



EDITING FILE
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NATURAL DEFENSE MECHANISMS

Color Index:

Main Text

Important

Female Slides

Male Slides

Dr's Notes

Extra

OBJECTIVES

01

To know First (non-specific immunity) and second (adaptive immunity) lines of defense

02

To understand the Complement system, its activation and how it involves in pathogen killing.

03

To recognize the importance of accumulation of inflammatory cells for clearance of infection

04

To know the role of cytokines as mediators which regulate inflammation

THE MAIN FUNCTION OF THE IMMUNE SYSTEM IS TO PROTECT FROM INFECTIONS:



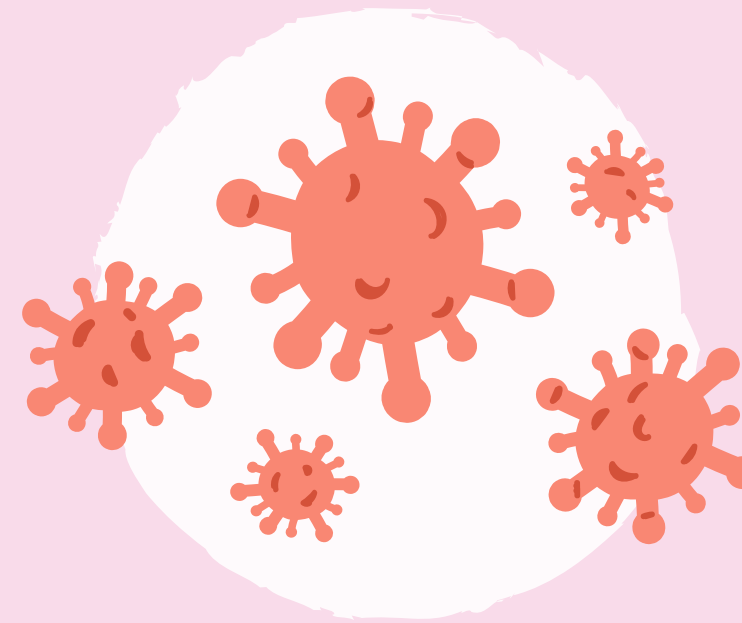
Bacteria

E.g
Tubercle bacillus
Staphylococcus



Parasites

E.g
Tapeworms
Malaria



Virus

E.g.
Influenza Polio



Fungi

E.g.
Candida
Albicans

FIRST AND THE SECOND LINES OF DEFENSE:

Non-specific defense mechanisms (Barriers)

Special defense mechanisms

First line defense

Second line defense

Other

Physical

Mechanical

Biochemical

- ◎ PHAGOCYtic (WBC)
- ◎ INFLAMMATORY RESPONSE

◎ **SKIN, IMPERMEABLE TO MICROBES.**

◎ **MUCOUS MEMBRANES** LINING THE GASTROINTESTINAL, GENITOURINARY AND RESPIRATORY TRACTS.

◎ SHEDDING OF OUTER SKIN LAYERS.

◎ COUGHING AND SNEEZING

◎ FLUSHING OF URINE.

◎ VOMITING.

◎ MUCUS AND CILIA IN RESPIRATORY TRACT

(CILIA BEATING UPWARD WILL REMOVE ALL FLUIDS RETAINED BY COUGHING)

◎ BODY SECRETIONS CONTAIN ANTIBACTERIAL SUBSTANCES E.G. SALIVA, TEARS AND SWEAT.

◎ ANTIMICROBIAL PEPTIDES (E.G. DEFENSINS, HEPICIDINS)

◎ NORMAL BACTERIAL FLORA (**COMPETES WITH PATHOGENIC BACTERIA FOR NUTRIENTS**).

◎ LYMPHOCYTES

◎ ANTIBODIES



Organ or tissue	Innate mechanisms protecting skin/epithelium
Skin	Antimicrobial peptides, fatty acids in sebum
Mouth and upper alimentary canal	Enzymes, antimicrobial peptides, and sweeping of surface by directional flow of fluid toward stomach
Stomach	Low pH, digestive enzymes, bile salts, antimicrobial peptides, fluid flow toward intestine
Small intestine	Digestive enzymes, antimicrobial peptides, fluid flow to large intestine
Large intestine	Normal intestinal flora compete with invading microbes, fluid/feces expelled from rectum
Airway and lungs	Cilia sweep mucus outward, coughing, sneezing expel mucus, macrophages in alveoli of lungs
Urogenital tract	Flushing by urine and mucus, low pH, antimicrobial peptides, and proteins
Salivary, lacrimal, and mammary glands	Flushing by secretions and mucus, antimicrobial peptides and proteins

