HKU Med
LKS Faculty of Medicine
School of Biomedical Sciences
香港大學生物醫學學院

Enrichment Course in Biology

BIO17-20 Body defense – A brief introduction to Immunology

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Sections covered in this lecture

I. a general concept of body defense

II. introduction to key immune components

III. introduction to two major types of immune response

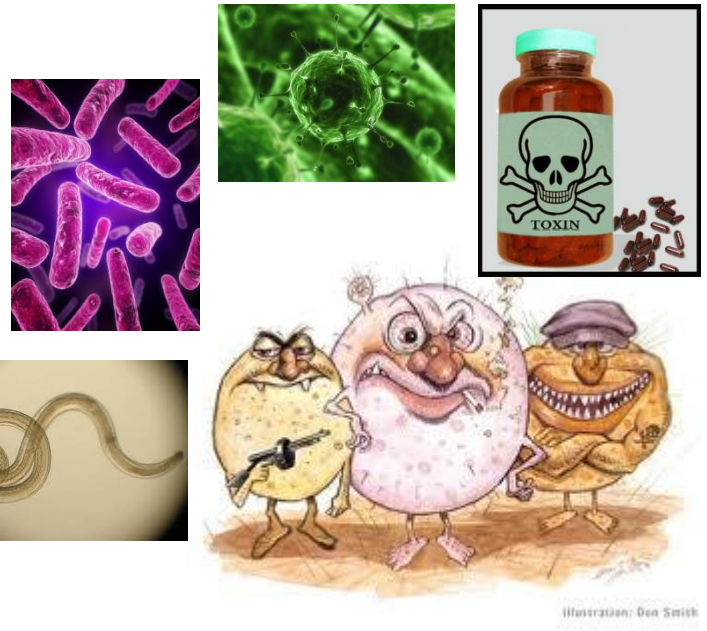
IV. examples of coordinated immune response in health and diseases

BIO17 Learning outcome

At the end of section I, you should be able to

- describe three levels of body defense
- list the characteristics of the first line of defense

The immune system is an army of body guards to defend against invading pathogens!

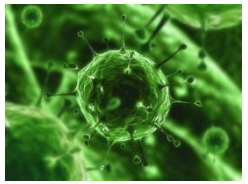


Warfare

Our body is equipped with three lines of defense against infection

Invading pathogens





1st : **Barriers** – physical, chemical and microbiological components that prevent entry

2nd : **Non-specific immune responses** that rapidly remove invading pathogens

3rd : **Specific immune responses** that target and "memorize" specifically to the invading pathogens and mount specific actions

Barriers: first line of defense

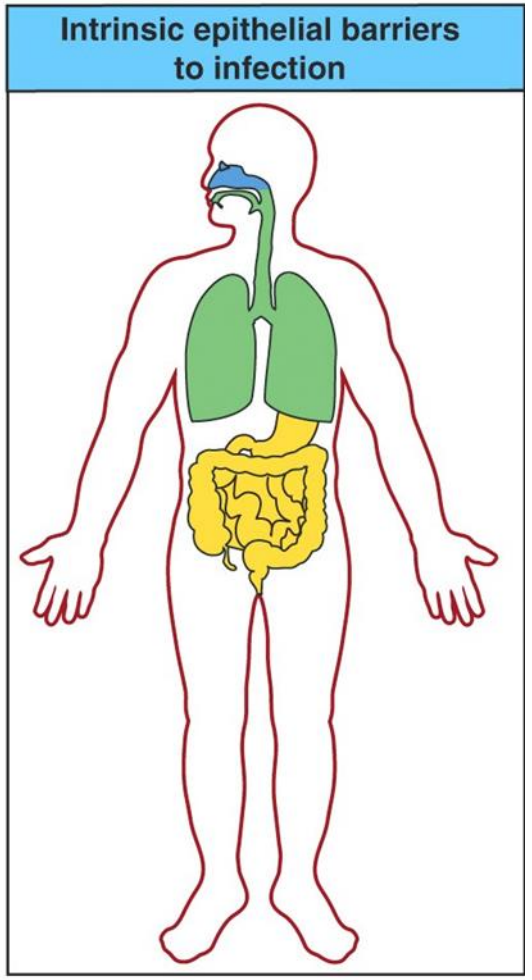
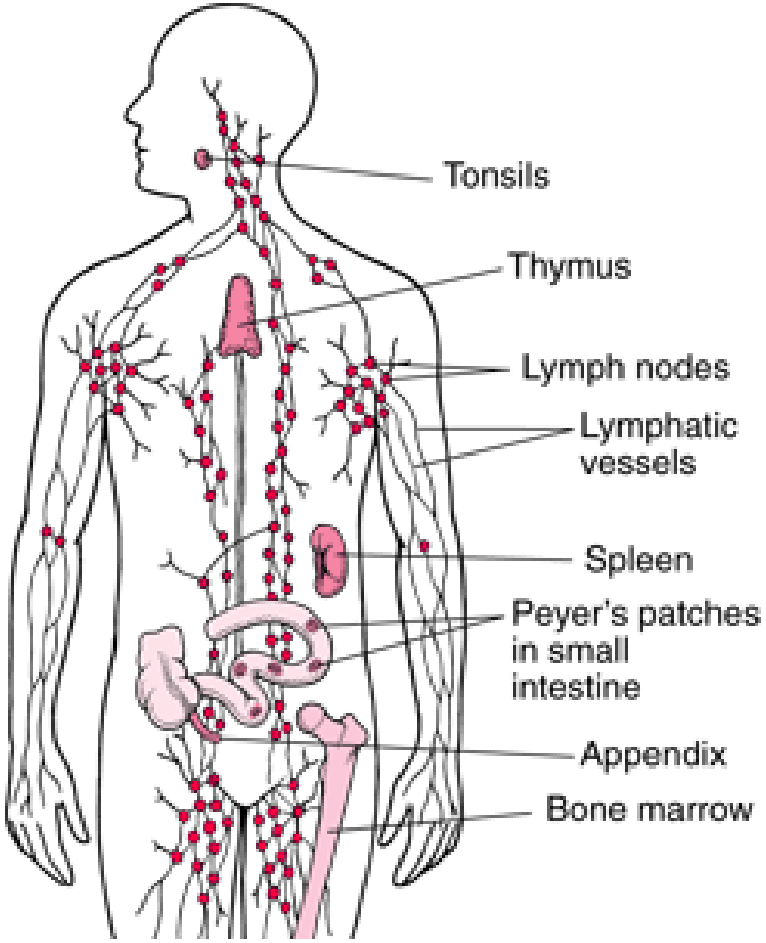


