

# Intro to the Immune System

## 451Micro

PRESENTED BY

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There are 2 major lines of defense:

**Non-specific**  
**(Innate Immunity)**

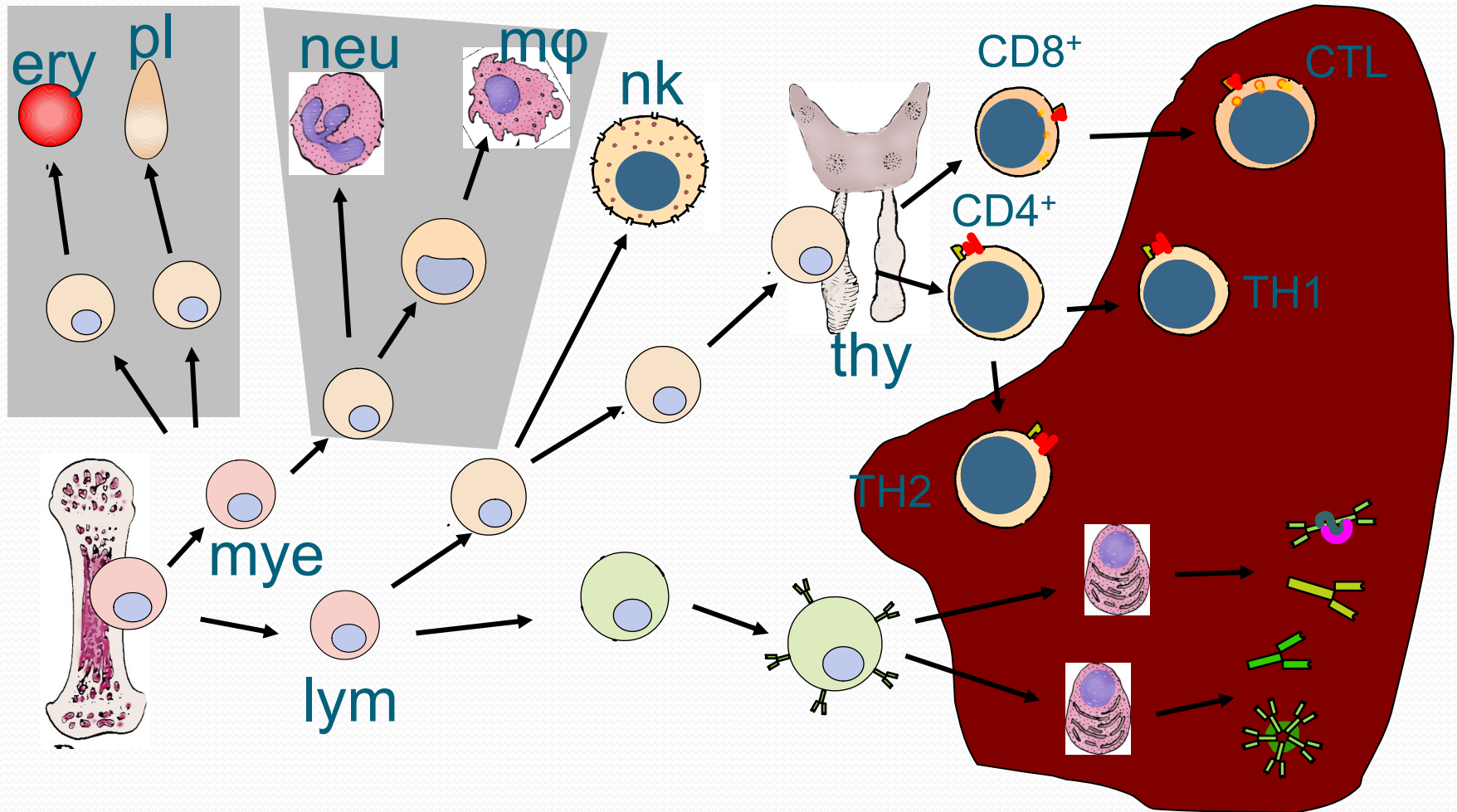
and

**Specific**  
**(Adaptive Immunity)**

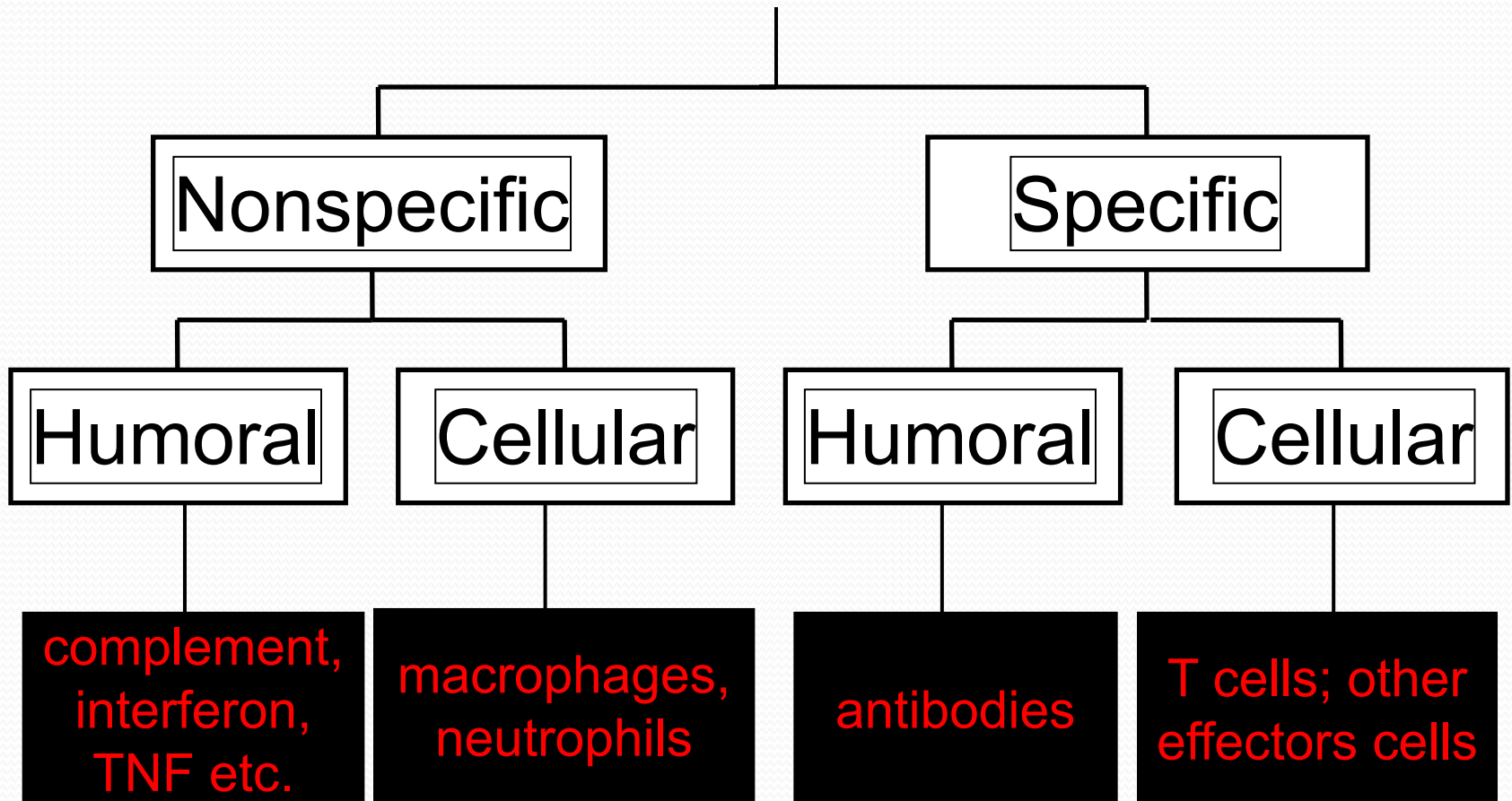
Photo of macrophage cell



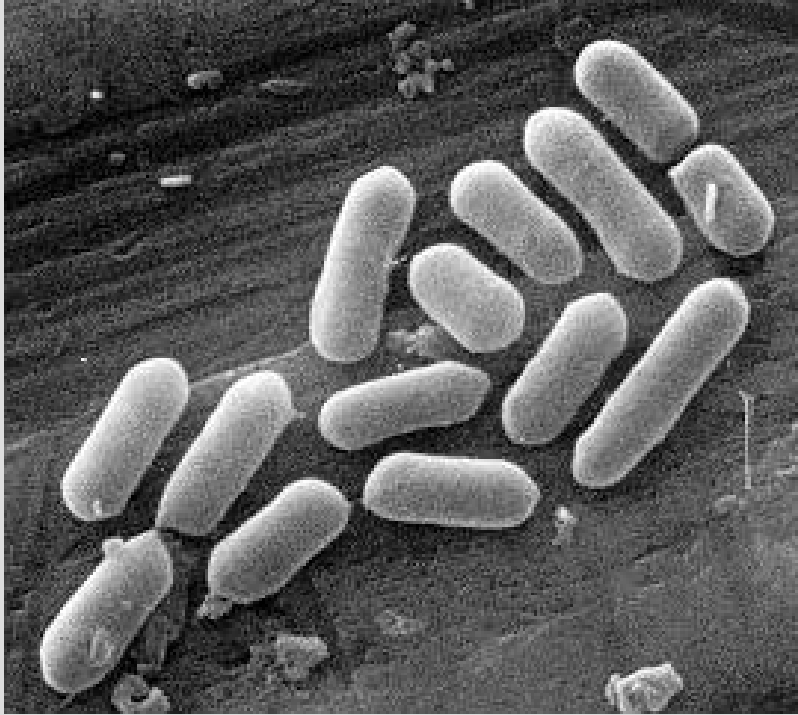
