University of Basrah, Medical College – Microbiology Department

Microbiology/ 3rd Year M.B.CH.B. Students

Part V: Basic & Clinical Immunology (17 hours)

Lecture 7

Duration: 1 hour

Complement system

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Reference: Roitt's Essential Immunology 13th Edition

For more detailed instruction, any question, cases need help please post to the group of session

Key Definitions

Cobra venom factor (CVF): is the non-toxic, complement-activating component of cobra venom (cobra: kind of snakes, venom: poison). Like naturally occurring C3b, CVF forms a complex, or convertase, with complement components Factor B and Factor D (alternative pathway).

C-reactive protein (CRP): a protein made by the liver, its levels in blood increase during inflammation. CRP test measure the amount of CRP in blood to detect inflammation due to acute conditions or to monitor the severity of disease in chronic conditions.

β-amyloid: peptides of 36-43 amino acids that are crucially involved in Alzheimer's disease as the main component of the amyloid plagues found in the brains of people with Alzheimer's disease.

Pathogen associated molecular patterns (PAMPs): expressed by bacteria, fungi, yeasts & not mammalian cells.

Mannose-associated serine proteases (MASPs): enzymes (proteases) that found in circulation bounded to MBL & Ficolin, involved in lectin pathway of complement system and responsible for cleaving C4 & C2 into fragments to form C3- convertase (activated when MBL bound to PAMPs).

Mannan Binding Lectin (MBL) & Ficolin: proteins found in circulation bounded with proteases, known as the (MASPs). MBL & Ficolin can bind with PAMPs leading to activation of MASPs.

Learning objectives (LOs)

Define the Complement System	(LO.1)
Mention the three pathways of Complement System	(LO.2)
Illustrate the initiators and initiation steps of each pathway	(LO.3)
Explain steps of complement activation	(LO.4)
Mention the biological activities of complement system	(LO.5)
Acute phase proteins increase in response to infection	(LO.6)

The Complement System (LO.1)

►Complement comprises approximately 30 circulating and membrane expressed proteins synthesized in the liver and by cells involved in the inflammatory response.

► Named for some of the earliest observations of its activity—a heat sensitive material in serum that "complemented" the ability of antibody to kill bacteria.

► Complement system plays a major role in defense against many infectious organisms as part of both the innate and antibody-mediated adaptive immune responses.

The three pathways of Complement System (LO.2)