Figure 2-4 Immunobiology, 6/e. (© Garland Science 200

Immune system: second and third lines of defense

Lymphoid organs

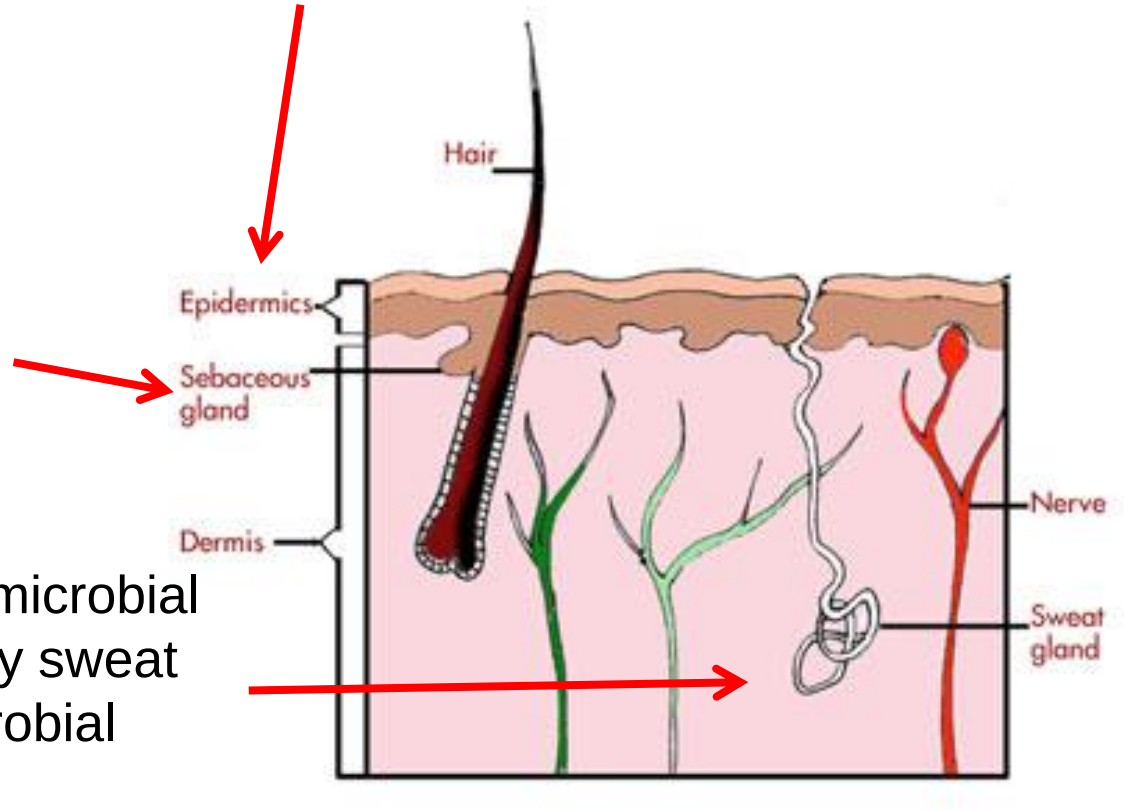


First line defense in skin

- Outermost epidermis is keratinized – layers of dead cornified cells form a physical barrier that prevent pathogen entry

- Fatty acids secreted by sebaceous gland is antiseptic

- Dermicidin, an anti-microbial peptide, produced by sweat gland suppress microbial growth

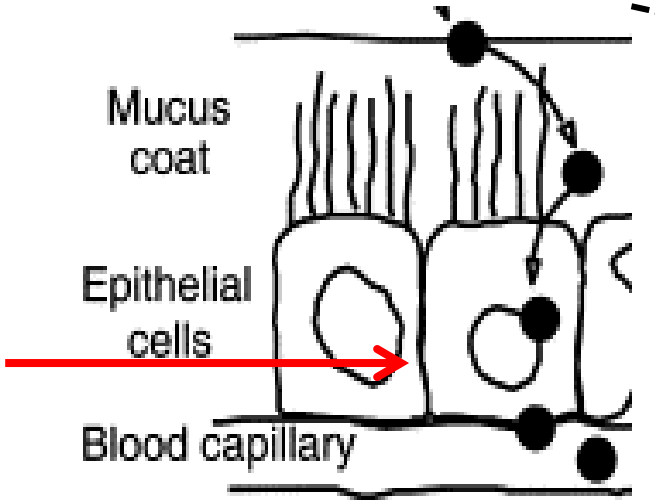


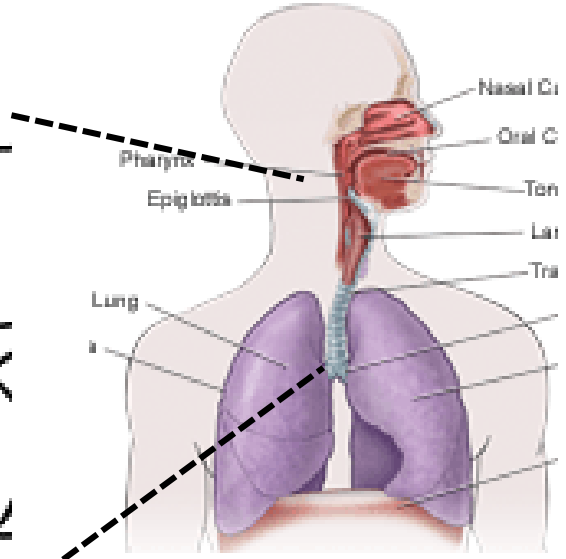
Barriers in respiratory tract

- Ciliated mucus secreting cells:
1. Slimy mucus traps microbes
2. Cilia beat towards upper respiratory tract to remove trapped microbes

- Defensins, antimicrobial proteins, secreted by respiratory epithelial cells to suppress microbial growth

- Tight junction formed a seal between epithelial cells to prevent entry of microbes into the blood stream





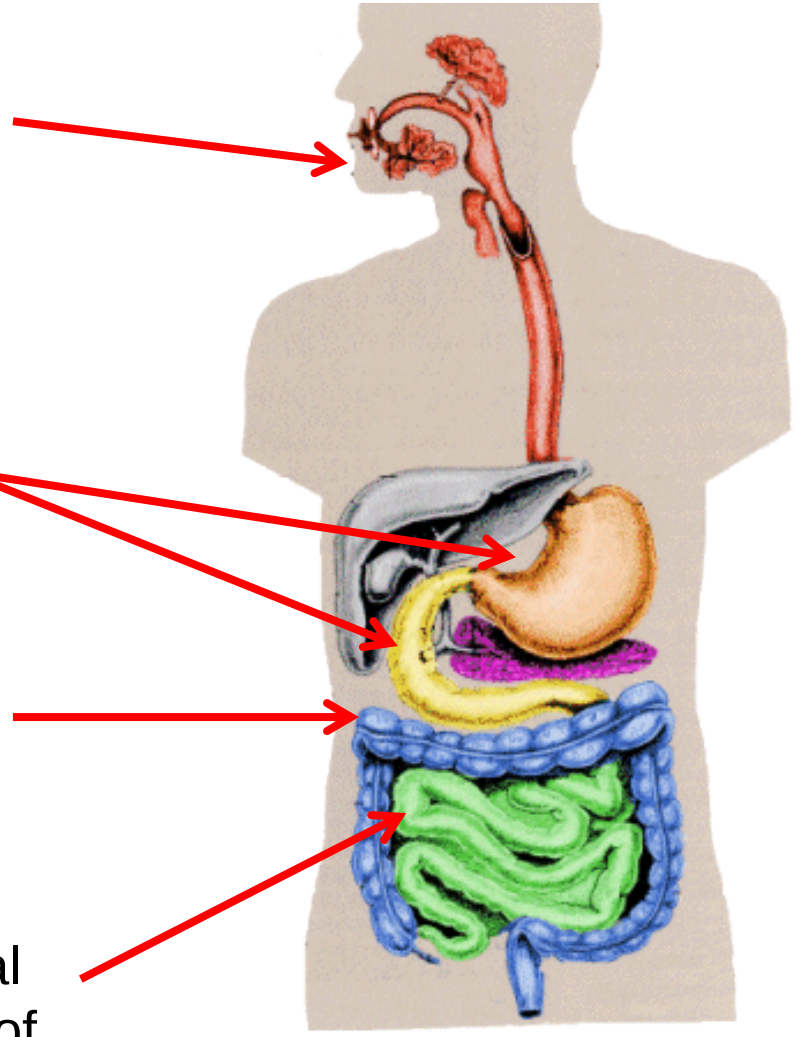
Barriers in gastrointestinal (GI) tract

- Saliva contain enzymes that digest microbes

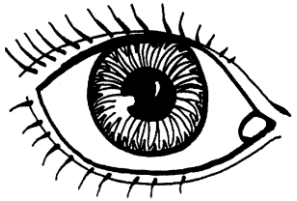
- Gastric and intestinal juices contain digestive enzymes
- Acidic pH in stomach kills microbes