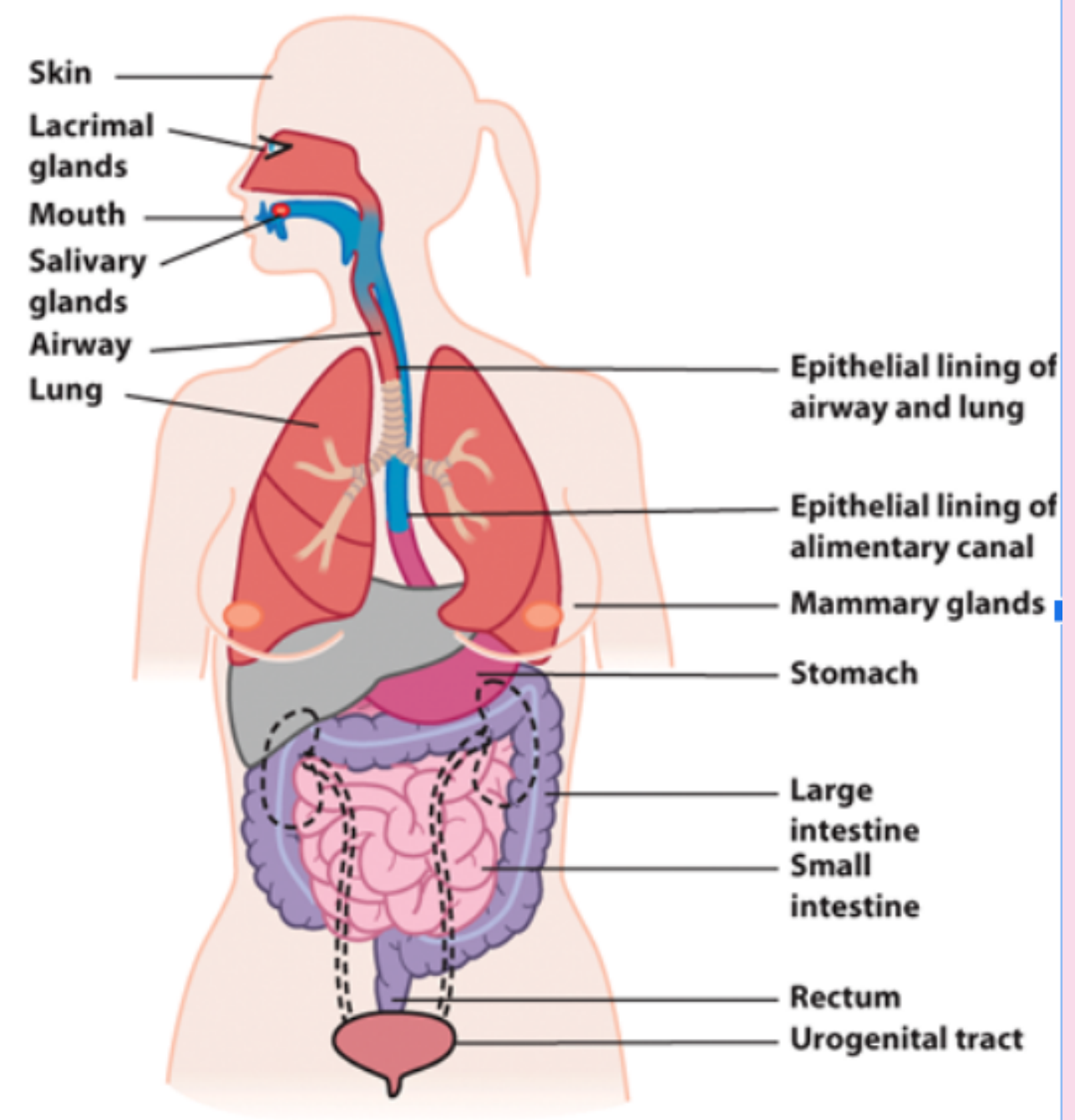


Figure 4-2
 Kuby Immunology, Eighth Edition
 © 2010 W. H. Freeman and Company



WATCH
VIDEO

INFLAMMATION

Inflammation is the first response of the immune system to infection or irritation.

It consists of a series of vascular and cellular changes that occur in response to various stimuli.
e.g. infections, injury, radiation etc.

Long-term inflammation is called Chronic inflammation.

GOALS OF INFLAMMATION

Prevent and limit infection and further damage.

Interact with the adaptive immune system

For example:
Monocytes / Macrophages serve as a link between adaptive and innate immunity by antigen presentation

Prepare the area of injury for healing.

MICROBIAL INFECTIONS INITIATE INFLAMMATION

As bacteria possess an array of pro-inflammatory molecules:

e.g.
Lipopolysaccharides (LPS)

LPS is a superantigen that quickly activates the immune system.