1. The classical pathway
2. The alternative pathway
3. Lectin pathway

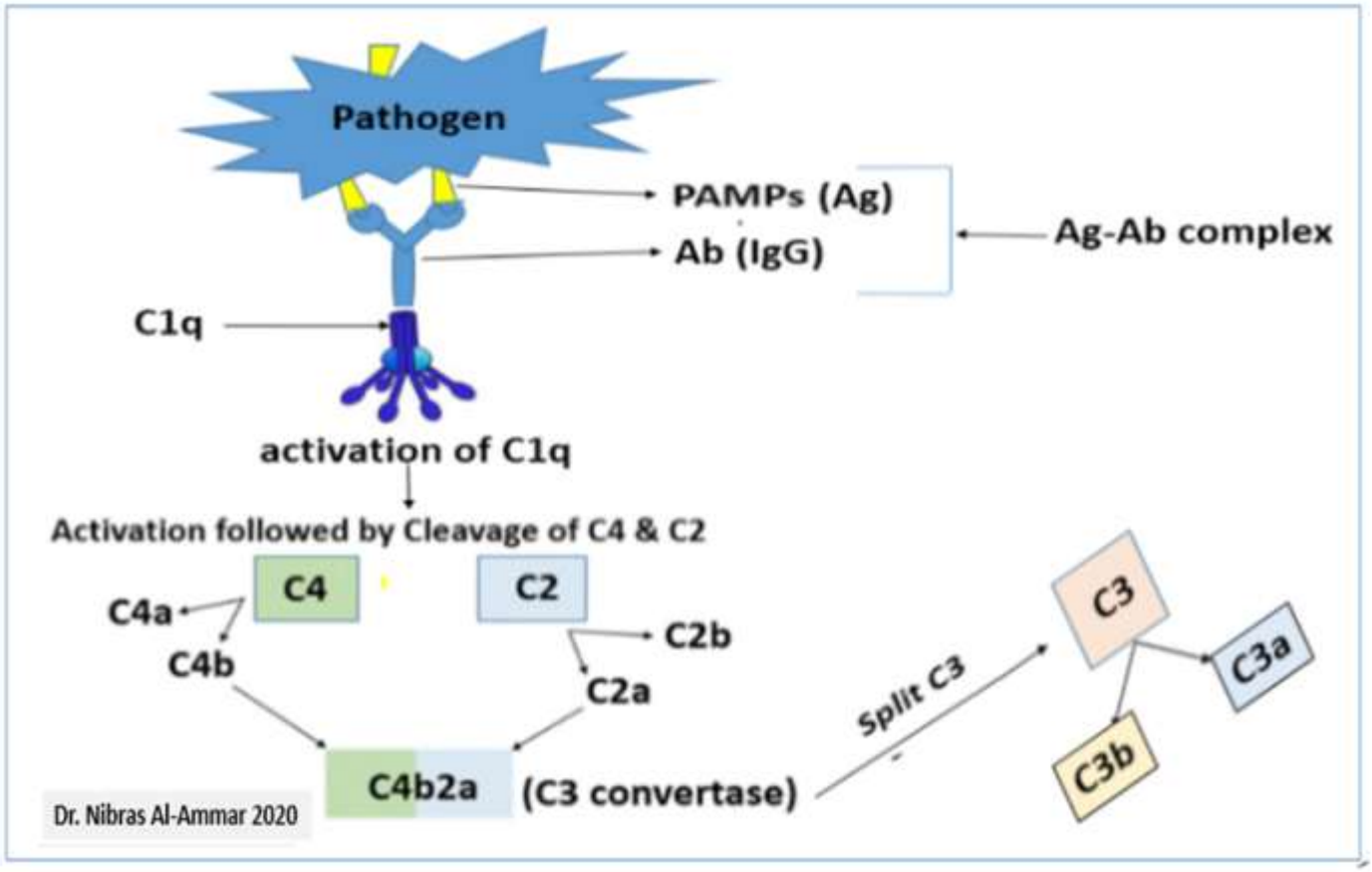
The initiators (activators) of classical pathway: (LO.3)

1. Ag-Ab complexes (Thus, the classical complement pathway is a major effector mechanism of the adaptive immune response and leads to elimination of pathogen).
2. Aggregated immunoglobulins
3. C-reactive protein (CRP)
4. β- amyloid (found in Alzheimer's disease plaques
5. Some viruses including HIV-1