# Development of the Immune System



# Components of the Immune System



# Innate (non-specific) Immunity



- 4 barriers to infection:

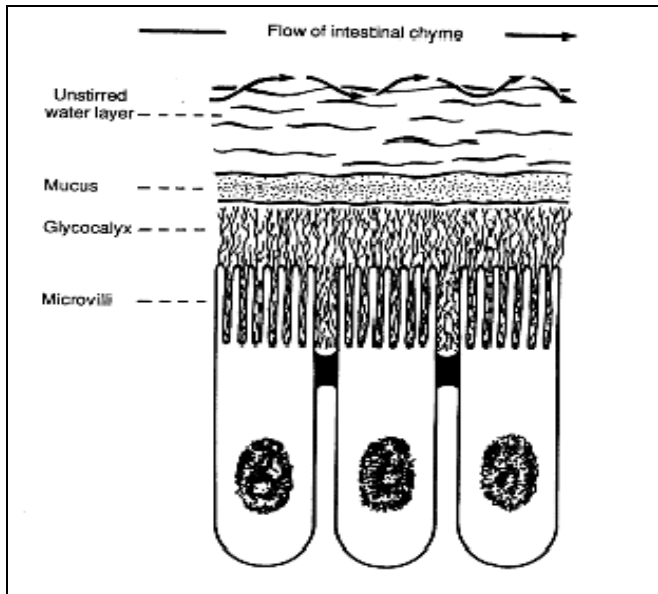
- Anatomic
- Physiologic
- Phagocytic
- Inflammatory

- 1<sup>st</sup> 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 innate immunity – **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

