

Host Defense Mechanisms

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.We live in a world dominated by microbes •

The atmosphere is full of bacteria, viruses,
.molds and parasites •

? What mechanisms prevent infections •

The discipline of immunology emerged out of the observation
:that

Individuals who had survived from certain
infectious diseases were thereafter protected from
.the disease •

The Latin term *immunis*, meaning “exempt,” is the
source of the English word immunity, meaning the
.**state of protection** from infectious disease •

Louis Pasteur
watching
Joseph Meister
receive
the anti-rabies
.vaccine



These observations marked the beginnings of the discipline of immunology

The term : **Immunity**

refers to the state of protection from infectious disease

:and the discipline is called

Immunology

The Immune System is Organized into Two Main Branches

The Natural (**innate**) or non-specific, .1
.immune system

The adaptive (**acquired**) or specific immune .2
.system

the two systems work together to provide protection

Recognition of microbes

To protect against infectious disease, the immune system (natural or acquired) must be able to recognize bacteria, bacterial products, fungi, . parasites and viruses •

This is achieved by recognition of specific molecules on the .surface of the microorganisms and not as a whole microbe •

.in natural immunity : pattern molecules - •

.in adaptive immunity : antigens - •

:Definitions

Antigens:

Are substances that are able to combine specifically
with antibodies and/or cell-surface receptors

Antibodies:

Are proteins that recognize and bind to a particular
antigen

:Natural (innate) immunity

: Anatomic barriers

Skin: Mechanical barrier prevents entry of .1
.microbes in body

Mucous membranes: Normal flora compete with .2
.microbes for attachment sites and nutrients

.Mucus entraps foreign microorganisms •

.Cilia propel microorganisms out of body •

:Physiological Barriers

Temperature: Normal body temperature inhibits •
.growth of some pathogens

Fever response: Inhibits growth of some •
.pathogens

Low pH: Acidity of stomach contents kills •
.most ingested microorganisms

:Chemical Mediators

:Lysozyme

Found in mucous secretions and in tears, is able
.to damage bacterial cell wall

:Interferons

Belong to a group of proteins produced by virus-
.infected cells and act as anti-viral agents

:Complement

The complement system consists of about 20 proteins in normal human serum •

They are synthesized mainly by the liver •

Complement is heat labile i.e. it is inactivated at 56°C for 30 minutes •

Main Functions of Complement

.Lysis of cell walls

•

Bacteria

—

Generation of mediators

•

Participation in inflammation and attract
neutrophils

—

Opsonization

•

Enhancement of phagocytosis

—

Complement Activation

Several complement components are pro-enzymes and require cleavage to form active enzymes

Activation of complement is initiated either by antigen-antibody complexes or by non-immunologic molecules such as endotoxin

:Pathways of activation

.Classical Pathway

—

.The Lectin Pathway

—

.The Alternative Pathway

—

Lectin and alternative pathways are activated with the first encounter with bacteria since the antibody required to trigger classic pathway is not present

•

:The complement system

: Pathways of activation 3

Classical. (Requires antigen-antibody binding) -

(C1,C4,C2,C3,C5,C6,C7,C8,C9) -

Lectin. (Activated by mannan binding protien -

binding manose groups of bacterial carbohydrates)

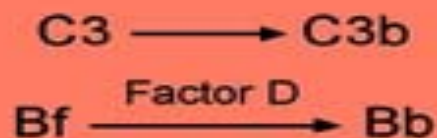
(C4,C2,C3,C5,C6,C7,C8,C9-) -

Alternative (Activated by bacterial products) -

(C3,C5,C6,C7,C8,C9 -) -

Alternative pathway

spontaneous activation



Lectin pathway

mannose binding

MBL
MASP-1
MASP-2



Classical pathway

antibody binding

C1q/r₂/s₂



C3b/Bb



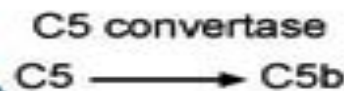
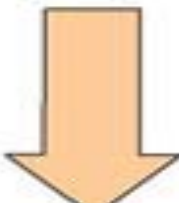
C4b/C2b