6. **Necrotic cells**

Q. Is there any difference between IgG & IgM in activation of complement?

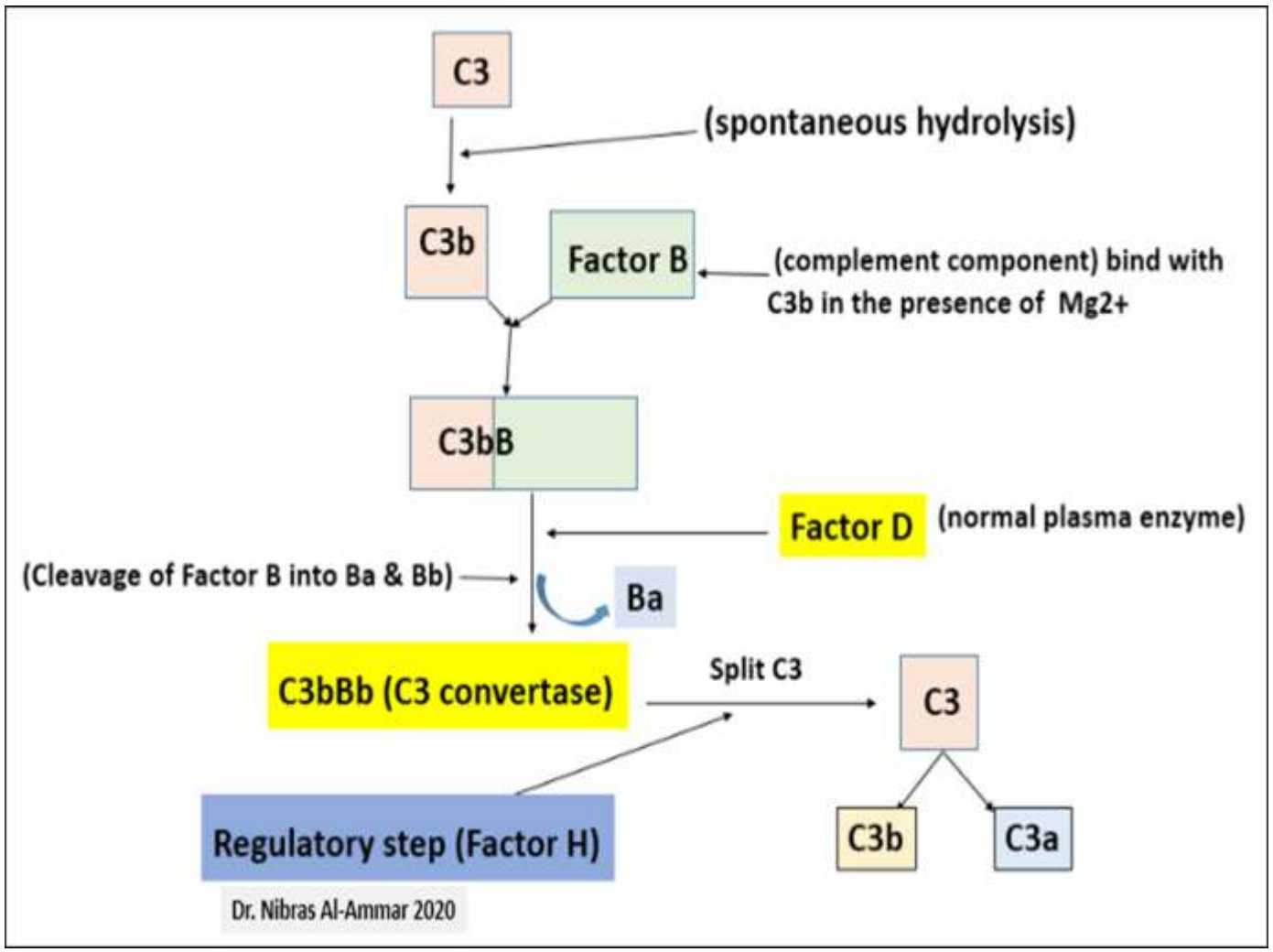
The initiation of classical pathway (LO.3)



The initiators (activators) of alternative pathway (LO.3)

1. **Any Foreign substance**
2. **Lipopolysaccharides of bacterial cell wall (Gm-ve), (endotoxins)**
3. **Cell wall of some yeasts**
4. **Cobra venom factor (poison of type of snakes called cobra)**
5. **Viruses**
6. **Aggregated immunoglobulins (Igs)**
7. **Necrotic cells**

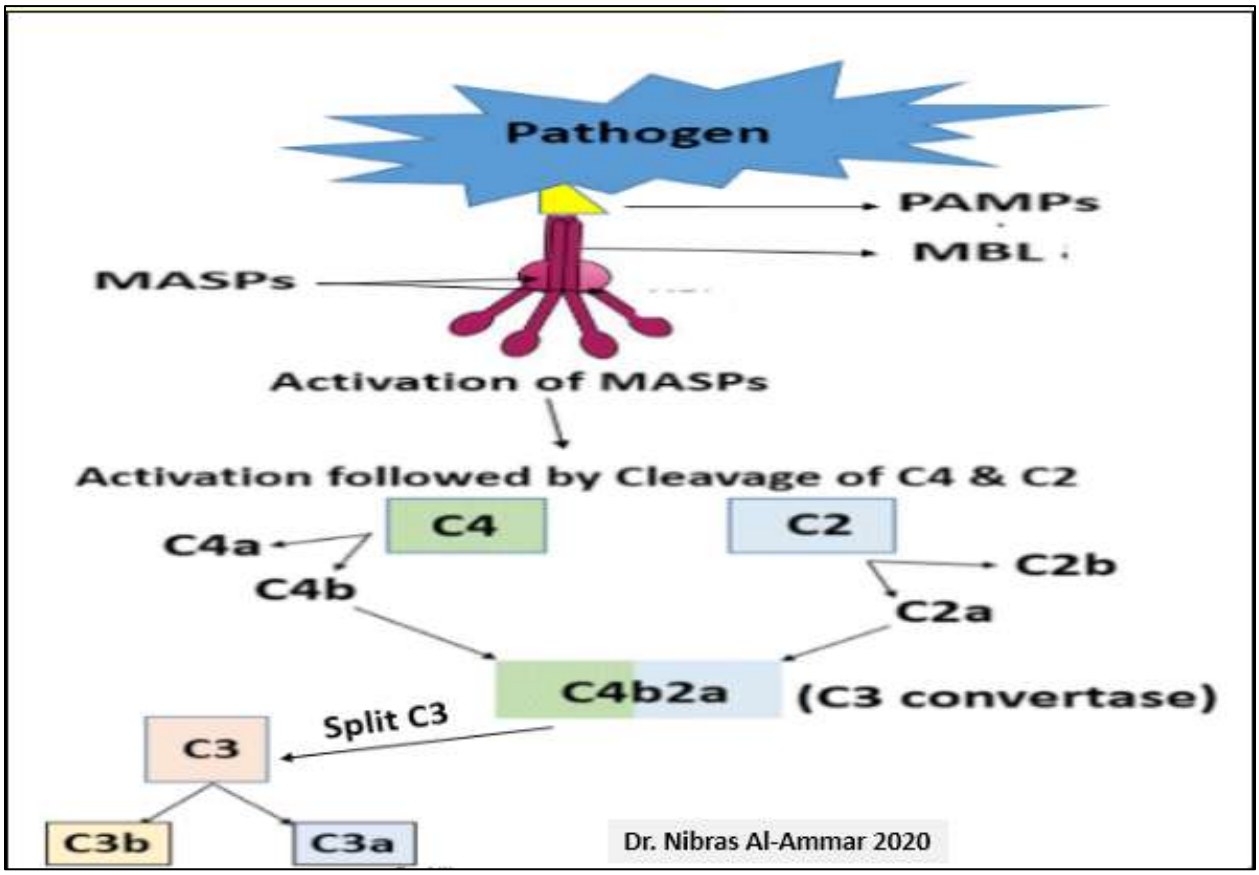
The initiation of alternative pathway (LO.3)