- Antimicrobial defensins are secreted by intestinal epithelial cells

- Symbiotic microbes (normal gut flora) suppress growth of invading pathogens

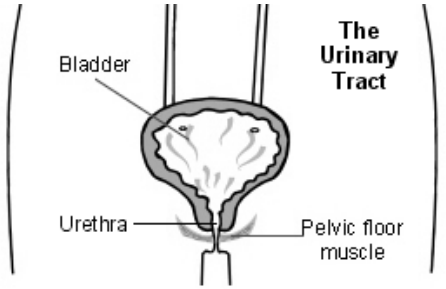


Other barriers



- Tear /lacrimal gland – produce <u>tears</u> that

1) contain enzymes that digest microbes
2) wash away trapped microbes or dust particles in the eyes and nose



- <u>Acidic secretion</u> in vagina that suppress microbial growth
- Normal vagina flora/microbiota

First line of defense: summary

The barriers can be:

- **Mechanical/physical**
  - Keratinization of skin
  - Hairs, cilia and mucus
  - Epithelial cells are joined by tight junctions
- **Chemical**
  - Acidic pH (skin, stomach, vagina)
  - Enzymes: lysozymes (in saliva, sweat, tears), pepsin (gut)
  - Fatty acids (skin)
  - Antibacterial peptides – e.g. defensins (intestine, lung) and dermcidin (sweat glands)
- **Microbial**
  - normal flora (in skin, gut and vagina) keep microbiological balance by competition for nutrients or produce substances toxic to other microbes

BIO18 Learning outcome

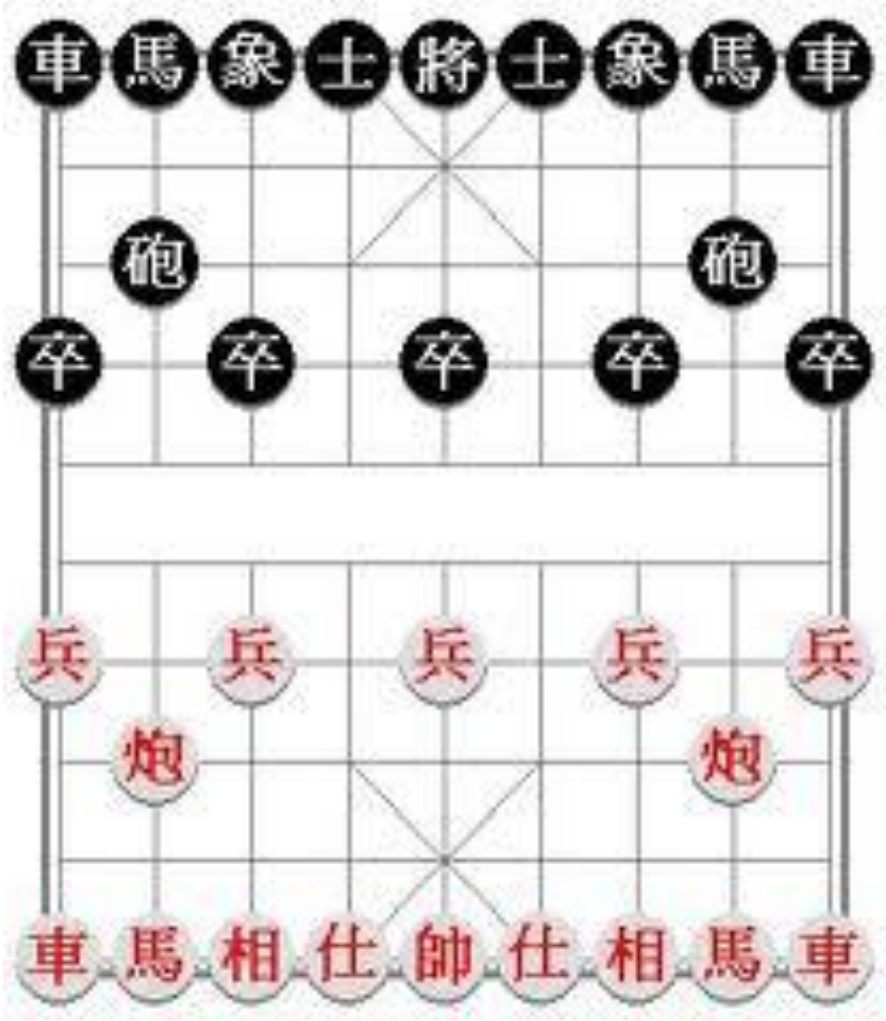
At the end section II, you should be able to

- list major components of the immune system

Common terminology in immunology

- Immune responses – cellular and molecular events that defend the host against pathogens or adverse events
- Antigen – any molecules/ cellular structures that induce immune responses; usually from foreign material but may derive from our own tissues (self/auto-antigen).
- Immunogenicity – ability of a substance to induce either humoral and/or cell-mediated immune responses
- Antigen receptors – specific proteins on cell surface of lymphocytes to interact with antigens and transduce intracellular signals for cell activation
- Antibody – also known as immunoglobulin, a protein produced by immune cells (plasma cells) to bind to specific antigens.
- Humoral immunity – antibody-mediated immune responses
- Cell-mediated immunity – the immune effector functions are carried out by activated immune cells

Immunology made easy



Our immune system is designed to detect and act upon:

1. Self vs non-self
   e.g. infection, transplant rejection

2. Danger signals
   e.g. cancer cells, tissue damages

Components of immune system

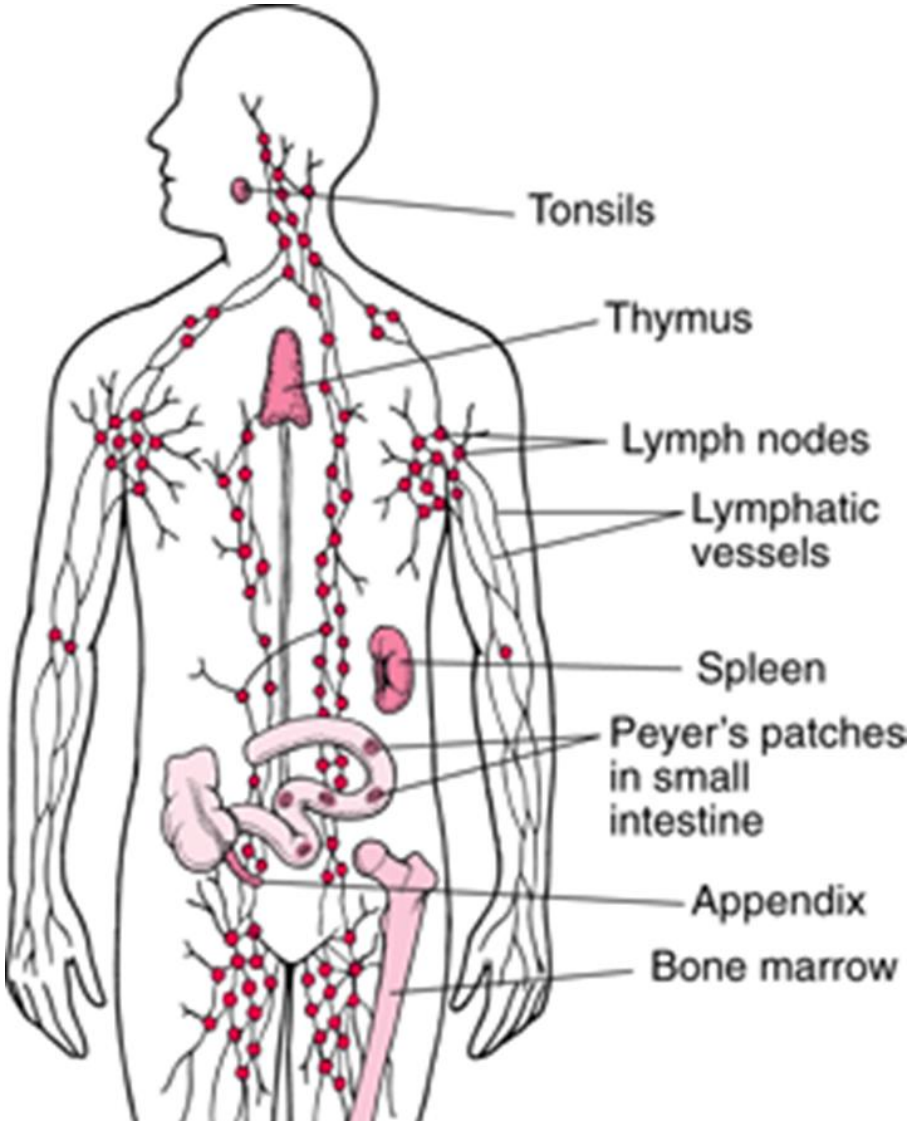
The immune system includes the body parts that help in the recognition and destruction/removal of foreign/harmful materials.

(i) organs and cells of immune system

(ii) Non-specific /innate immunity

(iii) Specific / adaptive immunity

Lymphoid organs/tissues



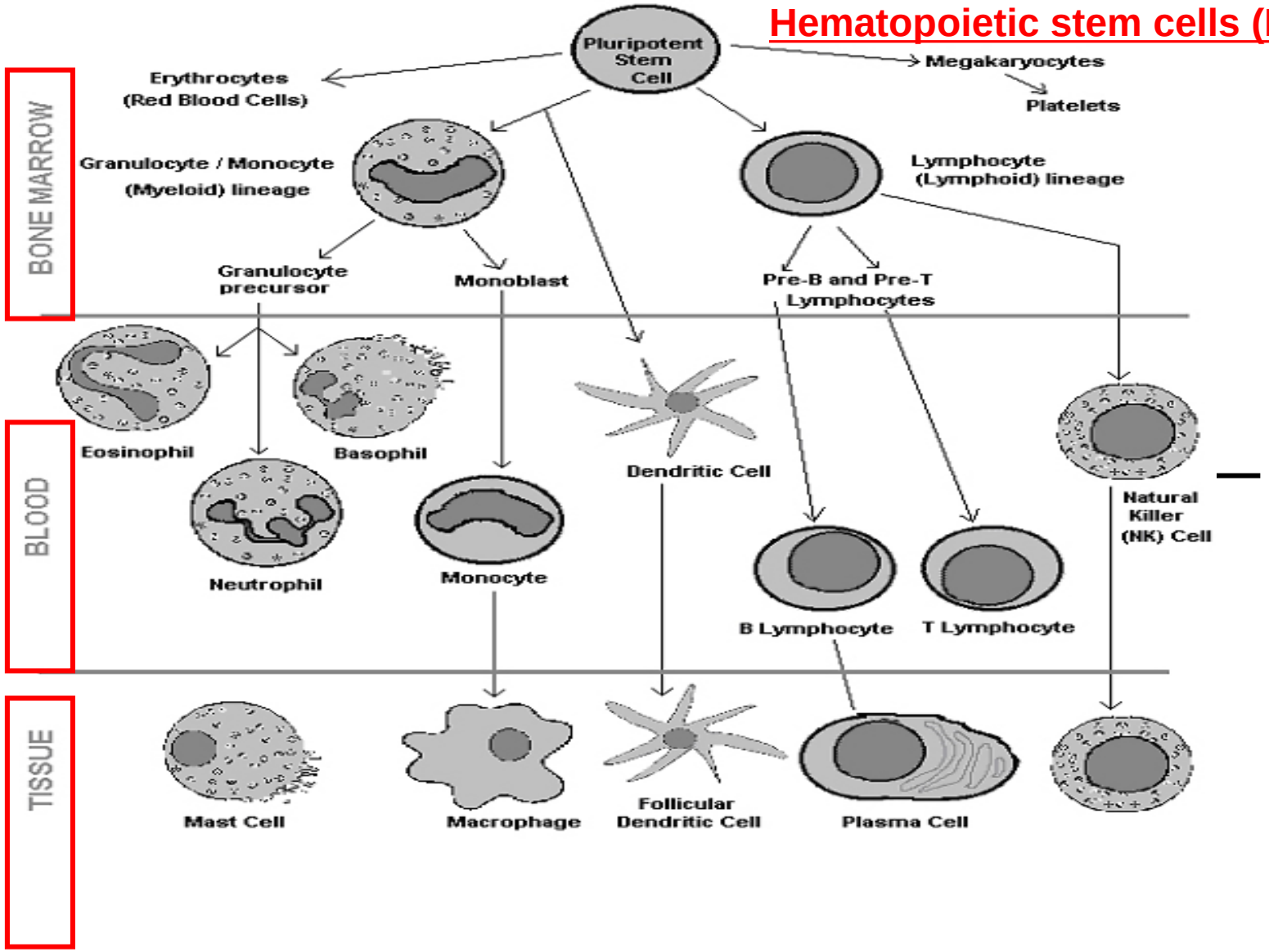
(I) Primary lymphoid organs – sites of leukocyte development from precursor cells

- **Bone marrow – source of haematopoietic stem cells (blood cell precursors)**
- **Thymus**

(II) Secondary lymphoid organs – sites of leukocytes interaction, activation and differentiation

- **Spleen**
- **Lymph nodes**
- **Tissue associated lymphoid tissues (e.g. Tonsils, Peyer's patches)**