C4b/C2b



C3 convertase



anaphylatoxin

*inflammation,
phagocyte recruitment*

C4a, C3a, C5a

opsonization

phagocytosis

C3b

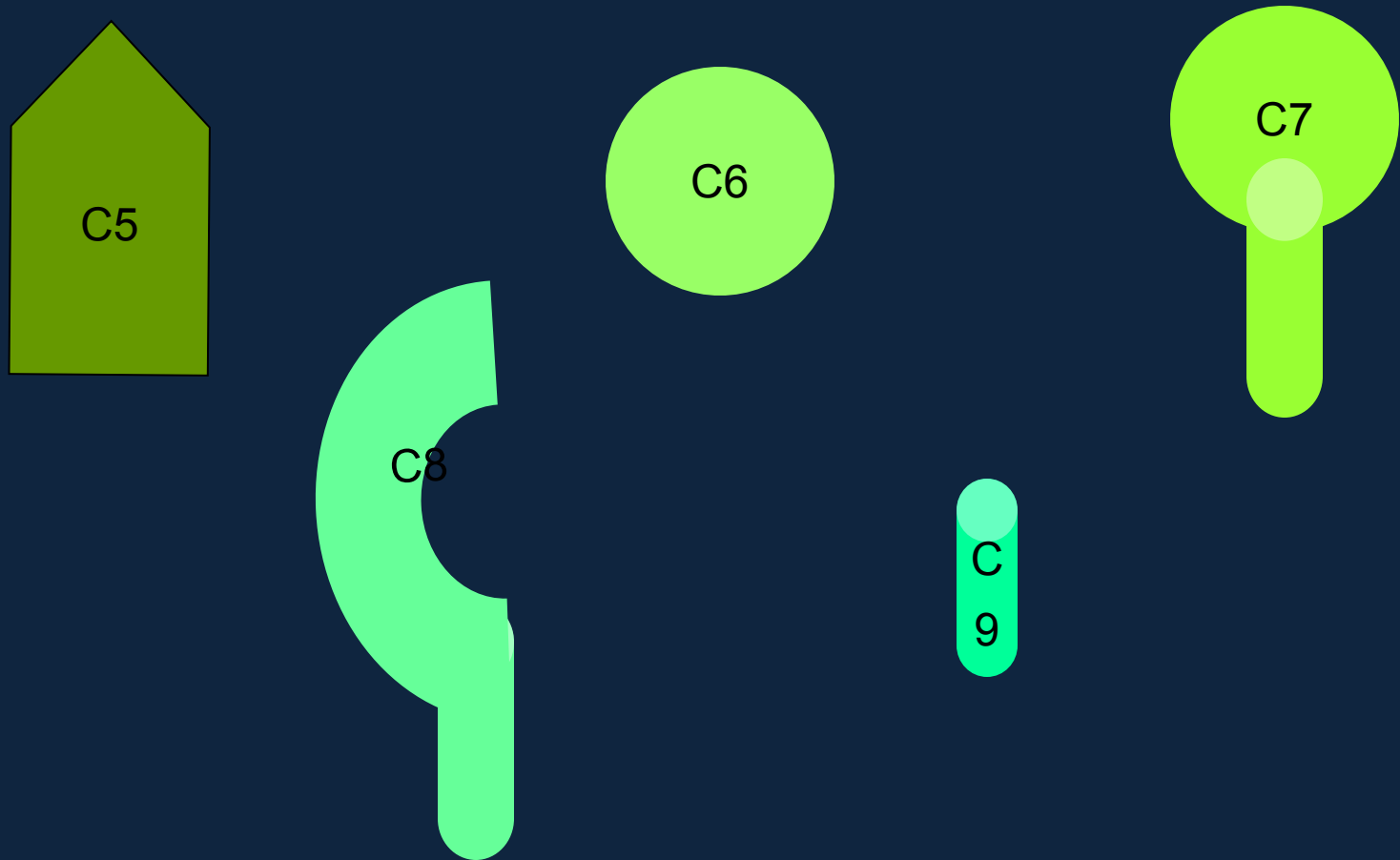