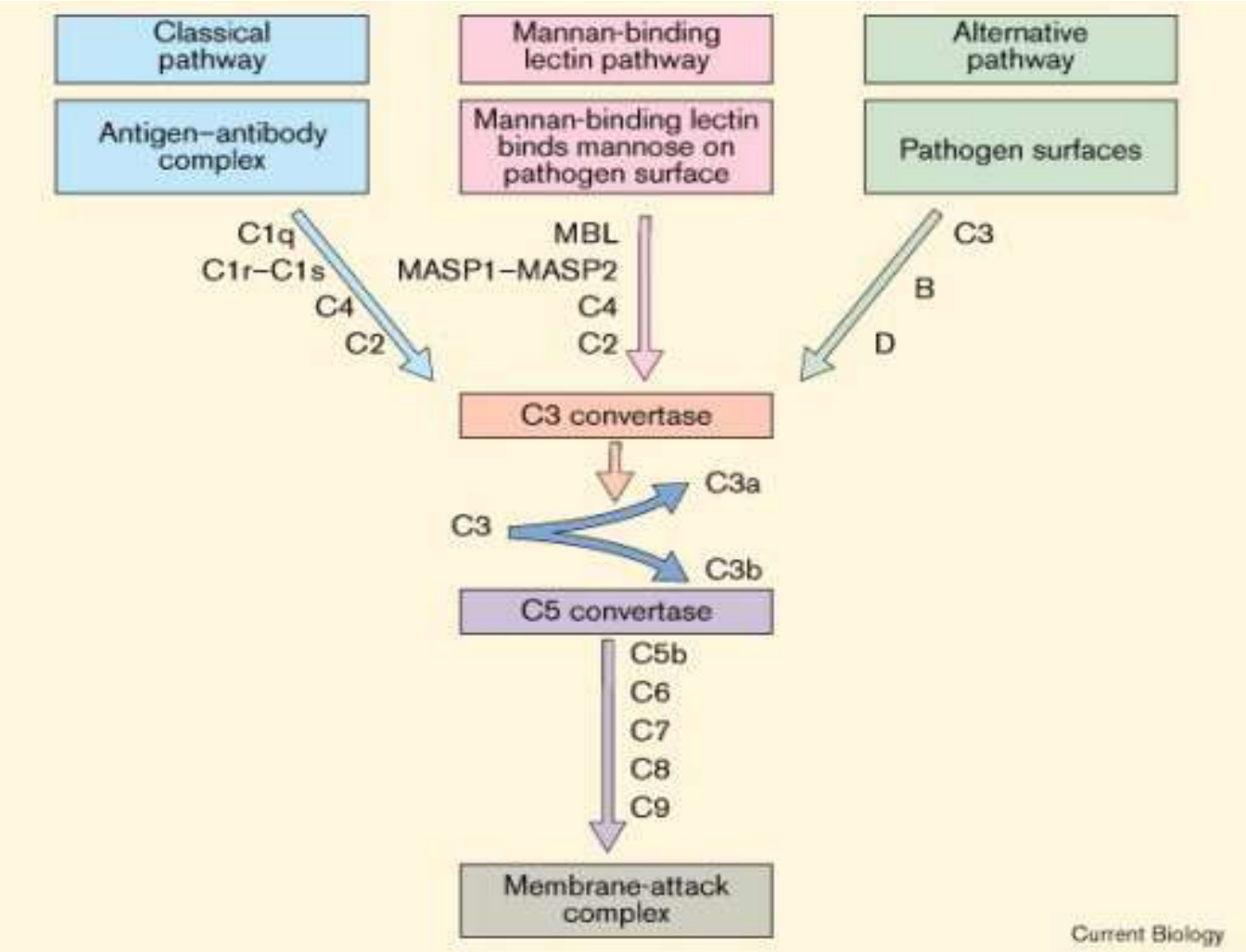
The activators and initiation of lectin pathway (LO.3)