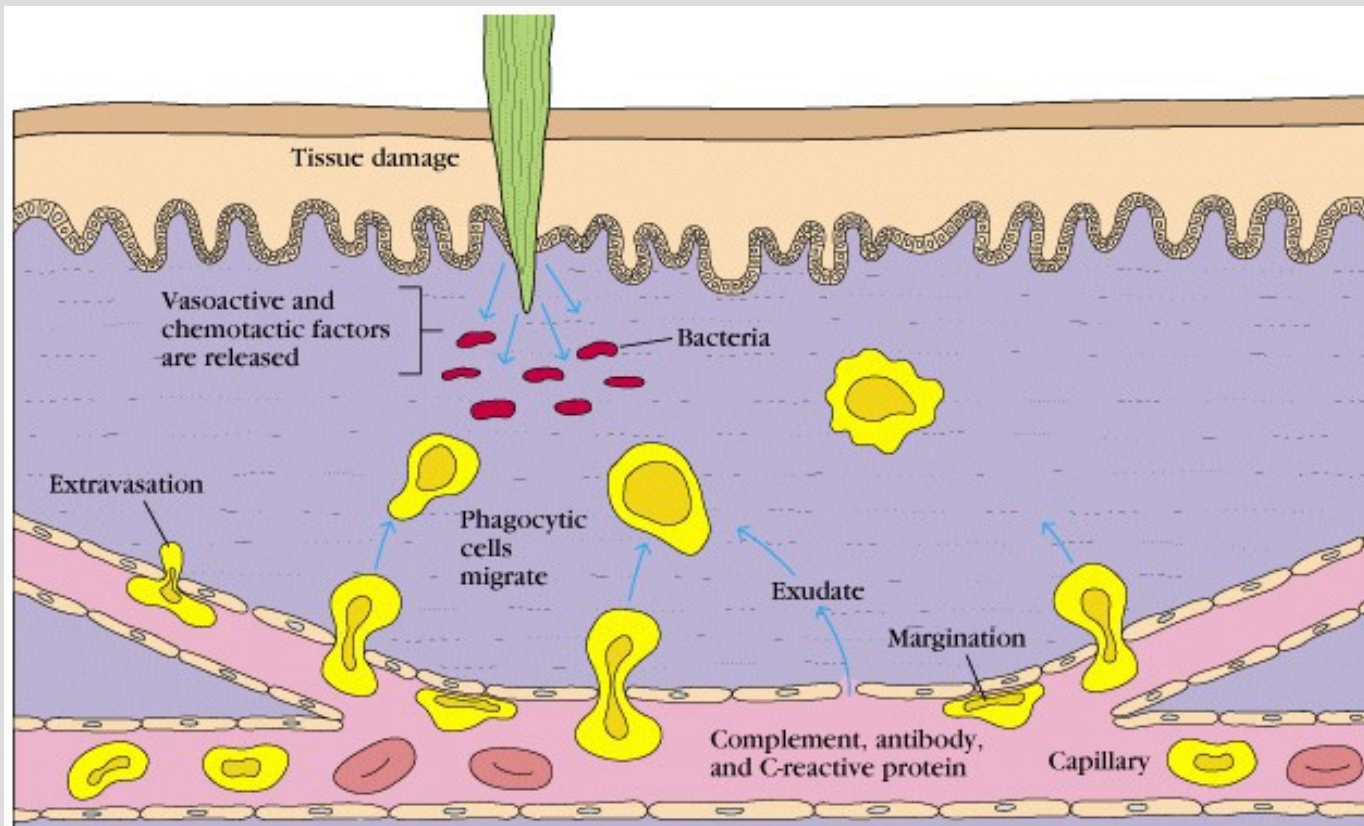
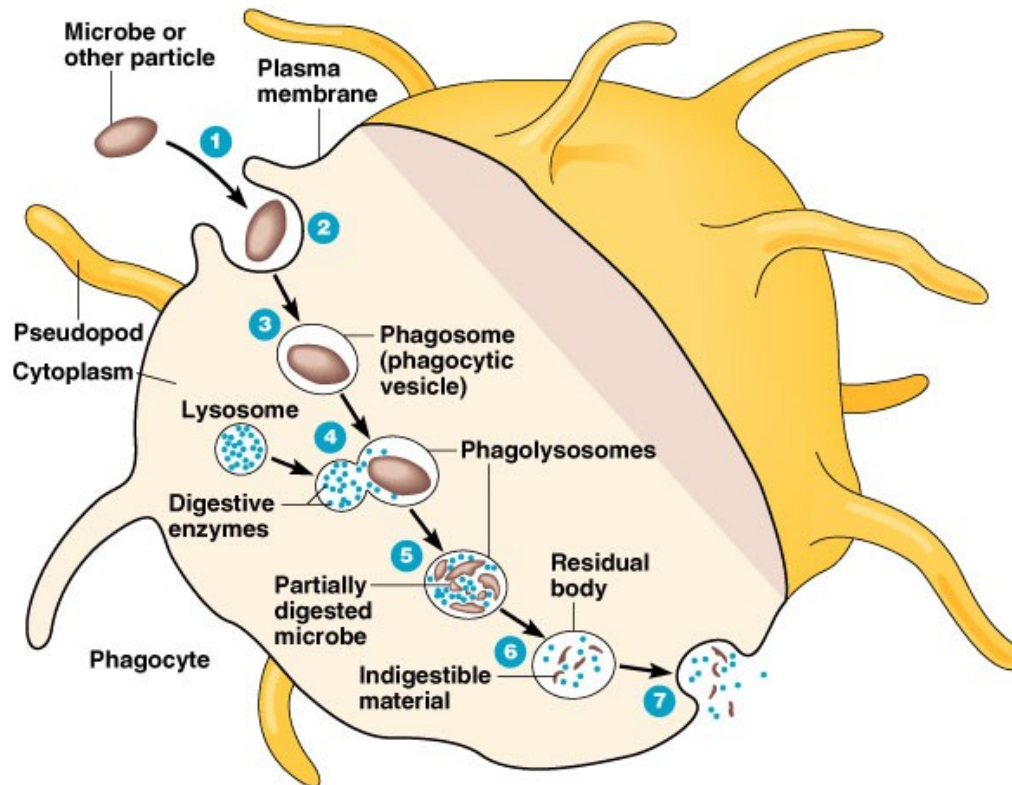


Fig 1-4 Kuby 5e





- 1 Chemotaxis and adherence of microbe to phagocyte.
- 2 Ingestion of microbe by phagocyte.
- 3 Formation of a phagosome.
- 4 Fusion of the phagosome with a lysosome to form a phagolysosome.
- 5 Digestion of ingested microbe by enzymes.
- 6 Formation of residual body containing indigestible material.
- 7 Discharge of waste materials.