lytic pathway

*formation of membrane-
attack complex,
lysis of pathogens*

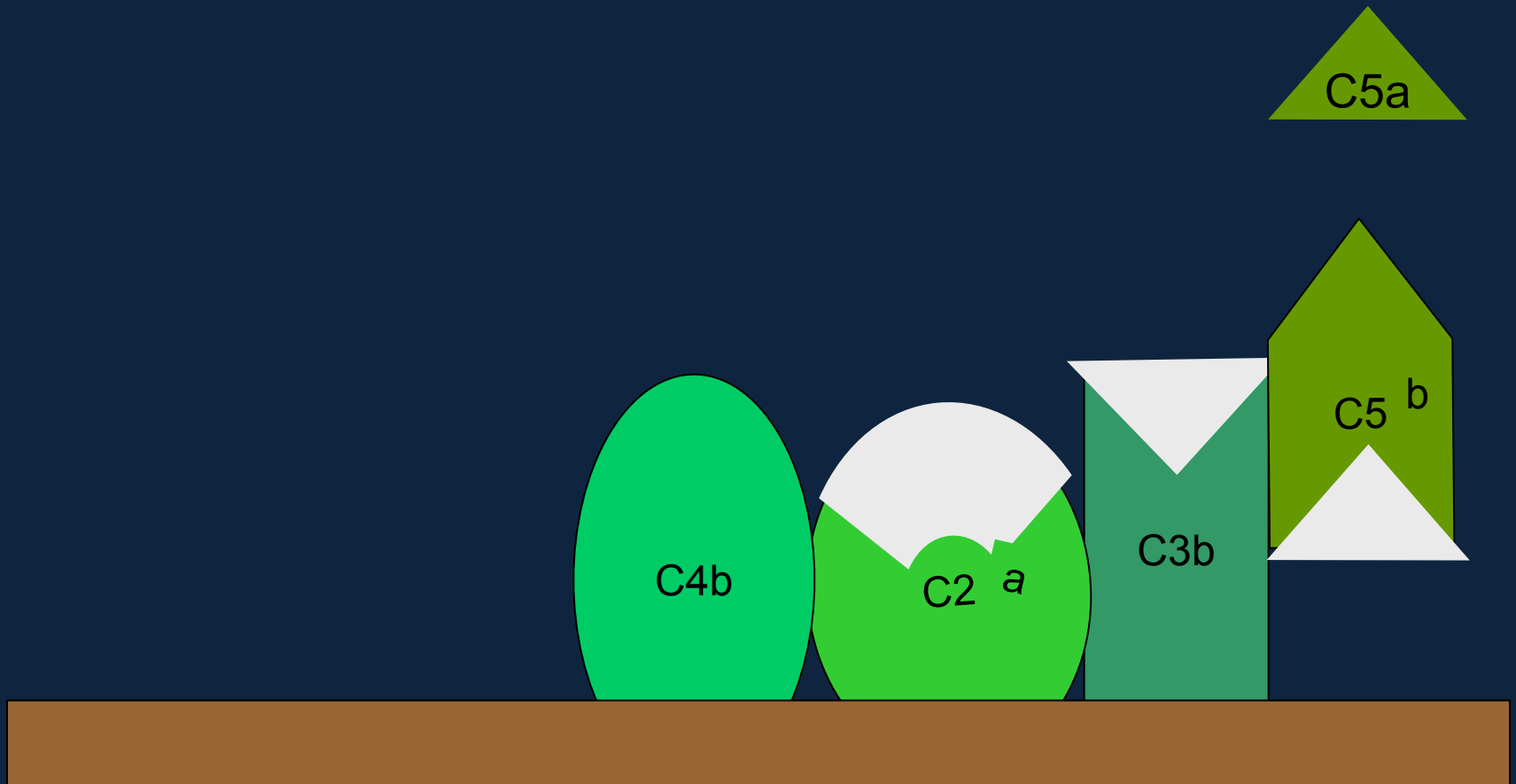
C5b, C6, C7, C8, C9

(adapted from Janeway 2001)