Initiation of lectin pathway (in the absence of antibody) by MBL & Ficolins that bind with PAMPs leading to activation of MASPs.

Lectin pathway is part of the innate immune defenses and is involved in the rapid response to pathogens.

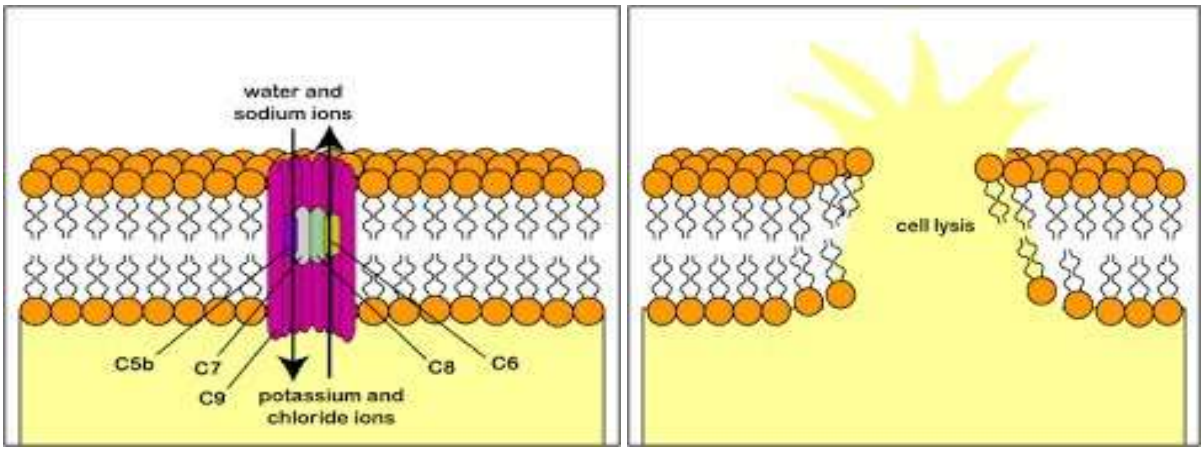


(LO.4)