**(a) Phases of phagocytosis**

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# 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

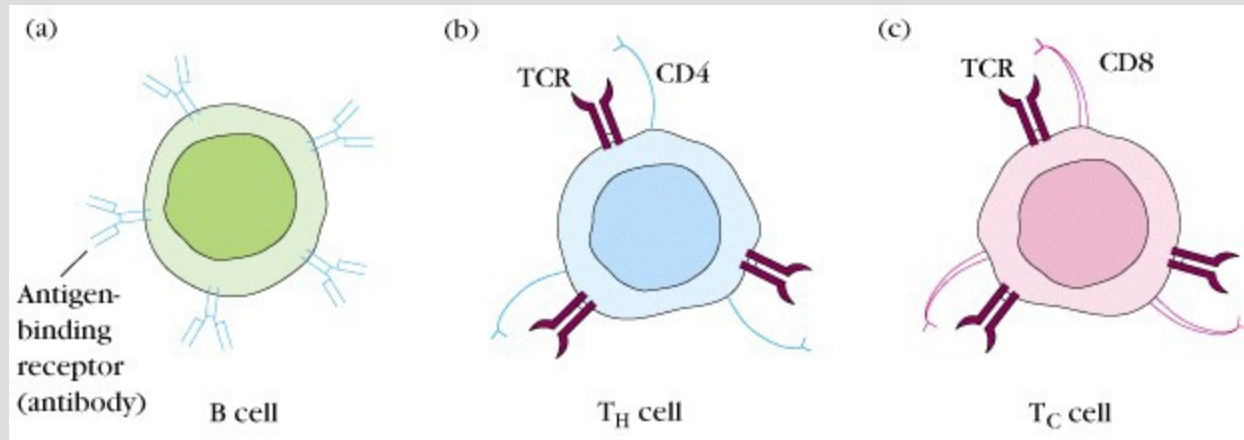
4) **self-nonself recognition** –the system typically responds only to foreign molecules

**\*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:

## B cell

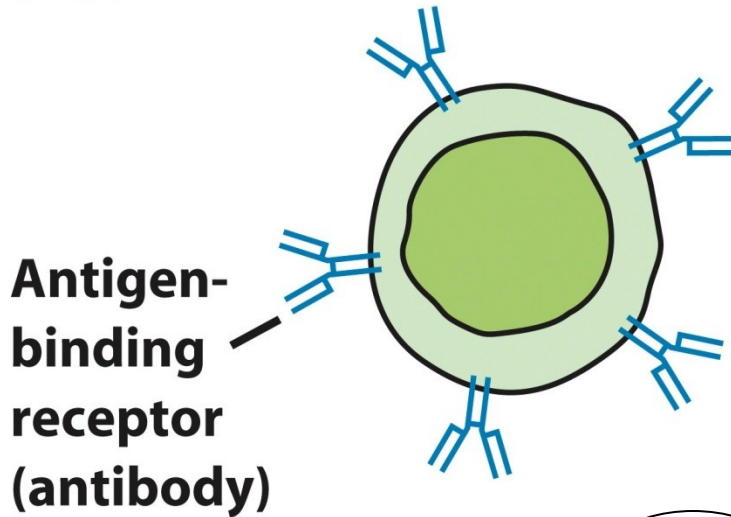


Figure 1-7a  
Kuby IMMUNOLOGY, Sixth Edition  
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Humoral Immunity

- 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

**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

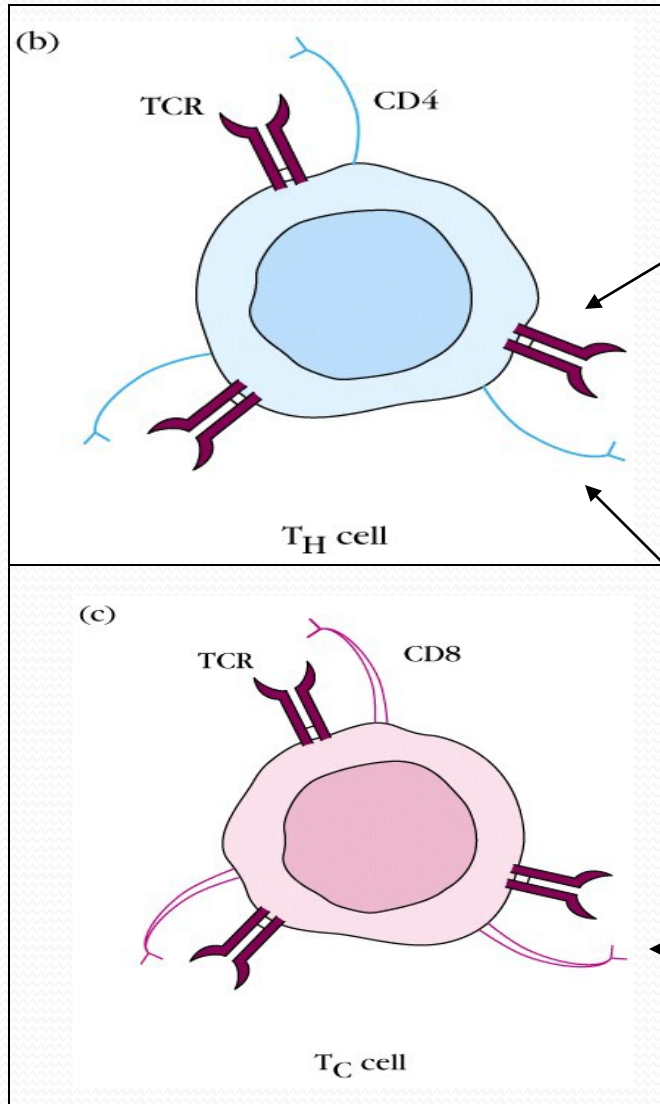
- MHC I – found on nearly all nucleated cells
- MHC II – found only on APC's

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:

