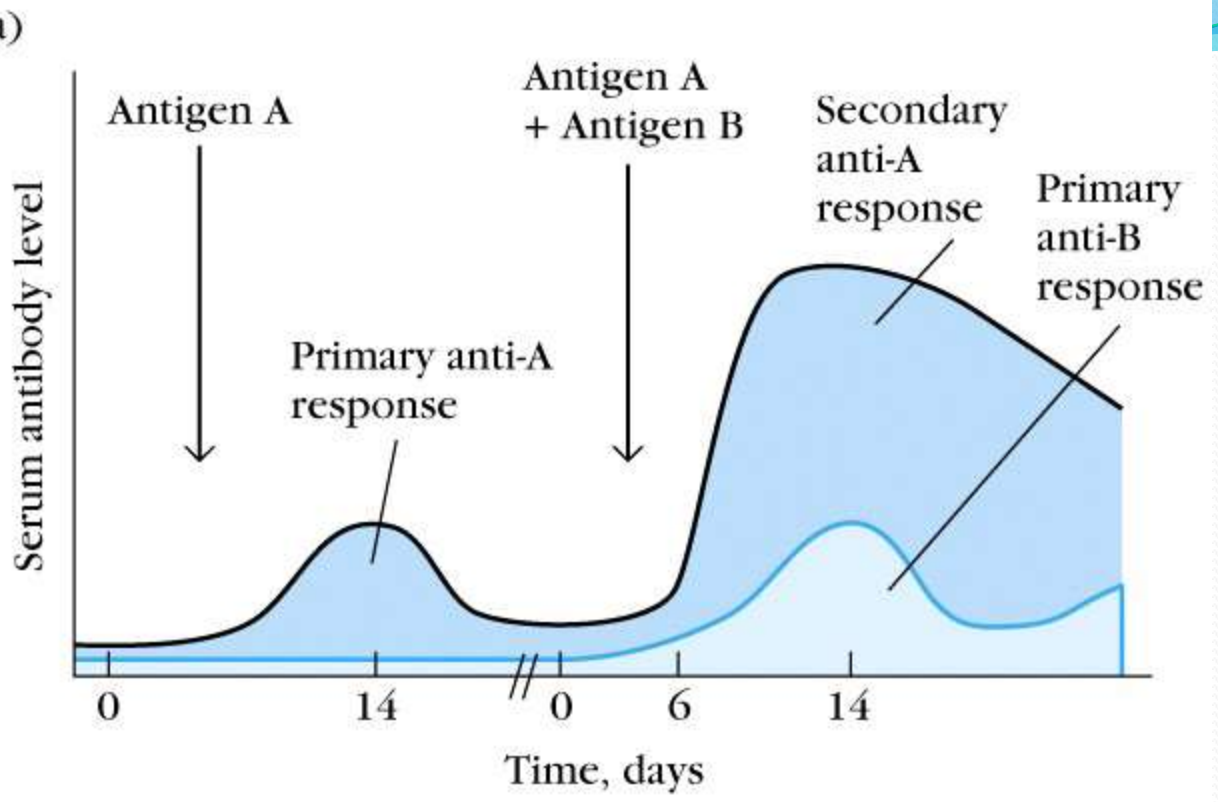


Fig 1-10 Kuby, 4e

Re: Self/nonself determination is accomplished by:

1. **Elimination** (during cell development) of lymphocytes bearing self-reactive receptors
2. **Functional suppression** of these cells in adults

Fig 1-11a



Initial encounter with Ag = **Primary (1°) immune response**; lag for 5-7 days, AB levels peak at ~14 days

Next encounter with same Ag = **Secondary (2°) immune response**; lags 1-2 days, Ab response is greater and sustained longer