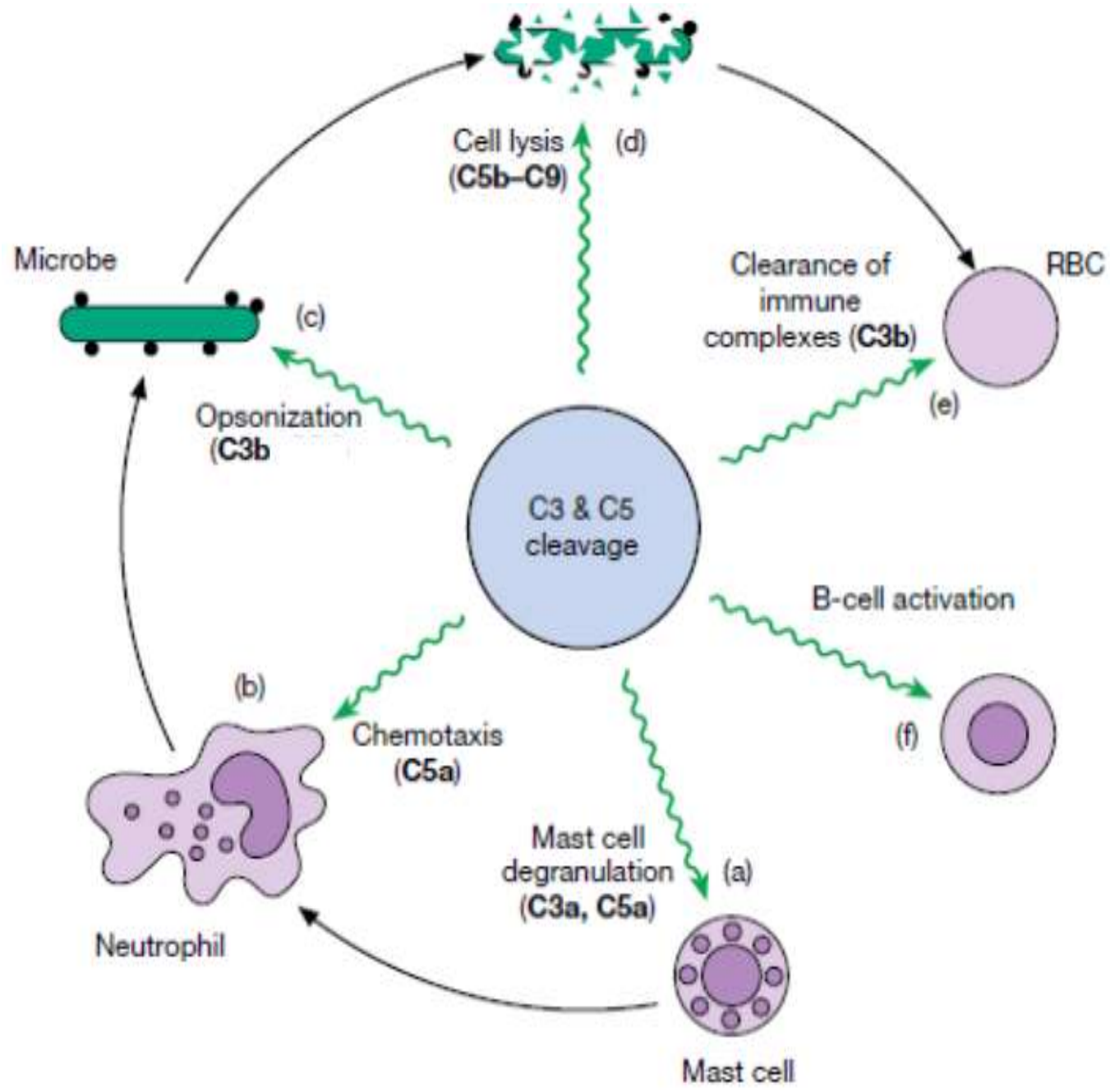

Classical pathway
Antigen–antibody complex
Mannan-binding lectin pathway
Mannan-binding lectin binds mannose on pathogen surface
Alternative pathway
Pathogen surfaces
C1q
C1r–C1s
C4
C2
MBL
MASP1–MASP2
C4
C2
C3
B
D
C3 convertase
C3a
C3
C3b
C5 convertase
C5b
C6
C7
C8
C9
Membrane-attack complex
Current Biology

(LO.4)