COMPLEMENT SYSTEM

WATCH
VIDEO

Consist of:

- Consist of a group of serum proteins initially present in **inactive** form.
(There are 30 different serum proteins involved (enzymes) , but only 9 that are major (C1,C2,C3,C4,C5,C6,C7,C8,C9)
- Activation occurs in a cascade (one component or more activating another) after enzymatic cleavage. Once components become activated they produce important biological effects that initiate inflammation.
 - (The 9 proteins are present normally as “pro-enzyme”, inactive form. When complements get activated it’s amount will decrease)
 - (During activation, protein will be broken into 2 pieces, the smaller gets the letter a, while the largest get b)
- ^{From 443} Because pro-enzymes are produced in the **liver**, people with chronic liver disease will have a problem with their complement system.
- Activation occurs in an enzyme cascade (the activation of one protein leads to the next protein’s activation and cleavage break)
- **This system plays an important role in linking Innate & Adaptive immunity**

THE COMPLEMENT SYSTEM

There are 3 main pathways:

01

CLASSICAL PATHWAY

(Requires antigen-antibody binding)
(C1,C4,C2,C3,C5,C6,C7,C8,C9)

WATCH
VIDEO

02

LECTIN PATHWAY

(Activated by mannan binding protein binding
mannose groups of bacterial carbohydrates)
(MASPs,C4,C2,C3,C5,C6,C7,C8,C9)

WATCH
VIDEO

03

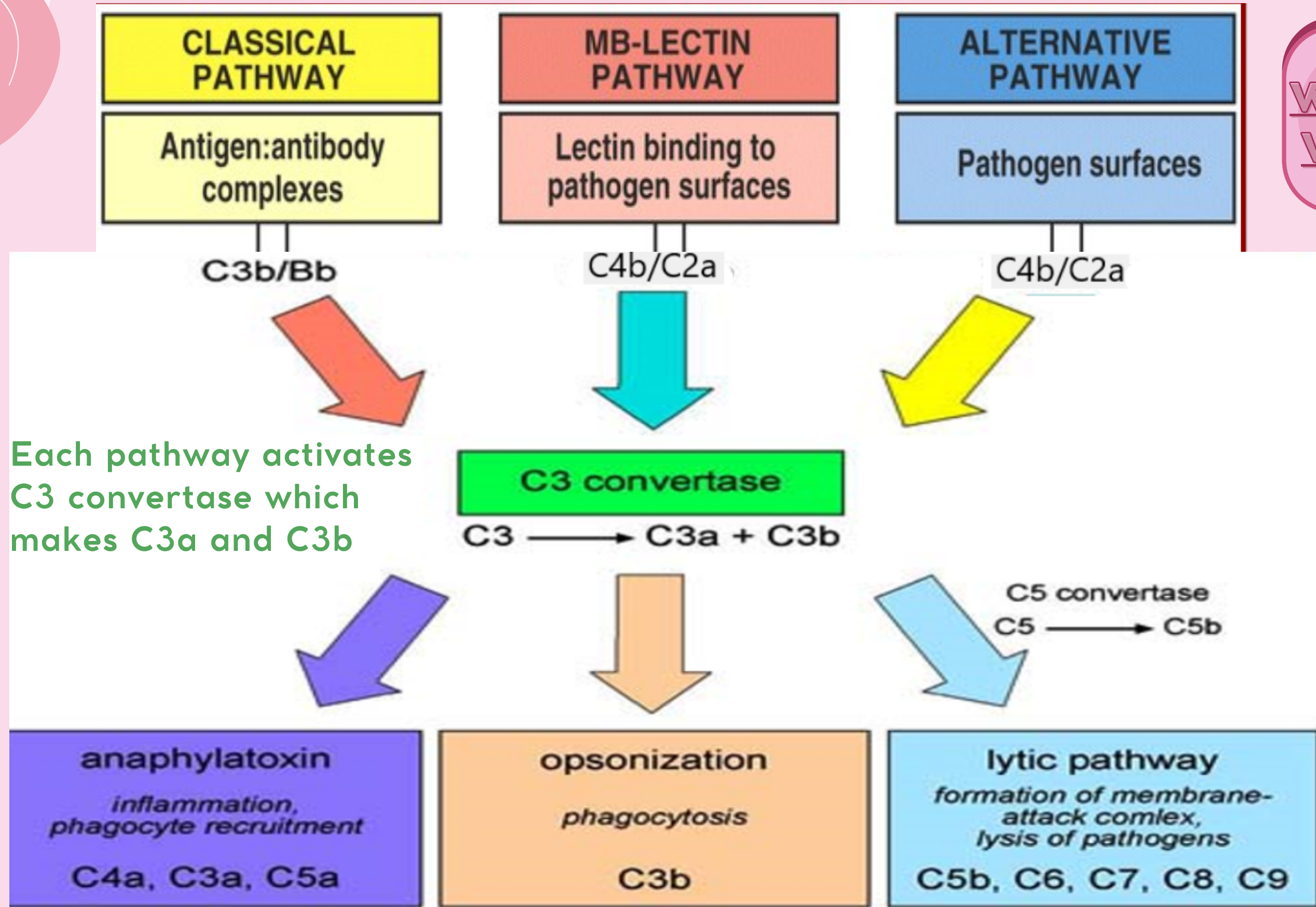
ALTERNATIVE
PATHWAY

(Activated by bacterial products)
(-C3,C5,C6,C7,C8,C9)

WATCH
VIDEO

C3 is the most common protein

ACTIVATING COMPLEMENT SYSTEM



Each pathway activates C3 convertase which makes C3a and C3b

The numbers are **VERY IMPORTANT** and you need to know the function of each complement

e.g What is the function of C5b?