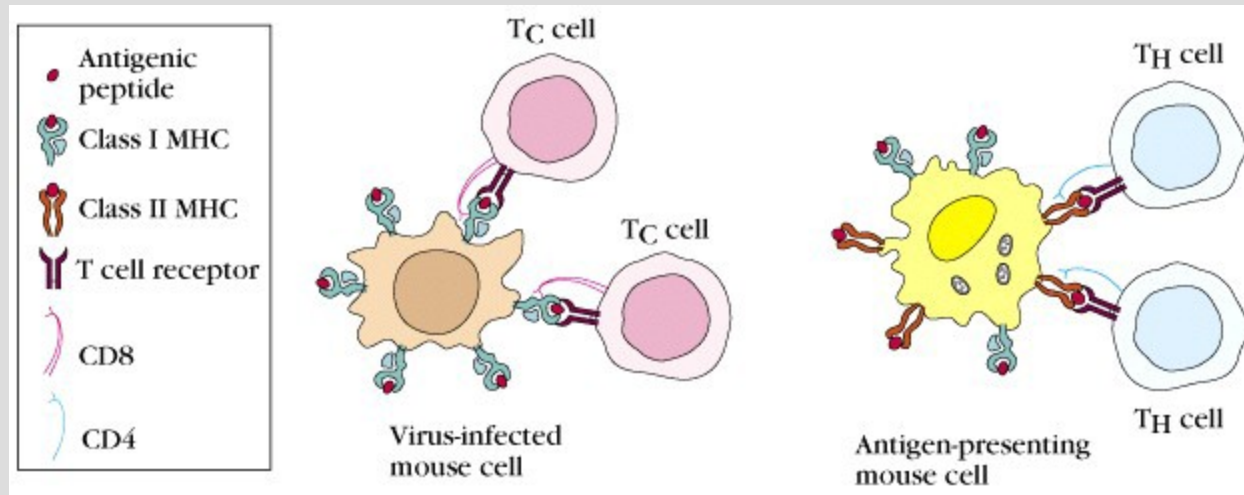


Fig 1-8 Kuby, 4e

Different patterns of cytokines determines types of IR:

-if T<sub>C</sub> cell recognizes an Ag/MHC I complex, it divides and differentiates to become CTL

if T<sub>H</sub> cell recognizes Ag/MHC II complex, it divides and stimulates B cells, T<sub>C</sub> cells, and MØ

# Humoral vs Cell-mediated Immune Response:

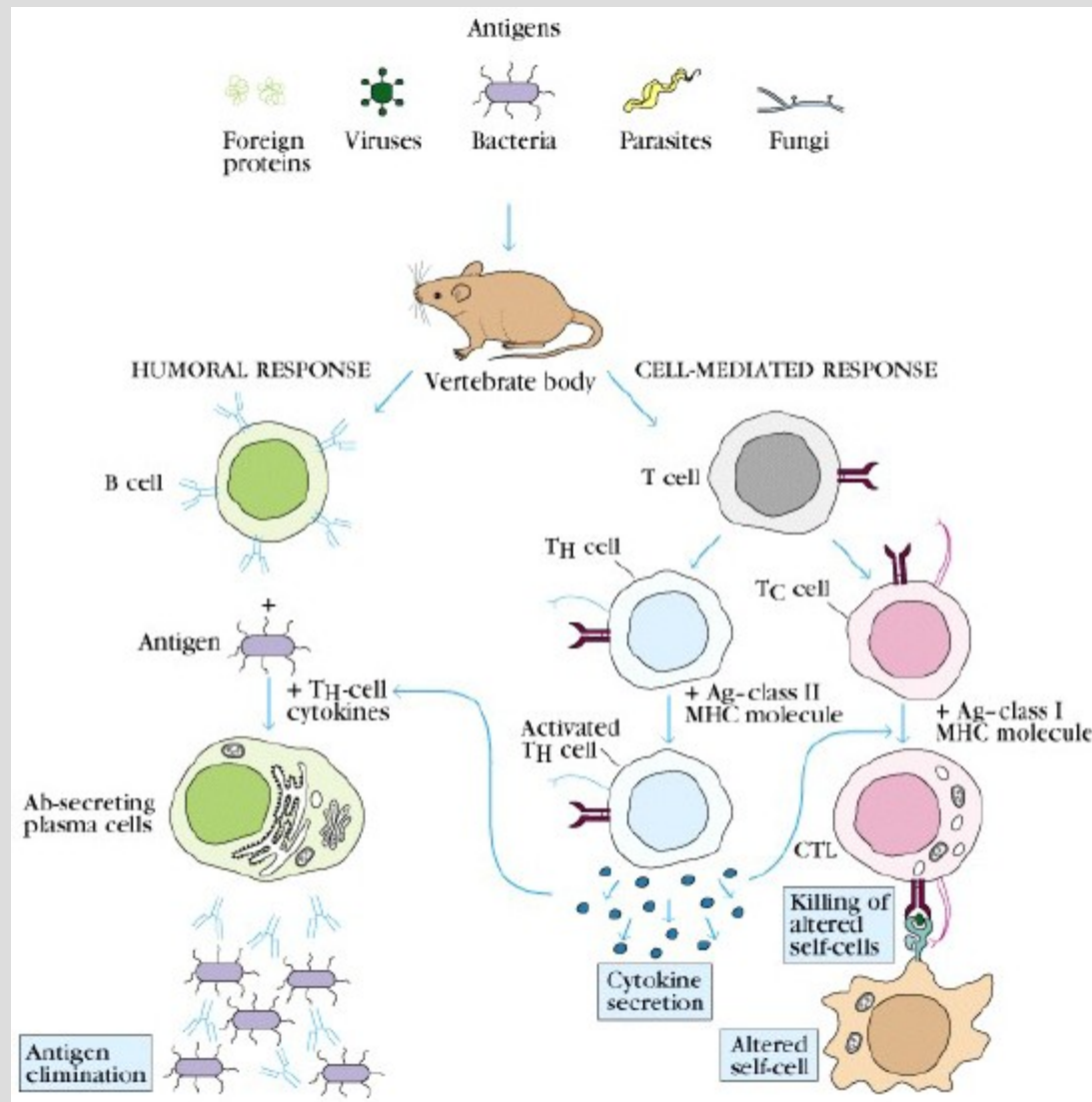
Humoral IR: occurs when Ag becomes coated with Ab which brings about the elimination of the foreign body