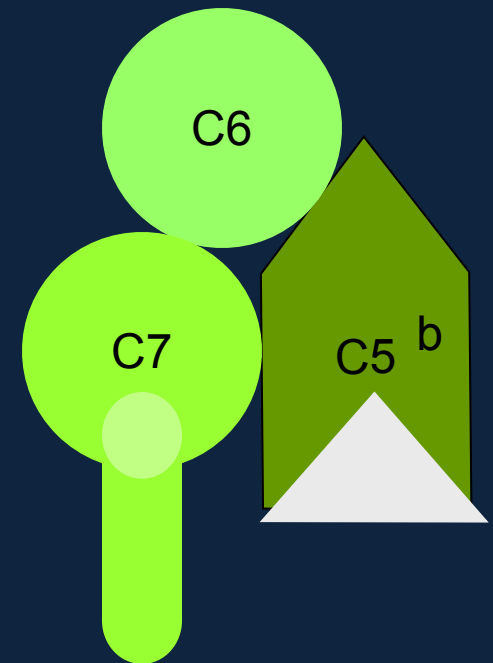
Components of the lytic pathway



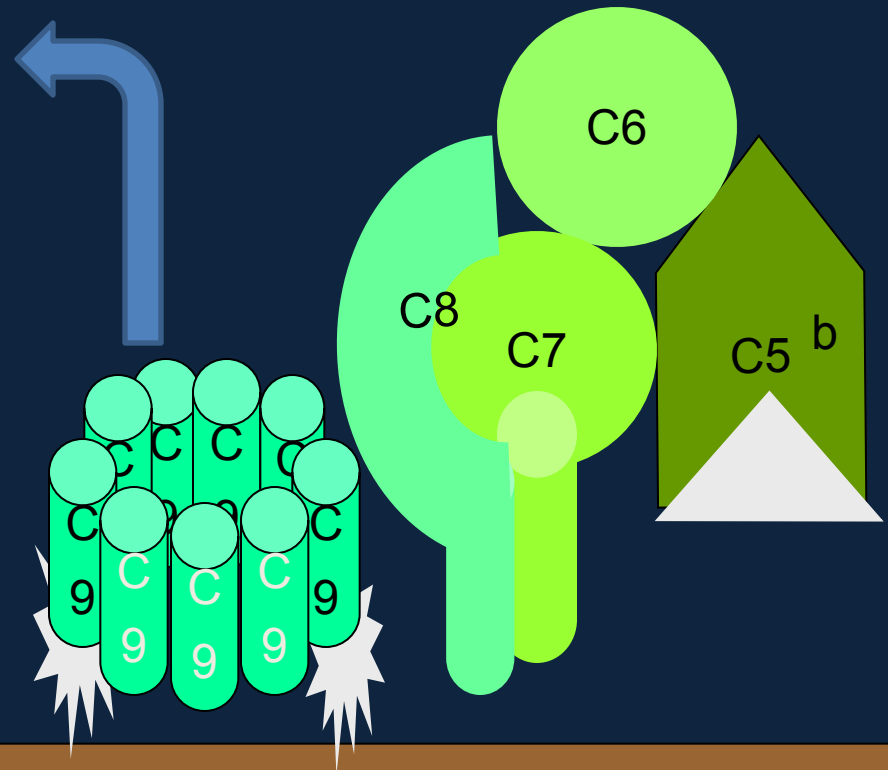
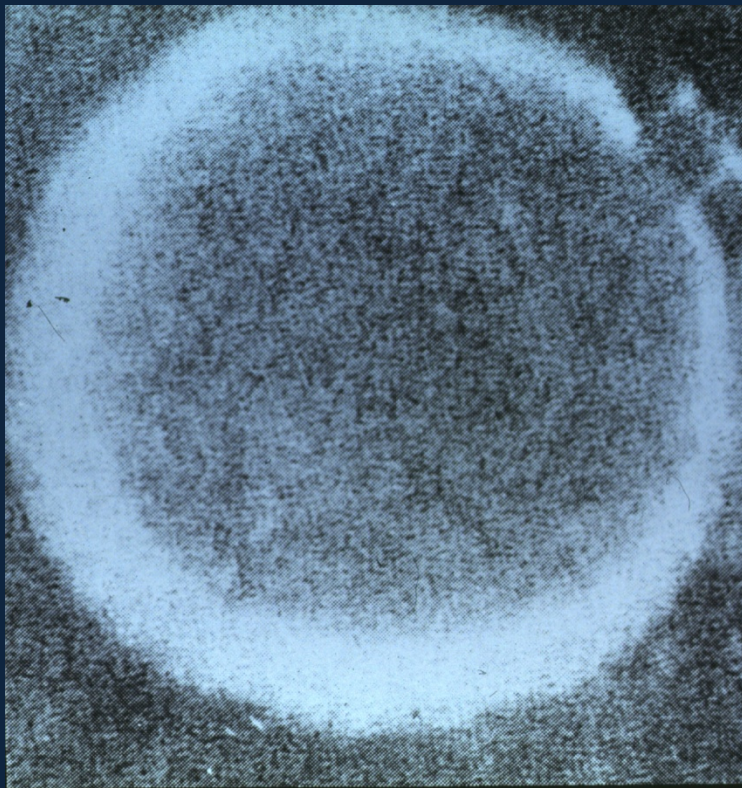
Lytic pathway C5-activation