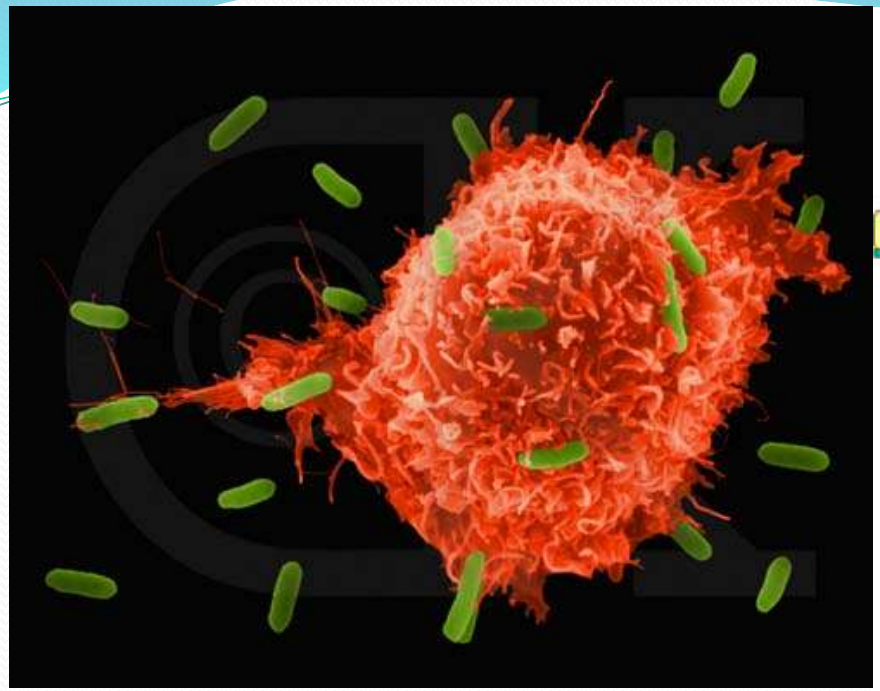
*more memory cells present →more plasma cells produced (100-1,000X more Ab's produced)

Components of Innate and Adaptive Immunity

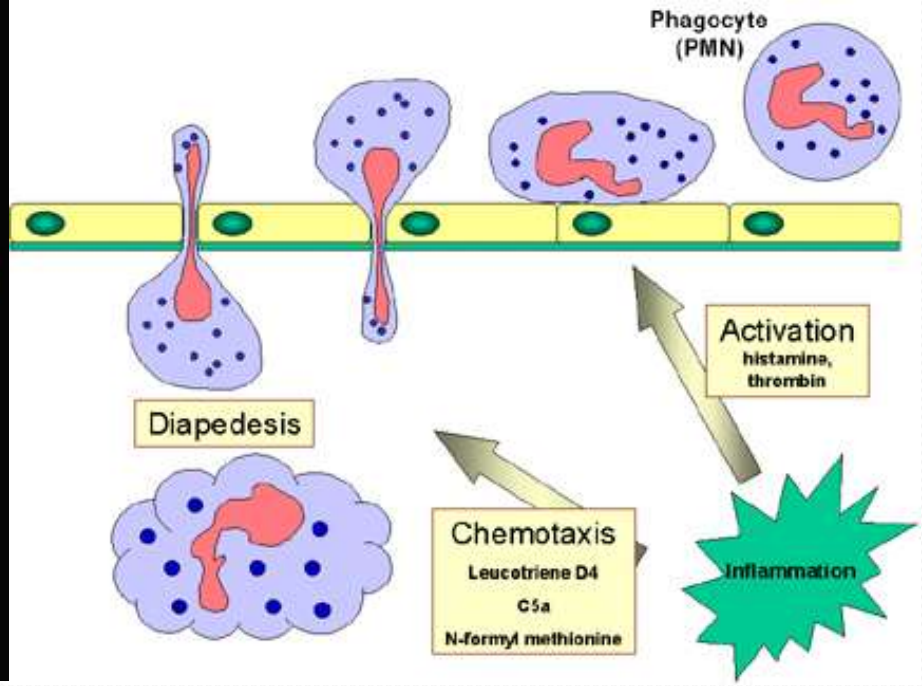
Innate Immunity	Adaptive Immunity
physical barriers	
skin, gut Villi, lung cilia,etc	none
soluble factors	
many protein and non-protein secretions	Immunoglobulins (antibody)
cells	
phagocytes, NK cell eosinophils, K cells	T and B lymphocytes