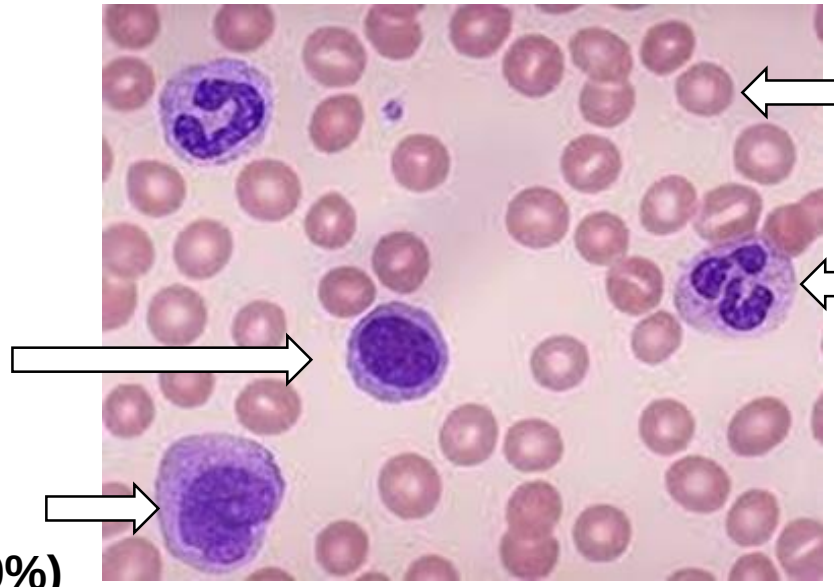
An overview of cells in the immune system



Common cell types in the blood

lymphocyte (20-40%)

- T cells – for adaptive immunity
- B cells - for adaptive immunity
- NK cells –killer cells, innate response



Erythrocyte

Polymorphonuclear (PMN) leukocyte (45-65%)

- **also refer as granulocytes**
- **most abundant granulocytes in blood is neutrophils**
- **phagocytic cells**

Monocyte (3-10%)

- Phagocytic,
- can turn into macrophages in tissues

The human immune system

- The **second and third** lines of defense are both part of our active immune system

- All immune cell populations are developed from haematopoietic (from Greek, means “blood making”) stem cells (HSC) of the bone barrow. Cord blood is also another source of hematopoietic stem cells.

- HSC can be differentiated into the major players in the immune system (granulocytes, monocytes, lymphocytes, dendritic cells) as well as cells not involved in immune action, such as erythrocytes (red blood cells) and megakaryocytes (for blood clotting).

- White blood cells (or called leukocytes) in the body are the immune cell populations that guard us against infections or danger signals

The human immune system

- Immune cells circulate in the body via blood vessels and lymphatics and take residence in lymphoid organs (e.g. spleen, lymph nodes) as well as any tissue organs (e.g. tissue macrophages)

- Some immune cells mainly perform non-specific immune actions (innate immunity) e.g. macrophages, granulocytes, monocytes, natural killer (NK) cells, dendritic cells

- and some immune cells specialize in antigen-specific immune responses (adaptive immunity) e.g. B cells and T cells

- Each cell type is specialized to carry out different functions and act synergistically to mediate protection

BIO19 Learning outcome

At the end of section III, you should be able to

- Understand the major differences between innate and adaptive immunity
- Give examples of innate and adaptive immunity

Non-specific immunity (innate immunity)

- If microbes evade first line of defense, the innate immune response will be ready to take action
- Innate responses pre-exist in all individuals, and is ready to act rapidly (within minutes or hours) upon exposure to microbes
- The action is non-specific because it responds in similar fashion to a broad category of micro-organisms, and there is no enhancement of responses in subsequent re-exposure to the same pathogens i.e. no immunological memory of pathogen
- Innate immune functions can be carried out by immune cells directly or by the macro-molecules (humoral factors) they produced.
- Examples of immune cells for innate responses: macrophages, neutrophils, natural killer (NK) cells, mast cells, eosinophils, basophils and dendritic cells

Examples of non-specific immune function -1

- Direct killing of microbes by phagocytosis – a mechanism of "eat and digest" of microbes or cell debris
- Phagocytes (e.g. macrophages, neutrophils) can engulf bacteria and digest them intracellularly

A bacterium being enclosed by a macrophage

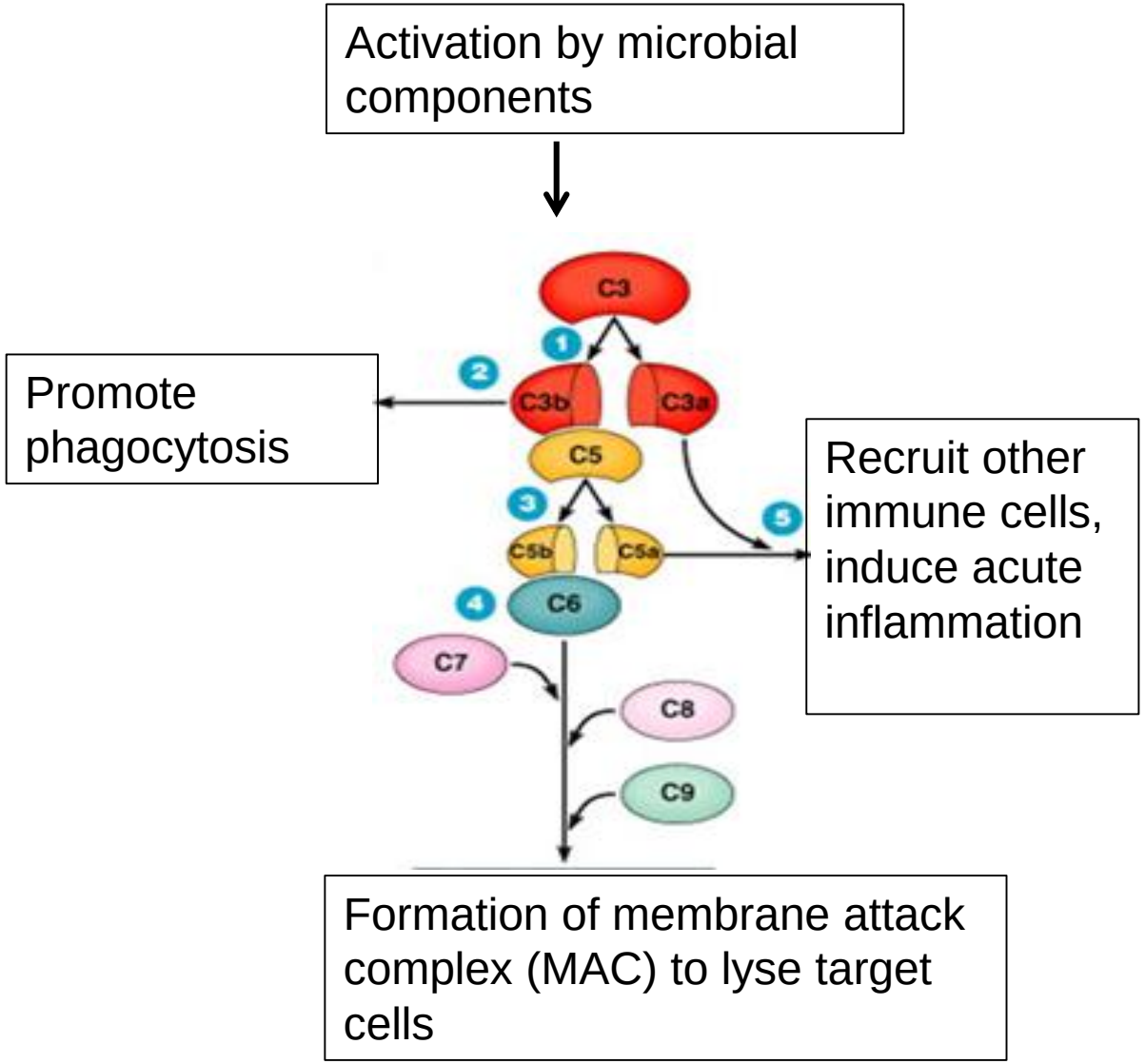
- Natural killer (NK) cells can kill infected or abnormal cells in close contact
- Kill by releasing toxic granules to penetrate and lyse the target cells directly