- 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



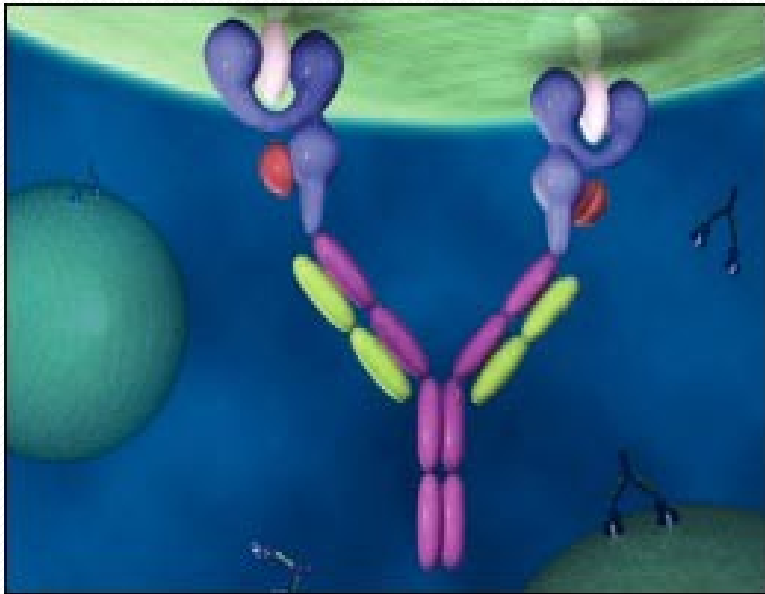


Next, a bit about antigens (Ag's)...

## 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)



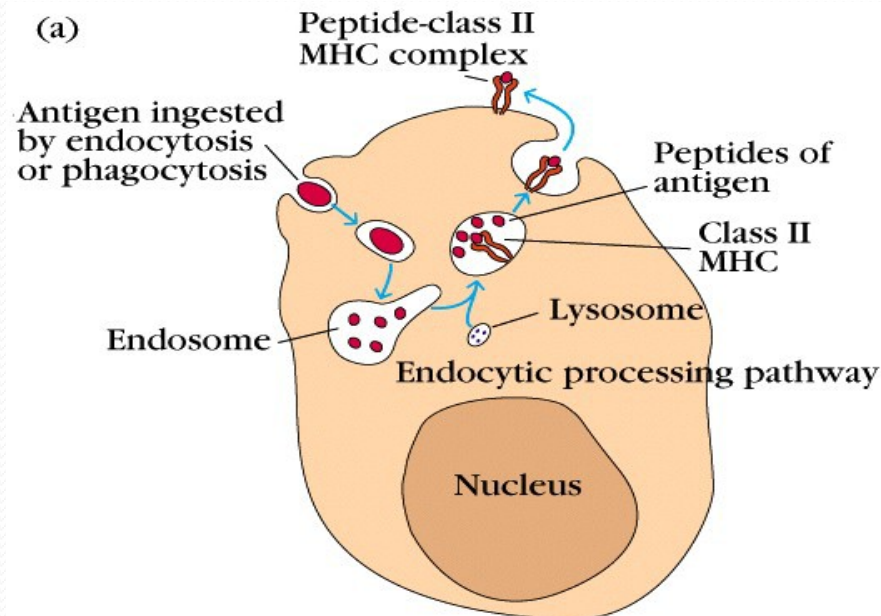
**\*\*Maturation of B & T cells creates enormous receptor diversity for binding foreign Ag**

## 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!

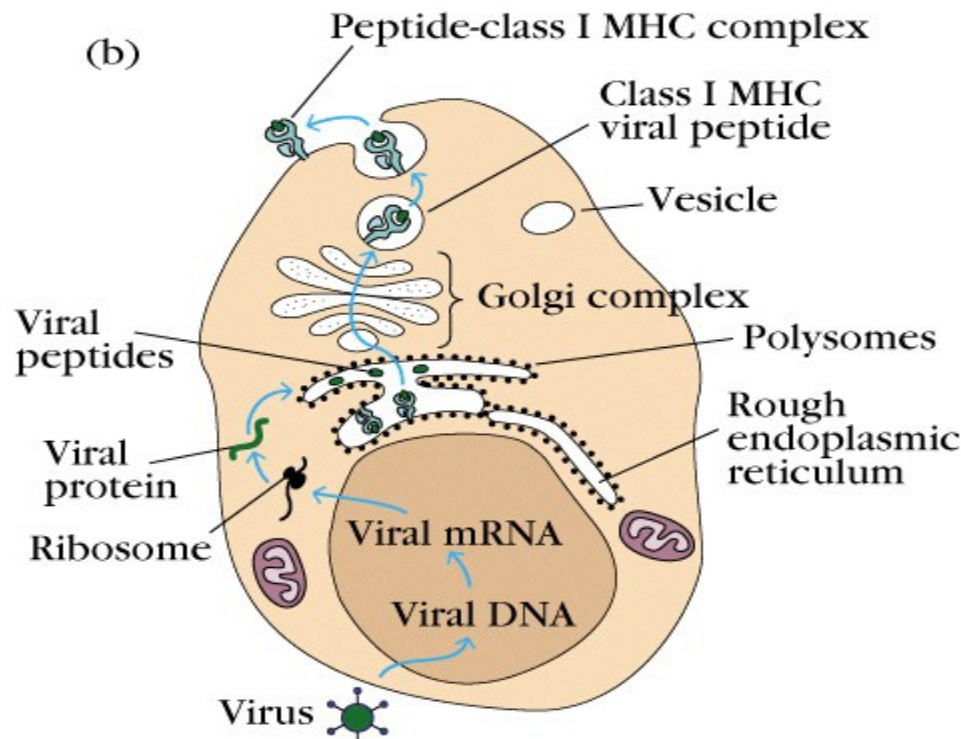
- then APC digests Ag into peptide fragments, combines fragments with MHC Class II within the cell and transports MHC II/ Ag peptides to surface of cell → for presentation to **CD4 T cells** (these T cells are MHC II restricted)