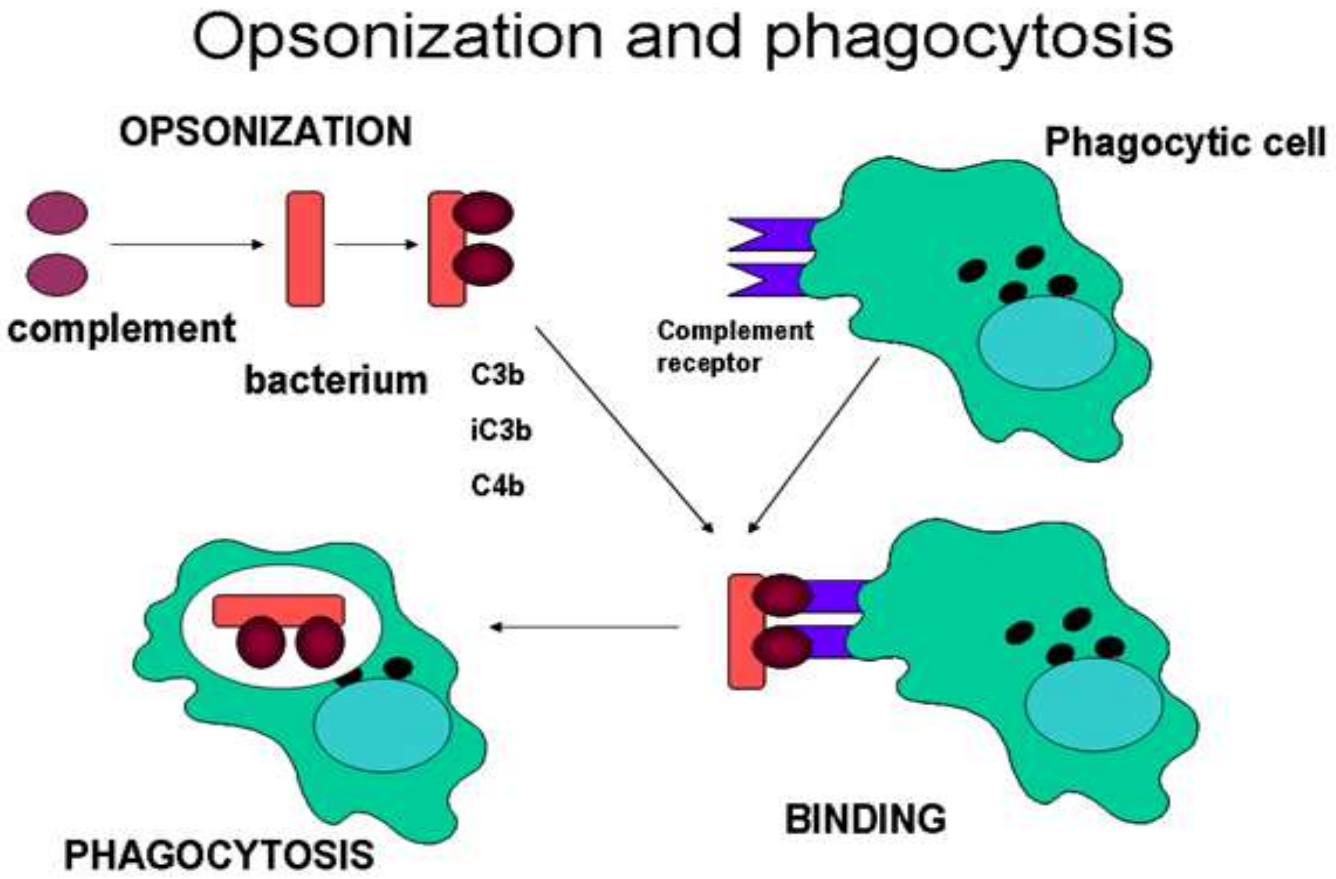
Formation of membrane attack complex (MAC)