A target cell being attacked by two NK cells

Examples of non-specific immune function - 2

Complement cascade

- Complement proteins are a family of serum proteins that elicit non-specific immune protection
- A chain reaction will be initiated by infectious microbes to produce several active complement components (e.g. C3b, C3a, C5a, MAC) which effect in various immune responses

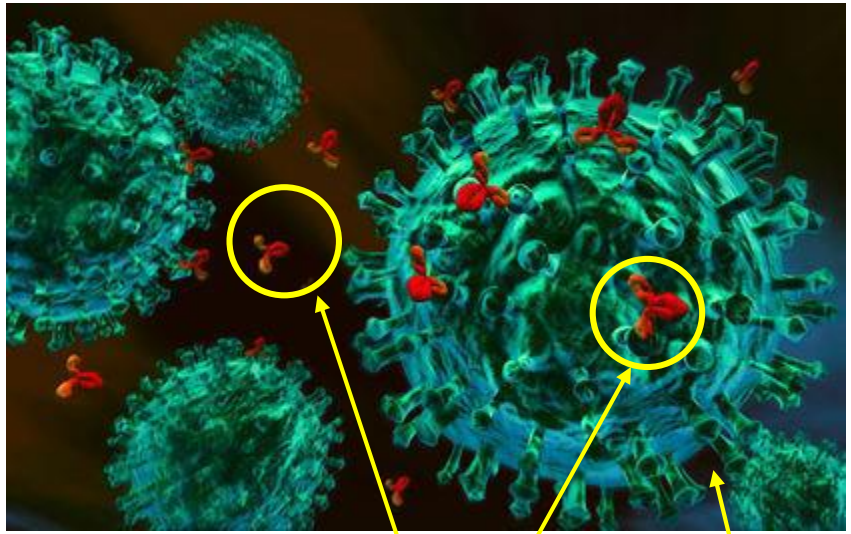


Specific immunity (adaptive/acquired immunity)

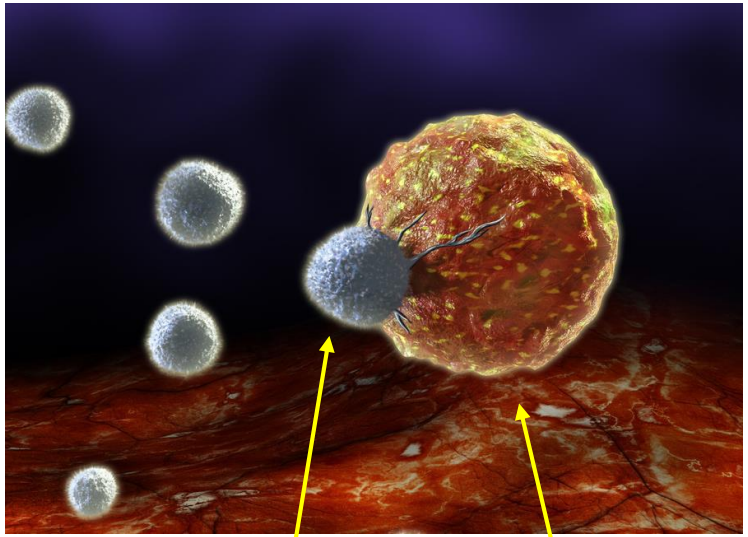
- Specific immunity is not inborn but need to be “acquired” upon exposure to microbes
- Specific immune response takes days to weeks to develop
- The response is antigen-specific as it only recognizes the invading pathogens that initiate the response. It does not cross react with other pathogens, even different strain of the same species.
- Specific immunity has “immunological memory” – it gives better and faster responses in the subsequent re-exposure of the same pathogens
- Two major cell types for specific immune responses: B cells and T cells

T and B cells have different mechanisms of effector action

B cells – humoral response

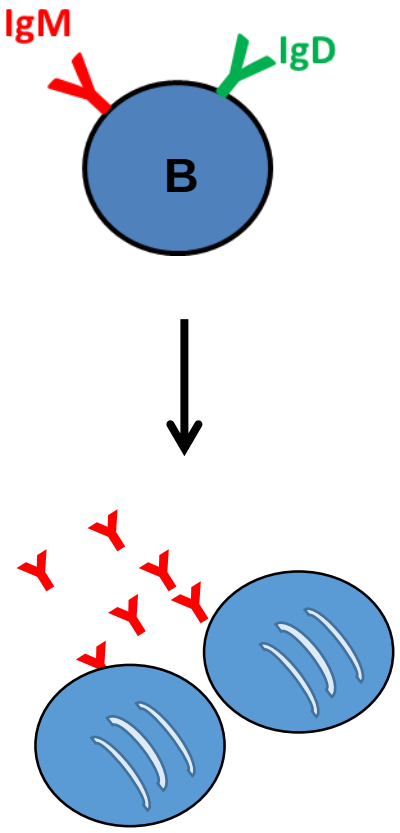


T cells – cellular response

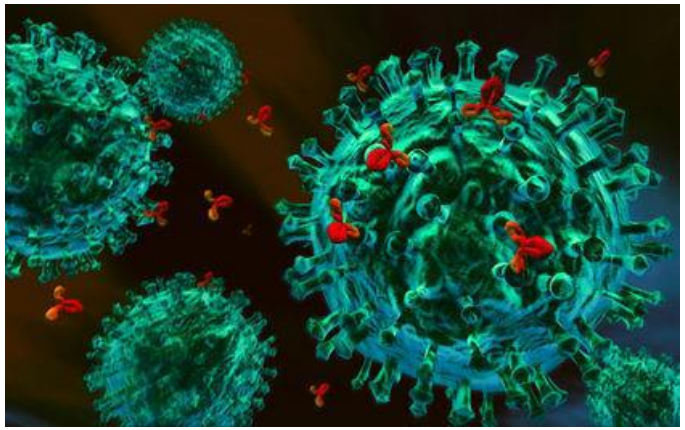


Two arms of adaptive immunity

A. Humoral immunity – B cells



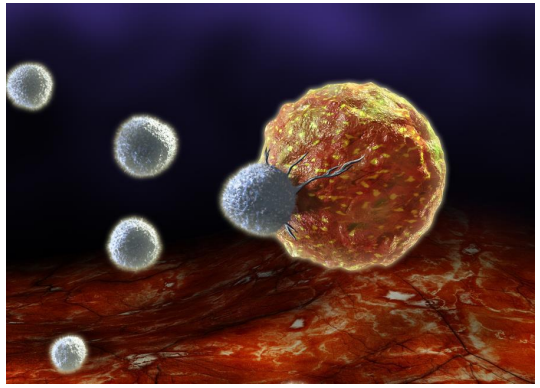
- B cells bear specific antigen receptors (B cell receptor, BCR) on cell surface for pathogens/antigen recognition
- Once activated by pathogens, B cells become plasma cells that secret specific antibodies
- Antibodies are proteins that interact with antigens directly
- Antibodies are antigen-specific, only respond to the initial activating antigen