## 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

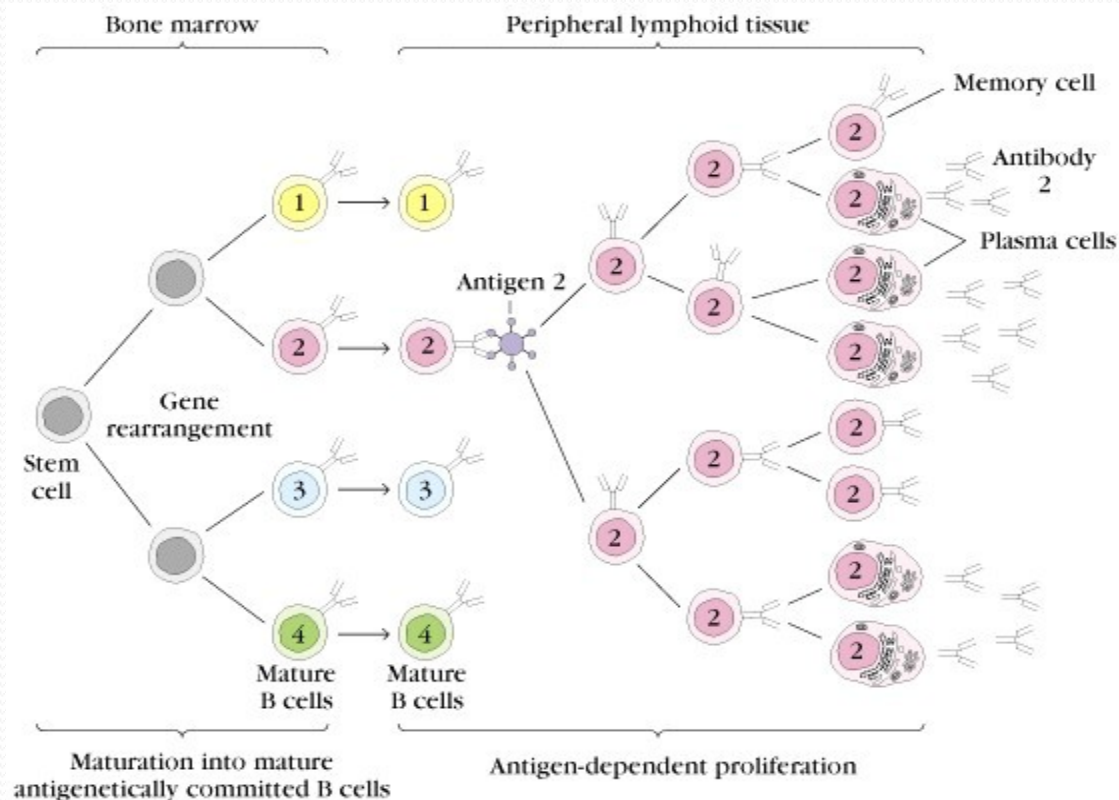
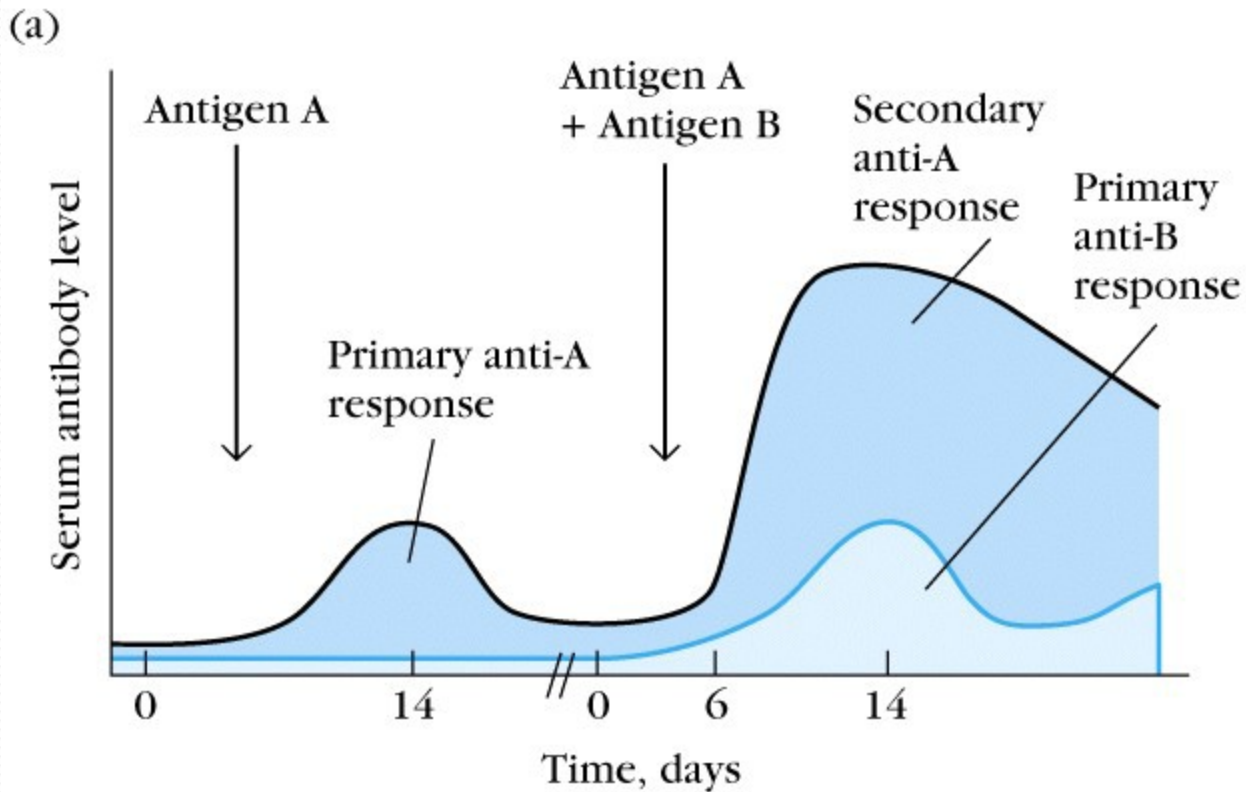