Answer: MAC

Membrane Attack Complex Formation (MAC)

thanks to
Team438

Insertion of lytic complex into cell membrane

- 1- **C5** gets activated How? The (**C4b**, **C2a**, **C3b**) complex works as a **C5 convertase** which breaks **C5** into **C5a** and **C5b**
- 2- **C5b** assembles with **C6**, **C7** and binds into the membrane
- 3- **C8** binds to the complex as well
- 4- **C9** binds and forms the hole (pore) in the membrane

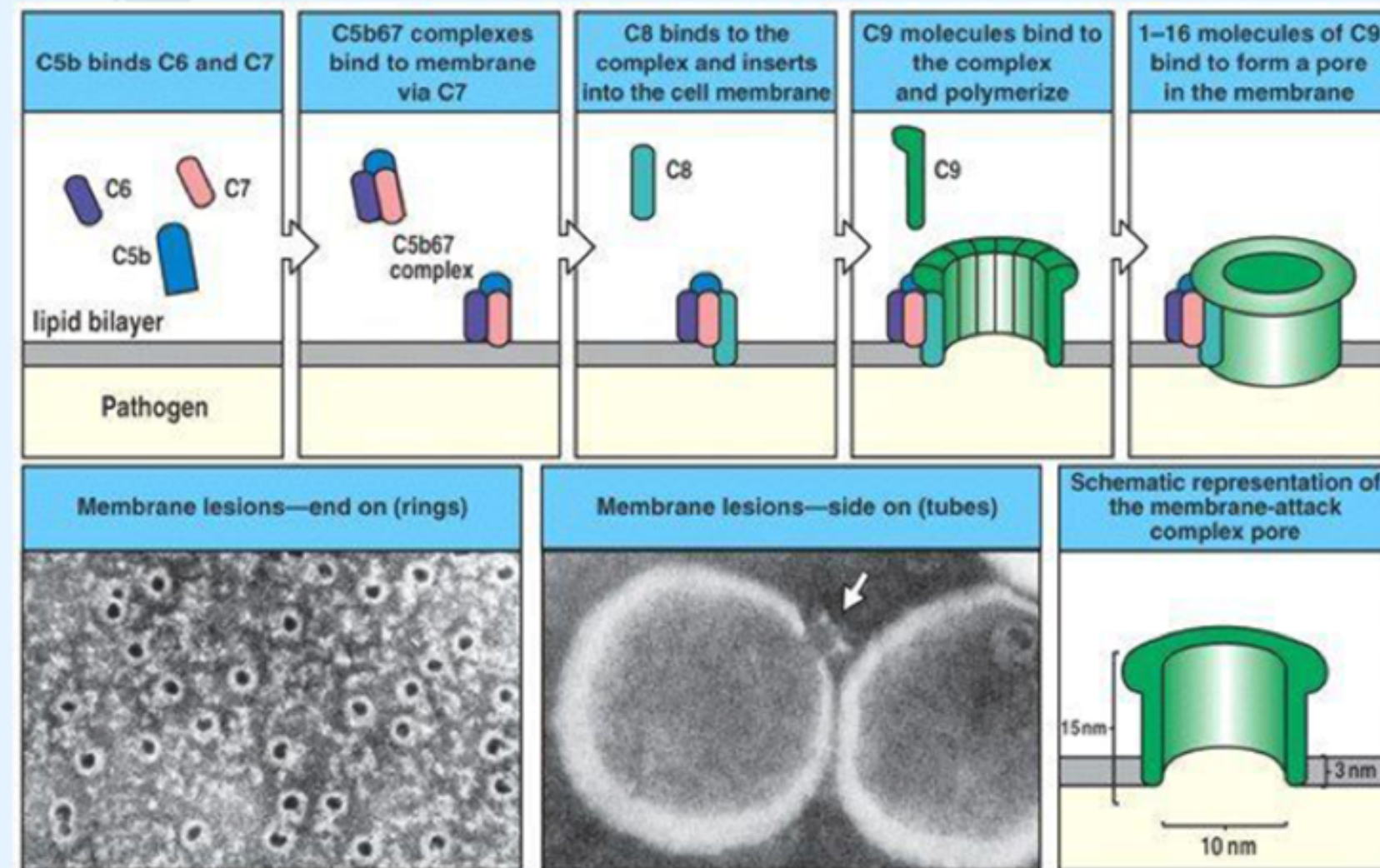


Figure 2-35 Immunobiology, 6/e. (© Garland Science 2005)

This structure (hole/pore) that is formed at the pathogen's cell membrane after the activation of the host's complement system, is called the Membrane Attack Complex Formation. This disrupts the cell membrane leading to cell lysis and death.

Biological Effect of Complement Activation

(start after pathway get activated)

1. ANAPHYLATOXIN FUNCTIONS (E.G. C3A, C5A)

- Trigger **degranulation** (release of substances) of endothelial cells, mast cells or phagocytes.
- Induce smooth muscle contraction and increased vascular permeability.
- Attract additional inflammatory cells to the site of activation.