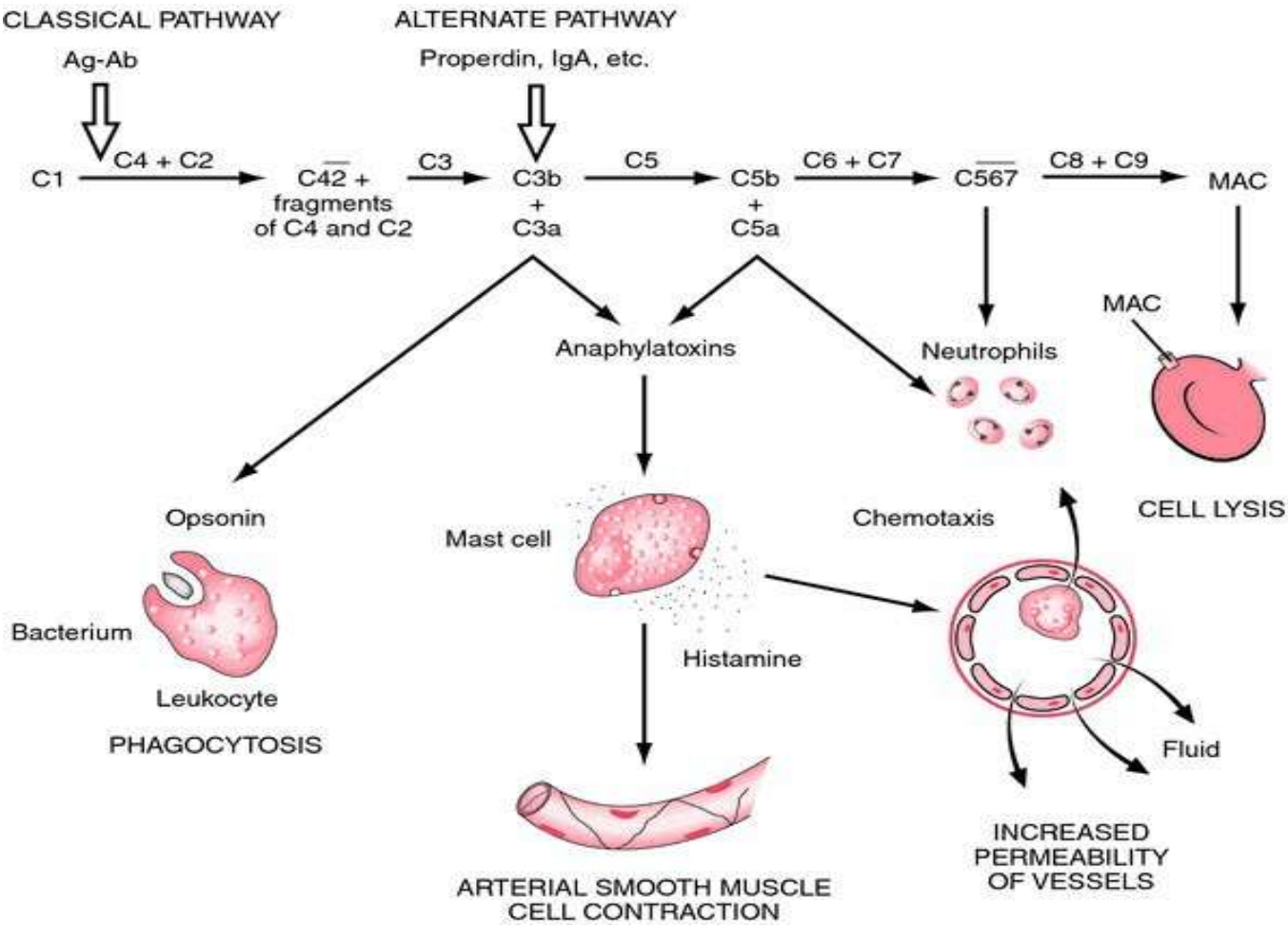
Biological activities of complement (LO.5)


Cell lysis
(C5b–C9)
(d)
Microbe
(c)
Clearance of
immune
complexes (C3b)
RBC
(e)
Opsonization
(C3b
C3 & C5
cleavage
B-cell activation
(b)
Chemotaxis
(C5a)
(f)
Mast cell
degranulation
(C3a, C5a)
(a)
Neutrophil
Mast cell

(LO.5)


Opsonization and phagocytosis
OPSONIZATION
Phagocytic cell
complement
bacterium
C3b
iC3b
C4b
Complement receptor
PHAGOCYTOSIS
BINDING

(LO.5)


CLASSICAL PATHWAY
Ag-Ab
ALTERNATE PATHWAY
Properdin, IgA, etc.
C1
C4 + C2
C42 + fragments of C4 and C2
C3
C3b + C3a
C5
C5b + C5a
C6 + C7
C567
C8 + C9
MAC
MAC
Anaphylatoxins
Neutrophils
CELL LYSIS
Opsonin
Bacterium
Leukocyte
PHAGOCYTOSIS
Mast cell
Histamine
Chemotaxis
Fluid
INCREASED PERMEABILITY OF VESSELS
ARTERIAL SMOOTH MUSCLE CELL CONTRACTION

Acute phase proteins increase in response to infection (LO.6)

Acute phase reactant	Role
Dramatic increases in concentration	
C-reactive protein	Fixes complement, opsonizes
Mannose binding lectin	Fixes complement, opsonizes
α_1-Acid glycoprotein	Transport protein
Serum amyloid P component	Amyloid component precursor
Moderate increases in concentration	
α_1-Protease inhibitors	Inhibit bacterial proteases
α_1-Antichymotrypsin	Inhibit bacterial proteases
C3, C9, factor B	Increase complement function
Ceruloplasmin	$\cdot O_2^-$ scavenger
Fibrinogen	Coagulation
Angiotensin	Blood pressure
Haptoglobin	Bind hemoglobin
Fibronectin	Cell attachment

☺

Thank You