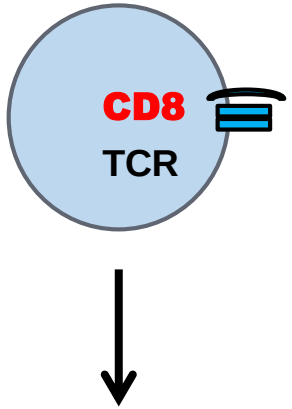


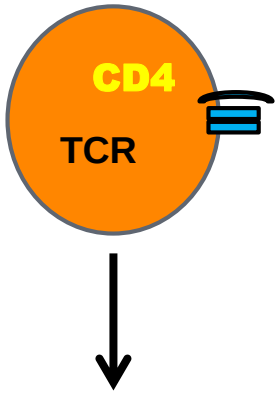
- antibodies can inactivate microbes to prevent further cell invasion
- neutralize toxins and infectious particles,
- facilitate response of other immune cells

Two arms of adaptive immunity

B. Cell-mediated immunity – T cells







- T cells also bear specific antigen recognition receptors (T cell receptor, TCR) on the cell surface
- two major subsets of T cells with distinct functions

Cytotoxic T cells

- Carry out direct killing by releasing toxic granules to the infected cells during cell-cell contact

Helper T cells

- Provide “help” for other immune cells (e.g. B cells, NK cells etc.) through secretion of cytokines (immune cells growth factors and function modulators) or by cell-cell contact

Summary:
A brief overview of immune system

1st line: Characteristics of barriers
- Mechanical, chemical, microbial

2nd line: Innate Immune defense
- characteristics
  - inborn, not antigen specific, quick response and short duration, no immunological memory
- examples of innate defense
  - Cellular: phagocytosis, natural killer cytotoxicity
  - Macro-molecules: complements

3rd line: Specific/adaptive immune defense
- Characteristics
  - acquired during life, antigen-specific in action, takes longer to initiate, develop immunological memory
- examples of adaptive response
  - Humoral: antibodies (B cells)
  - Cell-mediated: T cells

This is a very brief overview and many details will be covered in the relevant immunology lectures in the curriculum

BIO20 Learning outcome

Key learning points:

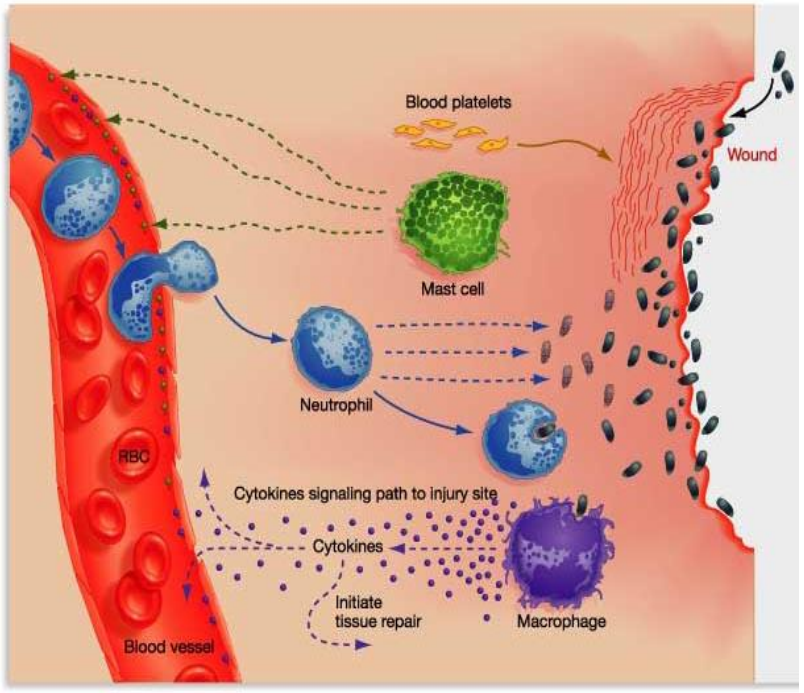
- a basic understanding on the coordinated events in the induction of acute inflammation
- Some examples to illustrate the role of immune responses in health and diseases

Inflammation

Inflammation - local accumulation of fluid, plasma proteins, and white blood cells that is initiated by physical injury, infection, or a local immune response.

- acute local Inflammation: coordinated actions of innate immune responses
- features of acute inflammation: redness, heat, swelling and pain
- These cardinal signs appear rapidly after injury

Key steps in inflammation induction



Step 1 – Tissue Injury

- e.g. caused by bacterial infection, physical cut or burn
- leads to bleeding, cell death and/or microbial invasion which activate resident immune cells

- Local resident immune cells (e.g. macrophages and mast cells) have damage or pathogen-sensing receptors

→ activated and release cytokines and chemokines

http://iahealth.net/inflammation/

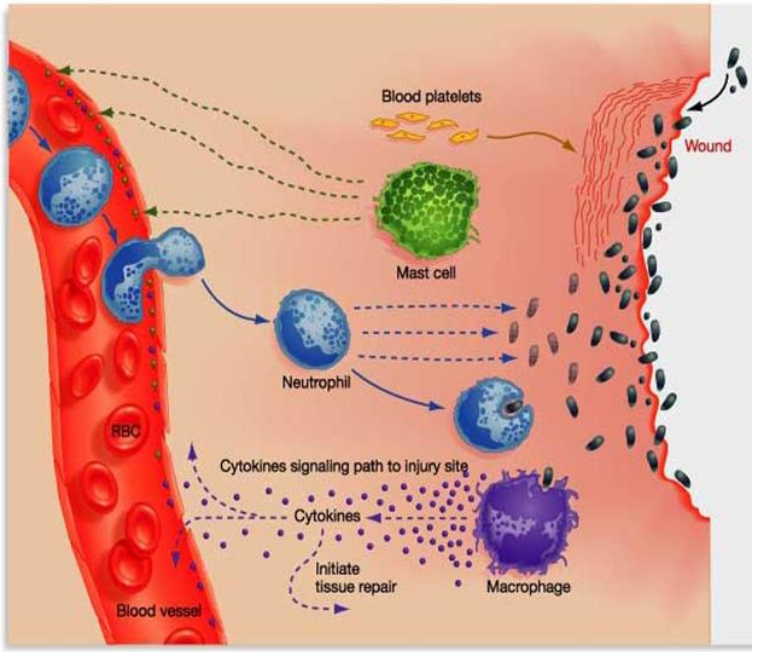
https://www.youtube.com/watch?v=iZYLeIJwe4w

Key steps in inflammation induction

Step 2: Release of chemical mediators

Chemical mediators include:

- Histamine and prostaglandins (lipid mediators) – induce local vascular responses
- Inflammatory cytokines – molecules that modulate the actions or growth of immune cells to elicit inflammation responses
- chemokines – molecules that attract other immune cells to the site of inflammation



Key steps in inflammation induction

Step 3: effector outcomes caused by the chemical mediators

(a) vasodilation

- Dilation of blood vessels or capillaries
  → increased blood flow to the affected area
  → **red** and **hot** (cardinal signs)
- Heat increases the metabolic rate of cells
  → promote healing

(b) Increased capillary permeability

- Fluid leaks into tissues forming an inflammatory exudate containing proteins and cells
- develop **swelling** which exerts pressure and cause **pain**

Key steps in inflammation induction

(c) Chemotaxis

- chemokines attract the migration of other immune cells into the affected site
- blood leukocytes (mainly neutrophils and monocytes) migrate to the injured area
- recruited neutrophils and resident macrophages are phagocytic, thus facilitate the killing and removal of invading micro-organisms
- activated neutrophils and macrophages further produce cytokines that suppress growth of microbes, activate immune cells and induce tissue repairs
- adaptive immune responses develop later and act upon it if the infection cannot be resolved by the innate responses.