2. OPSONIZATION: (MAIN OPSONIN C3B, C4B TO A LESSE EXTENT)

- C3b is the main opsonin and to a lesser extent C4b.
- Coating of bacteria enhance phagocytosis.

3. DIRECT CELL LYSIS: C5B, C6, C7, C8, C9

Destruction of bacteria.

Process of chemotaxis: is the movement of the responsible cells



to a **specific place of injury** in response to a chemoattractant

Diapedesis

Neutrophil squeeze its way out of the blood vessel

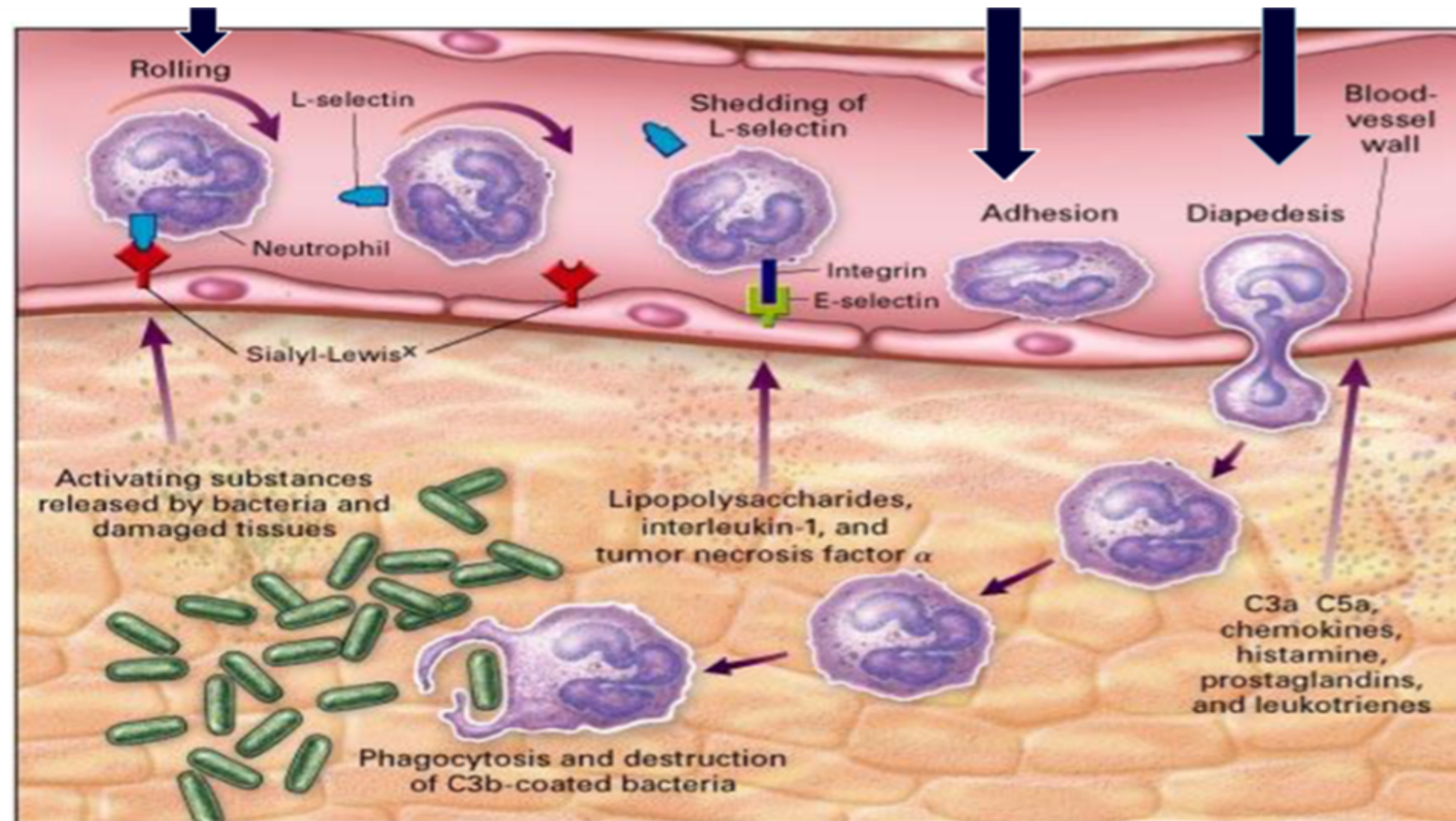
Adhesion

The attachment of the Neutrophil to Endothelial cells

Rolling

on vessel wall and slowing down of Neutrophils in the blood vessel

Thanks to team 441



What is Chemotaxis?

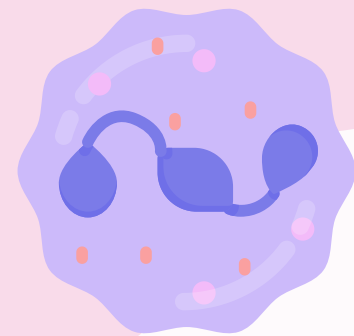
It is a chemically induced signaling process which would allow certain cells (such as macrophages or WBC) to go to the site of infection after they have left the circulation. It uses cytokines, chemokines which are molecules that are responsible for the chemical signaling to guide macrophages & neutrophils to the site of infection (making sure the pathogen is destroyed).