Fig 1-10 Kuby, 4e

# **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)

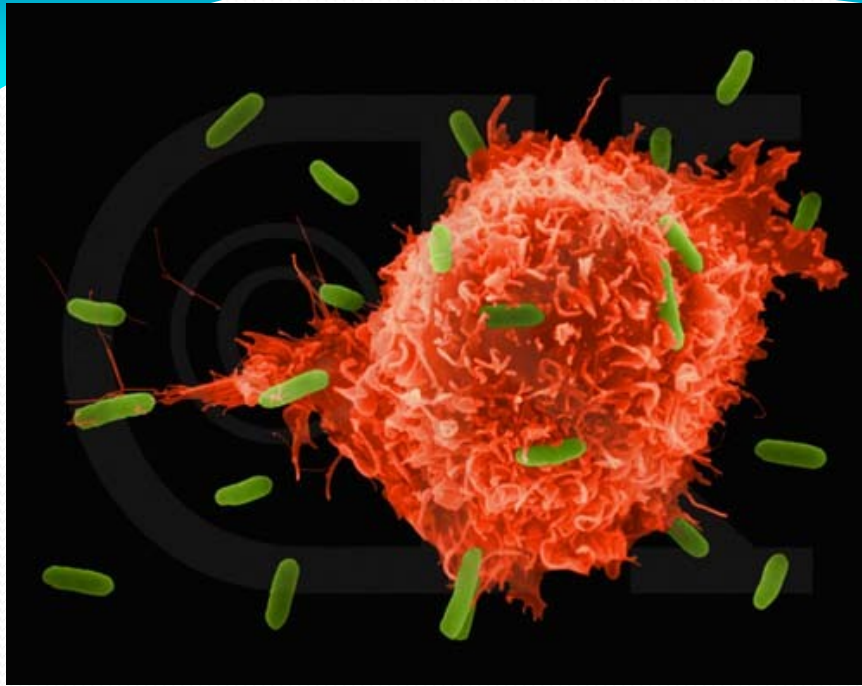
### cells

**phagocytes**, NK cell  
eosinophils, K cells

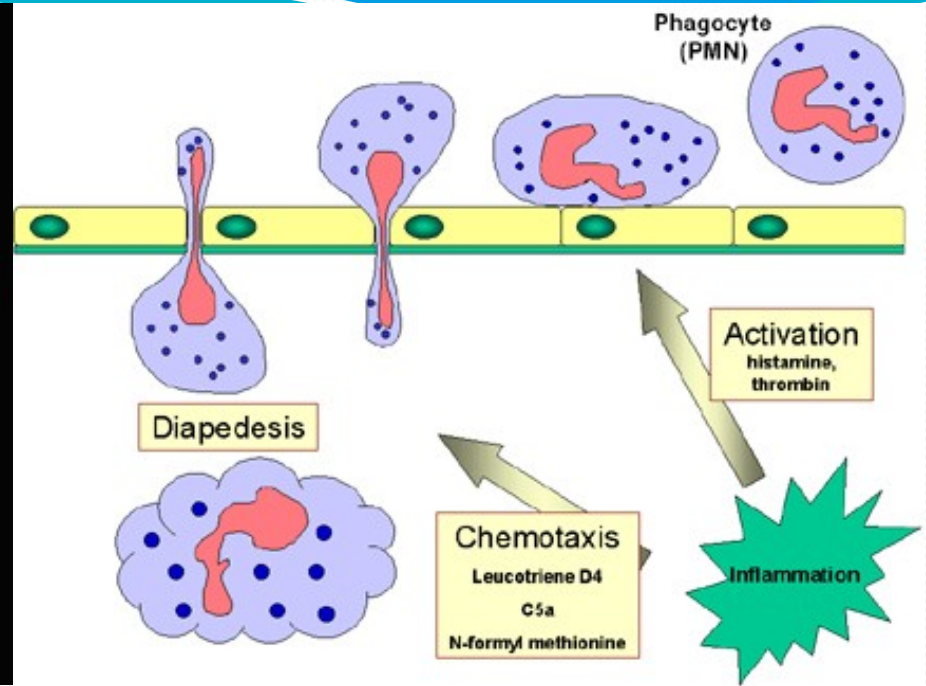
T and B lymphocytes

## 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	muco ciliary elevator surfactants
Nasopharynx and eye	mucus, saliva, tears	flushing, lysozyme
Blood and Lymphoid organs	Phagocytes	phagocytosis and intracellular killing
	K, NK & LAK cells	direct and antibody dependent cytotoxicity
Serum and other serous fluids	lactoferrin, transferrin	iron deprivation
	interferons, TNF- $\alpha$	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

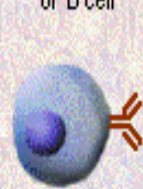
## Pathogens



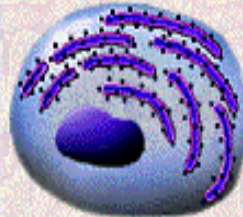
B lymphocyte  
or B cell

Plasma cell

Virus



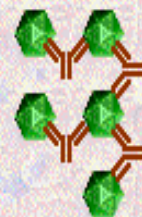
Matures into  
plasma cell



Secretes  
Antibodies

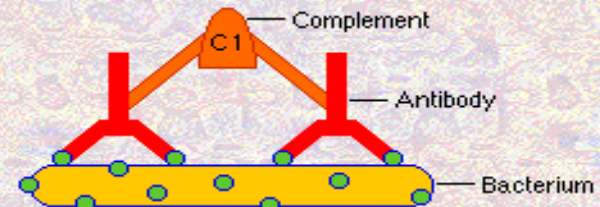


Binds

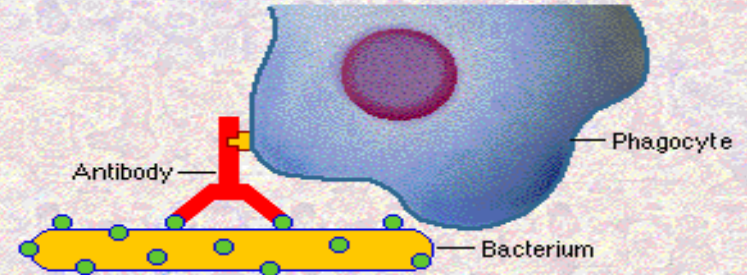


## Linking Function of Antibodies

Antibodies activate the classical pathway of the complement cascade when they link a bacterium to complement protein C1.



Antibodies act as opsonins when they link a bacterium to a phagocyte.



## Pathogens



T lymphocyte  
or T cell

Virus-infected  
cell

CTL

Lysis







Matures into  
active cytotoxic T  
lymphocyte (CTL)

Killing  
reaction

# Characteristics of Innate and Adaptive Immunity

## Innate Immunity

-  Antigen independent
-  No time lag
-  Not antigen specific
-  No Immunologic memory

## Adaptive Immunity

-  Antigen dependent
-  A lag period
-  Antigen specific
-  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 TH1 and 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 multiply.
- **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 create new antigenic phenotypes which evade the host's current immunity and allow reinfection with the virus.