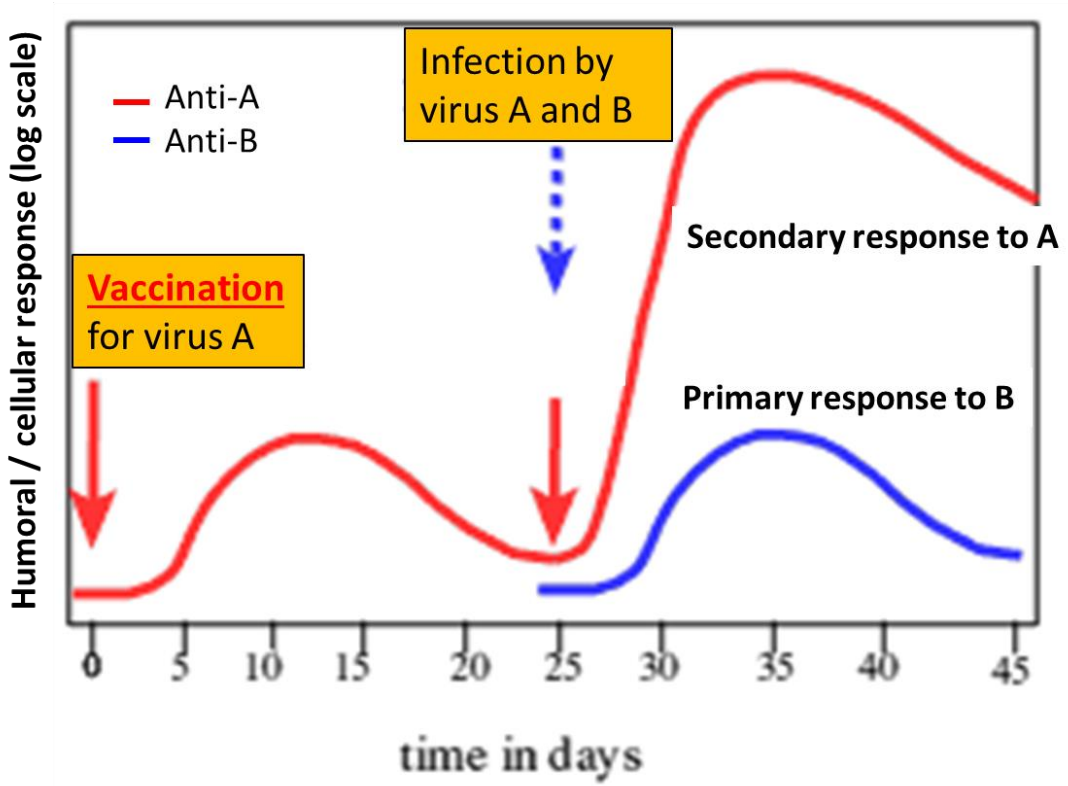
Vaccination – harnessing adaptive immunity

APPENDIX. Hong Kong Childhood Immunisation Programme

Age	Immunisation RECOMMENDED
Newborn	B. C. G. vaccine Hepatitis B vaccine — first dose
1 Month	Hepatitis B vaccine — second dose
2 Months	DTaP-IPV vaccine — first dose Pneumococcal vaccine — first dose
4 Months	DTaP-IPV vaccine — second dose Pneumococcal vaccine — second dose
6 Months	DTaP-IPV vaccine — third dose Pneumococcal vaccine — third dose Hepatitis B vaccine — third dose
1 Year	MMR (Measles, Mumps & Rubella) vaccine — first dose Pneumococcal vaccine — booster dose Varicella vaccine — first dose
1.5 Years	DTaP-IPV vaccine — booster dose
Primary 1	MMRV (Measles, Mumps, Rubella & Varicella) vaccine — second dose DTaP-IPV vaccine — booster dose
Primary 6	dTaP-IPV vaccine — booster dose

Note: DTaP-IPV vaccine: Diphtheria, Tetanus, acellular Pertussis & Inactivated Poliovirus vaccine; dTaP-IPV vaccine: Diphtheria, Tetanus, acellular Pertussis (reduced dose) & Inactivated Poliovirus vaccine

Vaccination – development of immunological memory for pathogens



Allergy: over-reaction of immune responses

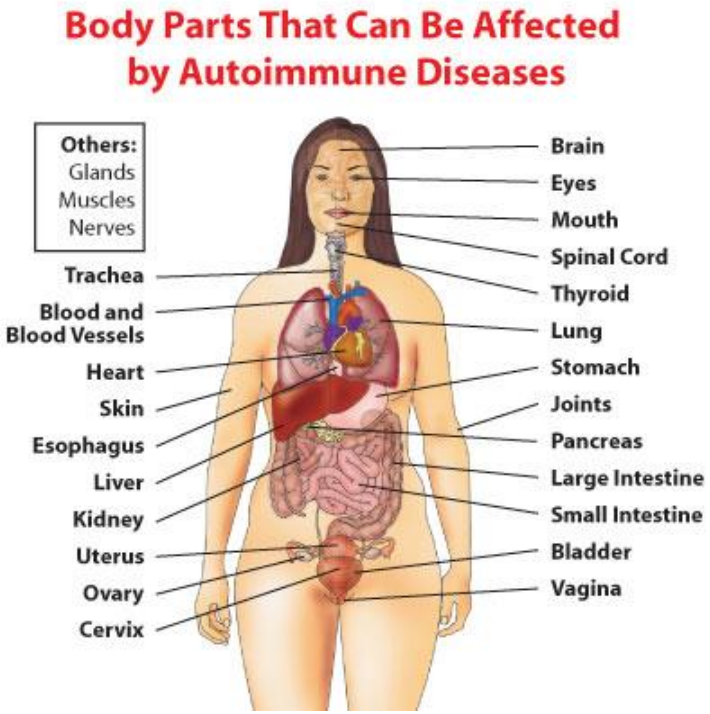
- Hypersensitive immune reactions against environmental substances
- involve antibody-mediated and/or cell-mediated mechanisms to produce distinct clinical manifestations
- clinical manifestations can be divided into:
  - (i) IgE-mediated allergy e.g. allergic rhinitis (hay fever), allergic asthma, food/drug allergy
  - (ii) Cell-mediated allergy e.g. allergic contact dermatitis (allergy induced by poison Ivy)

Diseases of the immune system

- *Autoimmune diseases (AID)* arise when chronic inflammatory response against self antigen is causing tissue damages or malfunctioning of organ systems

Lupus

Rheumatoid arthritis



Diseases of the immune system

(SCID, severe combined immunodeficiency)

Immunodeficiency

- defects (congenital or acquired) leading to reduced or absence of specific immune components
- recurrent infections – ↑ susceptibility, severity and duration
- ↑ Opportunistic infections – caused by microbes that normally do not easily cause serious disease in healthy individuals e.g. candidiasis, streptococcus, HSV etc.
- ↑ malignancies incidence

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