Types of cells attracted to the site of infection that mediate inflammation:



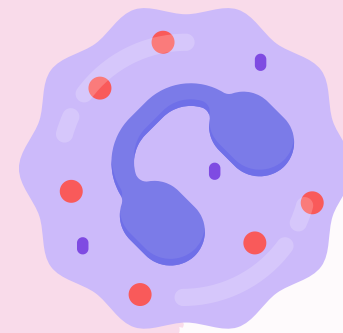
Monocytes

Become
Macrophages when
they leave the blood
and enter the tissues.



Neutrophils

Phagocytic cells



Eosinophils

Allergy and
Parasitic
infections.



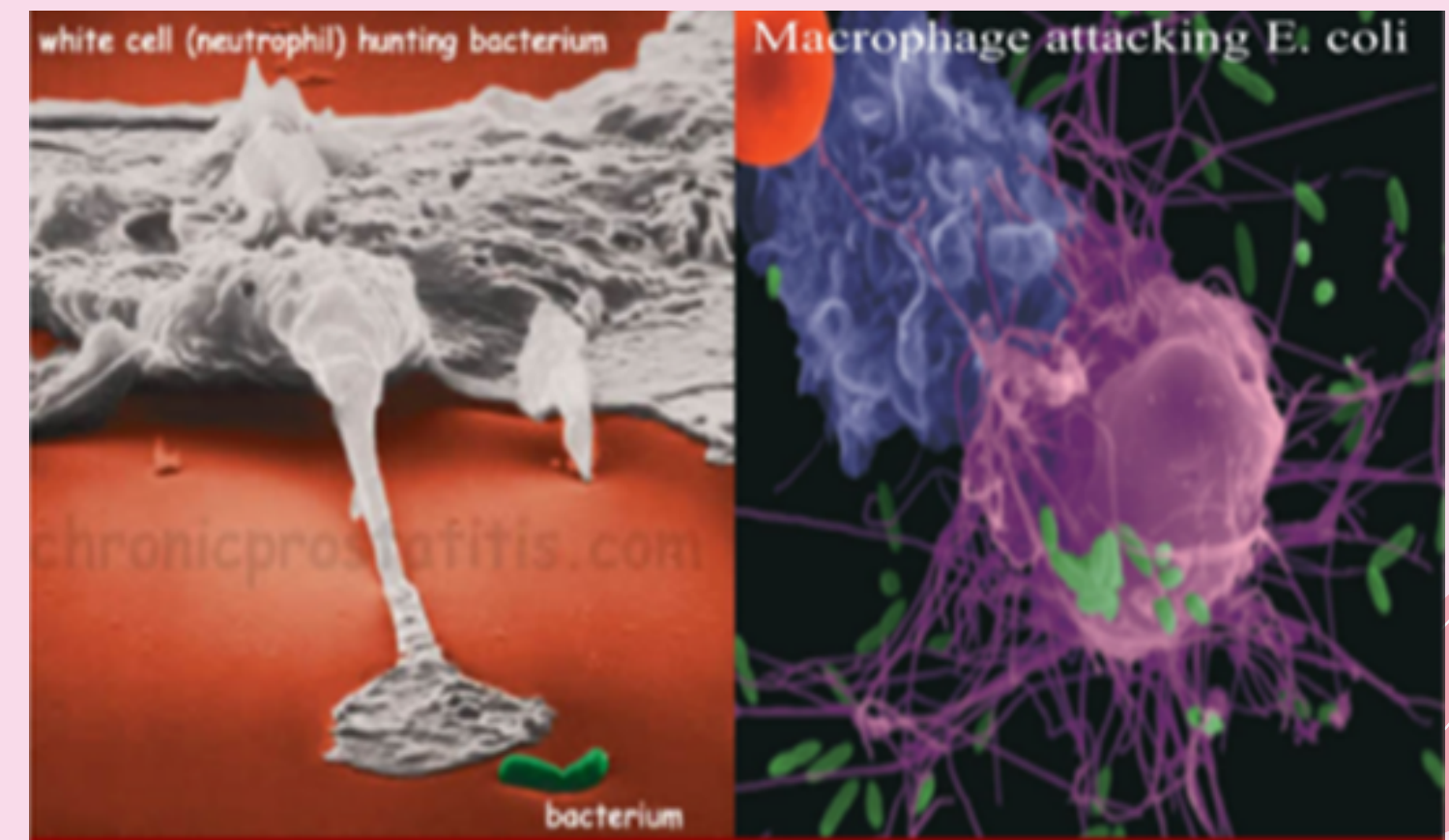
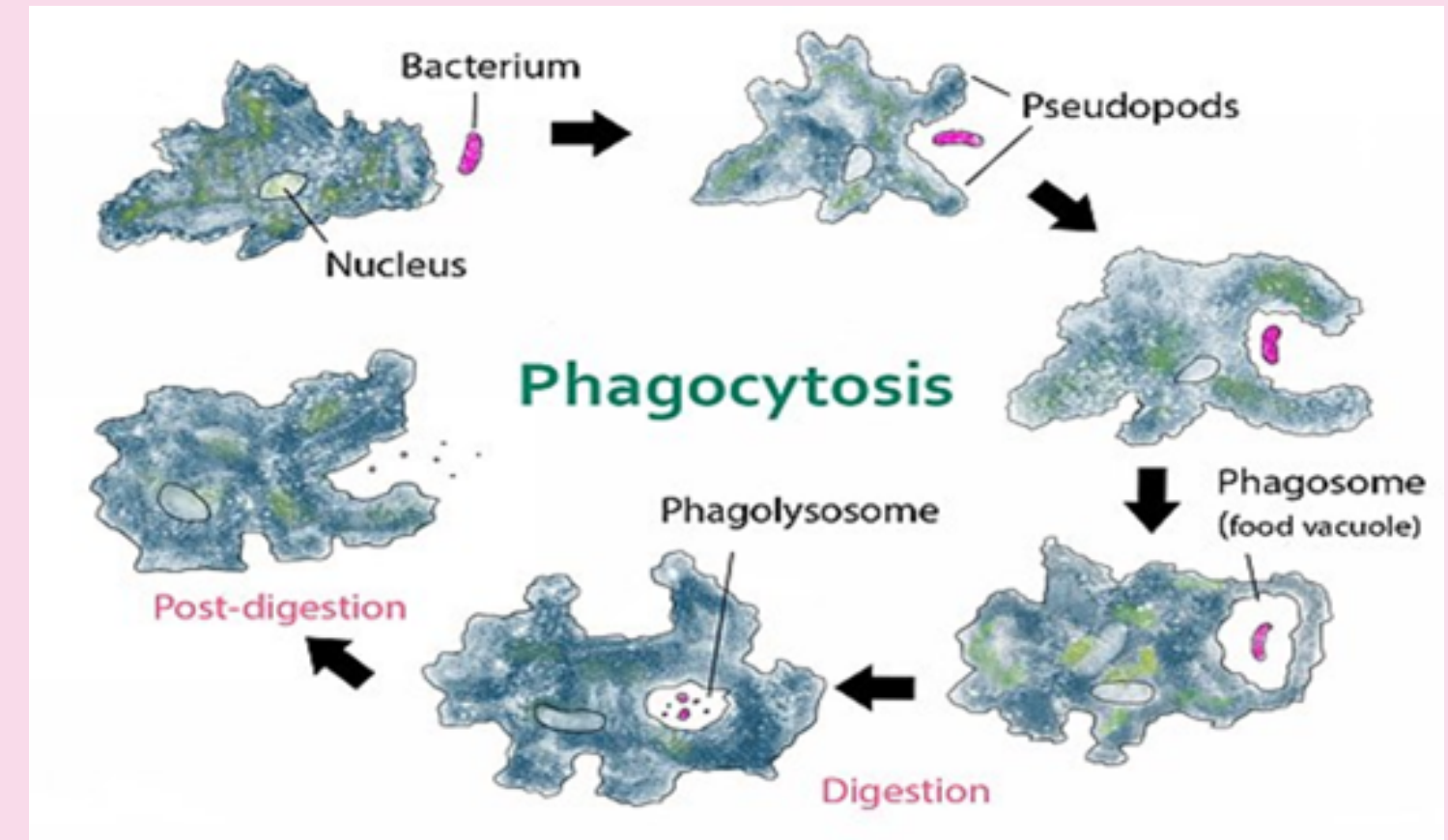
**Natural Killer
(NK) cells**