Effector mechanisms in Innate Immunity

Site	Component	Functions
Skin	squamous cells sweat	Desquamation flushing, fatty acids
GI tract	columnar cells	Peristalsis, low pH bile salts, fatty acids
Lung	tracheal cilia	mucociliary elevator surfactants
Nasopharynx and eye	mucus, saliva, tears	flushing, lysozyme
Blood and Lymphiod organs	Phagocytes	phagocytosis and intracellular killing
	K, NK & LAK cells	direct and antibody dependent cytolysis
Serum and other serous fluids	lactoferrin, transferrin	iron deprivation
	interferons, TNF-a	antiviral proteins phagocyte activation
	lysozyme	peptidoglycan hydrolysis
	Fibronectin & complement	opsonization, enhanced phagocytosis, inflammation

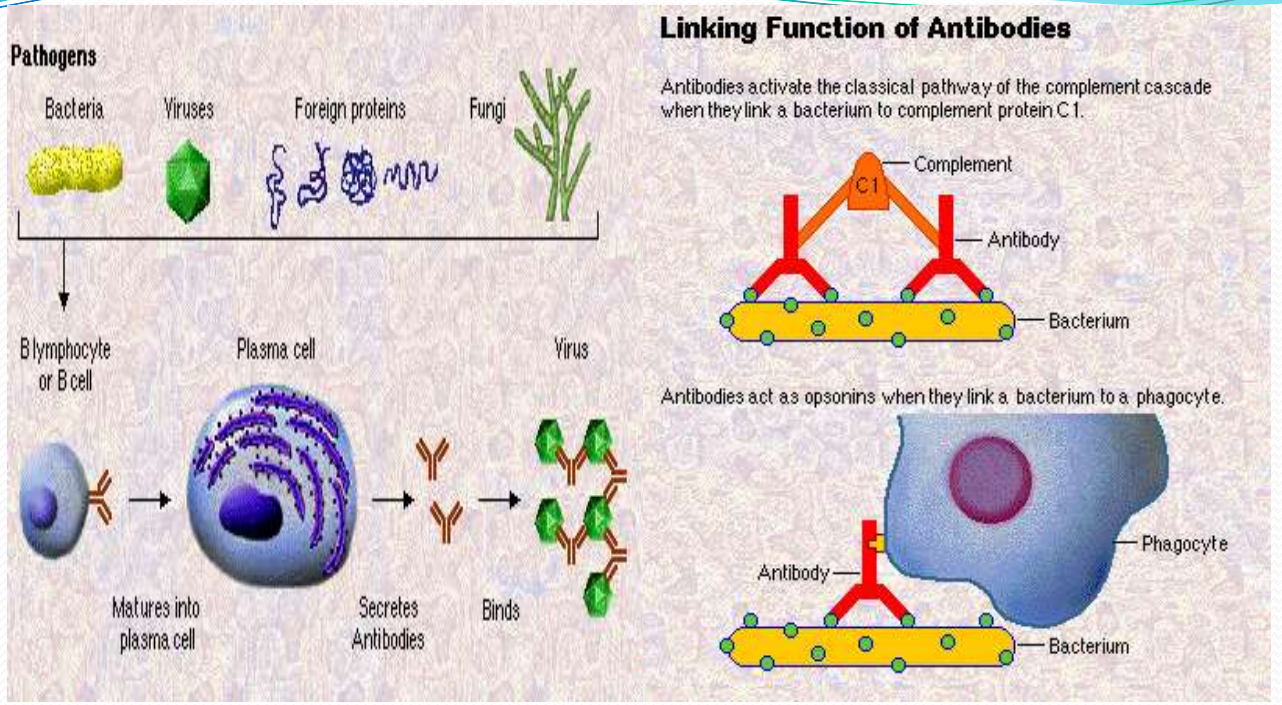


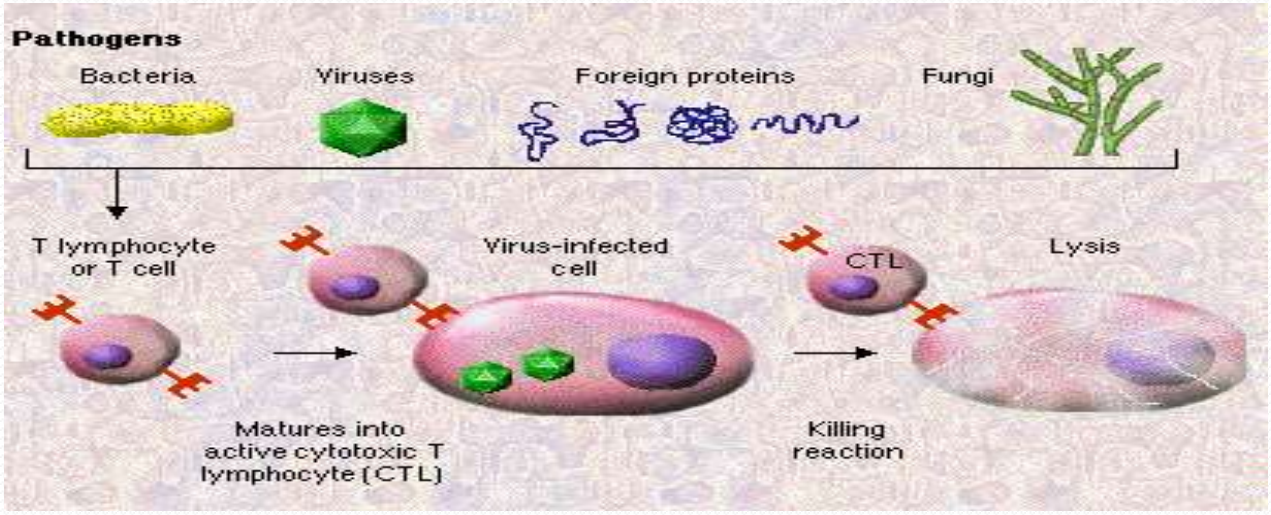
Macrophage Attacking E.coli (SEM x8,800)



Chemotactic response to inflammatory stimulus

Adaptive Immunity





Characteristics of Innate and Adaptive Immunity

Innate Immunity	Adaptive Immunity
Antigen independent	Antigen dependent
No time lag	A lag period
Not antigen specific	Antigen specific
No Immunologic memory	Development of memory

- **Immunity of extracellular bacterial infection:** antibodies (IgG, IgM, SIgA); phagocytes (neutrophils); complement; humoral immunity mainly.
- **Immunity of intracellular bacterial infection:** cell-mediated immunity (delayed-type hypersensitivity, DTH response (DTH) involving TH1and macrophages) mainly.

INADEQUATE IMMUNE RESPONSES TO INFECTIOUS AGENTS

- Causes **immune** **suppression**—an example is infection with HIV, which alters T cell immunity and allows further infection with opportunistic pathogens.
- Release toxins that function as **superantigens**, initially stimulating large numbers of T cells to proliferate but, because of the release of cytokines from T cells, ultimately suppressing the immune response and allowing the pathogen to multilply.
- Evade the immune defenses by altering their antigenic structure—an example is that influenza virus undergoes antigenic variation by two mutational mechanisms called **antigenic shift** and **antigenic drift** that creat new antigenic phenotypes which evade the host's current immunity and allow reinfection with the virus.