Kill tumor cells and
virus infected cells.

Phagocytosis:

WATCH
VIDEO

Phagocytic cells (neutrophils & macrophages) at site of infection start the process of **phagocytosis** which is the process by which a cell **engulfs** a solid particle such as a bacteria to form an **internal vesicle known as a phagosome**.



Cytokines

Soluble molecules (**small proteins**), produced by different cells, that control cell functions e.g. differentiation, proliferation activation or inhibition.

Cytokines play an important role in **Innate Immunity and Adaptive Immunity**

01 INTERLEUKINS

Produced primarily by **macrophages** and **lymphocytes** in response to a pathogen.

Has many types Examples
IL-1, IL-2, IL-3...etc...

02 INTERFERONS

Protects against viral infections.

Produced and released by virally infected cells in response to **viral infections**.

03 TUMOR NECROSIS FACTOR (TNF)

Secreted by macrophages.

Induces fever by acting as an **endogenous pyrogen** (a substance released from inside the body that produces fever).

- Increases synthesis of inflammatory serum proteins.
- Increase expression of adhesion molecules on endothelial cells and vascular permeability.



THE SIX MAJOR CYTOKINE FAMILIES

This is just for reading, it's not one of the exam questions

Family name	Representative members of family	Comments
Interleukin-1 family	IL-1 α , IL-1 β , IL-1R α , IL-18, IL-33	IL-1 was the first non interferon cytokine to be identified. Members of this family include important inflammatory mediators.
Class 1 (hematopoietin) cytokine family	IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-12, IL-13, IL-15, IL-21, IL-23, GM-CSF, G-CSF, growth hormone, prolactin, erythropoietin/hematopoietin	Members of this large family of small cytokine molecules exhibit striking sequence and functional diversity.
Class 2 (interferon) cytokine family	IFN- α , IFN- β , IFN- γ , IL-10, IL-19, IL-20, IL22, IL-24	While the IFNs have important roles in antiviral responses, all are important modulators of immune responses.

THE SIX MAJOR CYTOKINE FAMILIES

This is just for reading, it's not one of the exam questions

Family name	Representative members of family	Comments
Tumor necrosis factor family	TNF- α , TNF- β , CD40L, Fas (CD95), BAFF, APRIL, LT- β	Members of this family may be either soluble or membrane-bound; they are involved in immune system development, effector functions, and homeostasis.
Interleukin-17 family	IL-17 (IL-17A), IL-17B, IL-17C, IL-17D, IL-17E	This is the most recently discovered family; members function to promote neutrophil accumulation and activation, and are proinflammatory.
Chemokines	IL-8, CCL19, CCL21, RANTES, CCL2 (MCP-1), CCL3 (MIP-1 α)	All serve chemoattractant function.

Take Home Messages

01

1. Non-specific (innate immunity) acts as a first line of defense against invading pathogens.

02

2. Innate immunity is an important initial step for generation of adaptive immune response.

03

3. Inflammation is vital for controlling infection and limiting tissue damage.



MCQ'S

ANSWERS:

1-C 2-B

1

What is the function of C3b?

A

MAC

B

Lytic functions

C

Opsonization

D

Inflammatory
cells

2

Which pathway of activation require Mannose binding protein ?

A

Alternative

B

Lectin

C

Classical

D

MASPs

MCQ'S

ANSWERS:

3-D 4-A

3

Where are pro-enzymes produced?

A

Spleen

B

Kidney

C

Lymph nodes

D

Liver

4

WHICH OF THE FOLLOWING ARE NOT PART OF THE FIRST LINE OF DEFENSE?

A

Antibodies

B

Skin

C

Inflammation

D

Antimicrobial
proteins

MCQ'S

ANSWERS:

5-B 6-D

5

WHICH OF THE FOLLOWING CELLS PLAYS AN IMPORTANT ROLE IN PARASITIC INFECTIONS AND ALLERGIES?

A

Natural killer cells

B

Eosinophils

C

Monocytes

D

Macrophages

6

WHICH OF THE FOLLOWING CELLS SECRETE THE TUMOR NECROSIS FACTOR (TNF)?

A

Eosinophils

B

T-Lymphocytes

C

B-Lymphocyte

D

Macrophages

MEET THE TEAM

Abdullah Alzoom ← **LEADERS** → **Sadeem Alsaadoon**

MEMBERS

Abdulahdi Alqahatani

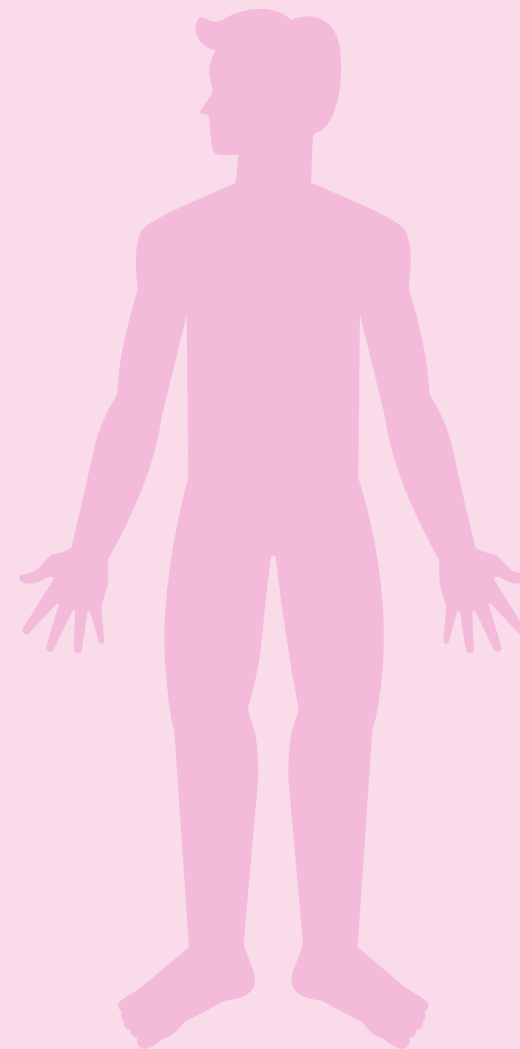
Bandar Alzaaidi

Faisal Alaowairdhi

Homoud Alsuhali

Omar Alattas

Ziyad Bukhari



Alanoud Alnajawi

Basmah Alghamdi

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