Lytic pathway assembly of the lytic complex

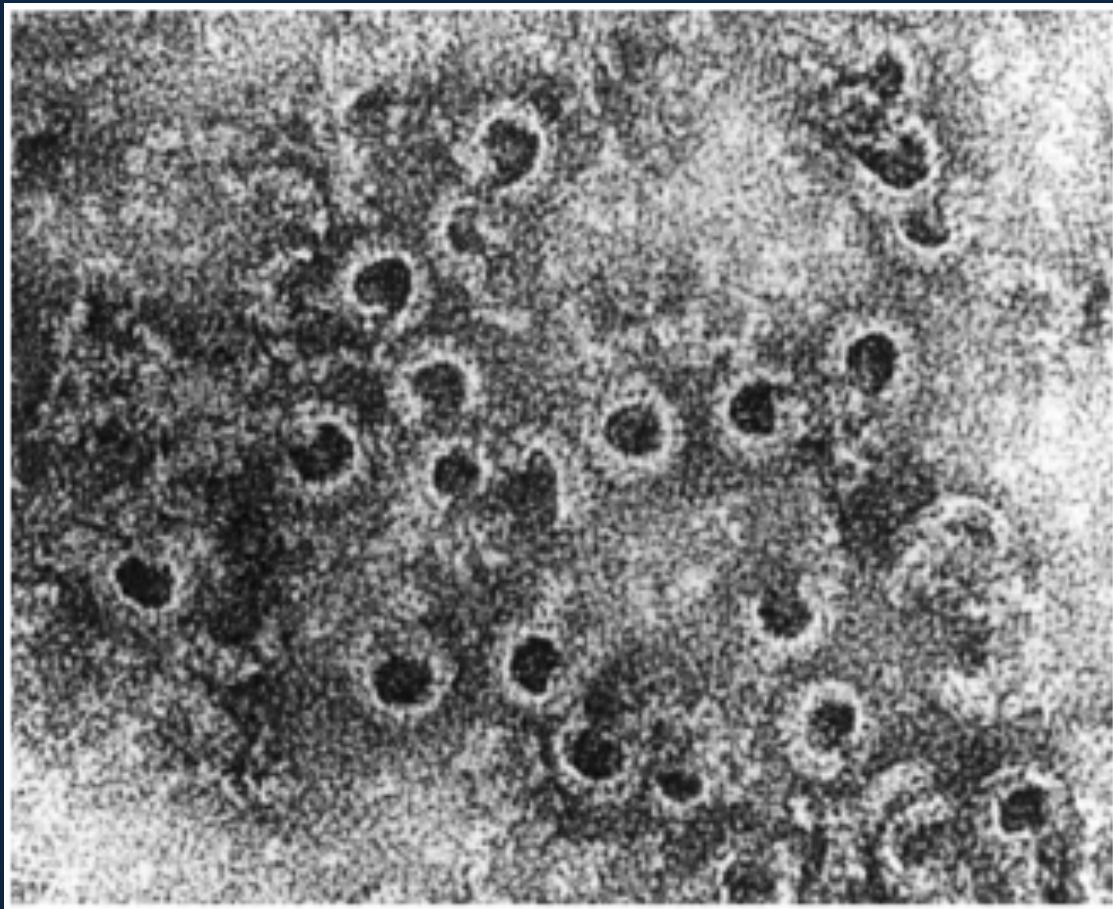
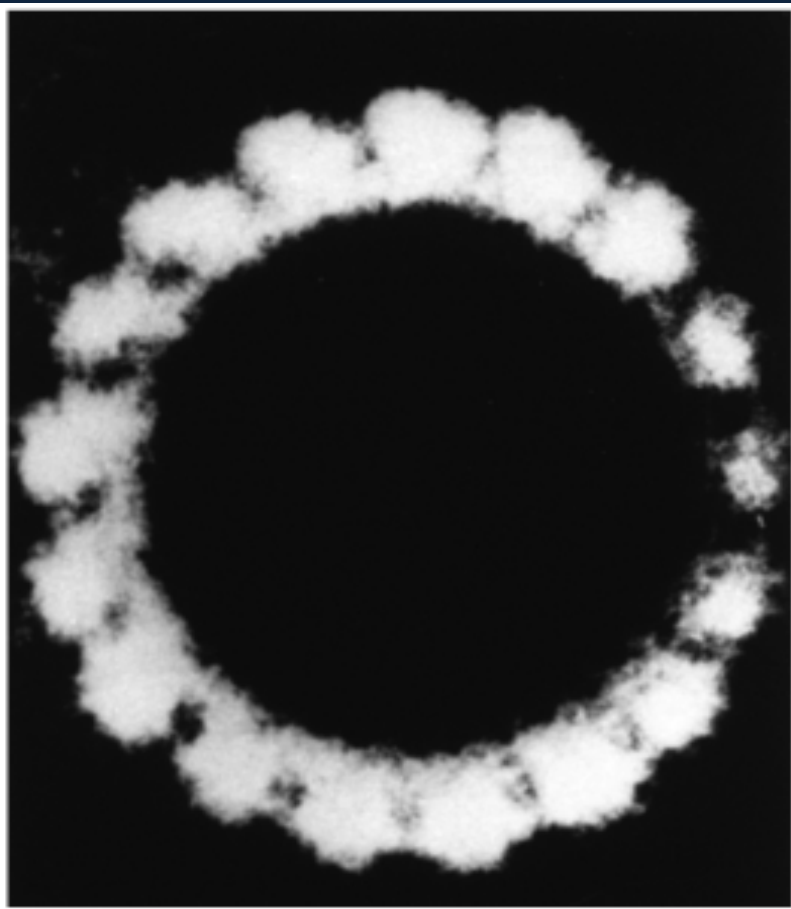


Lytic pathway: insertion of lytic complex into cell membrane



C9 complex

*Complement-induced lesions on the
membrane of a red blood cell*



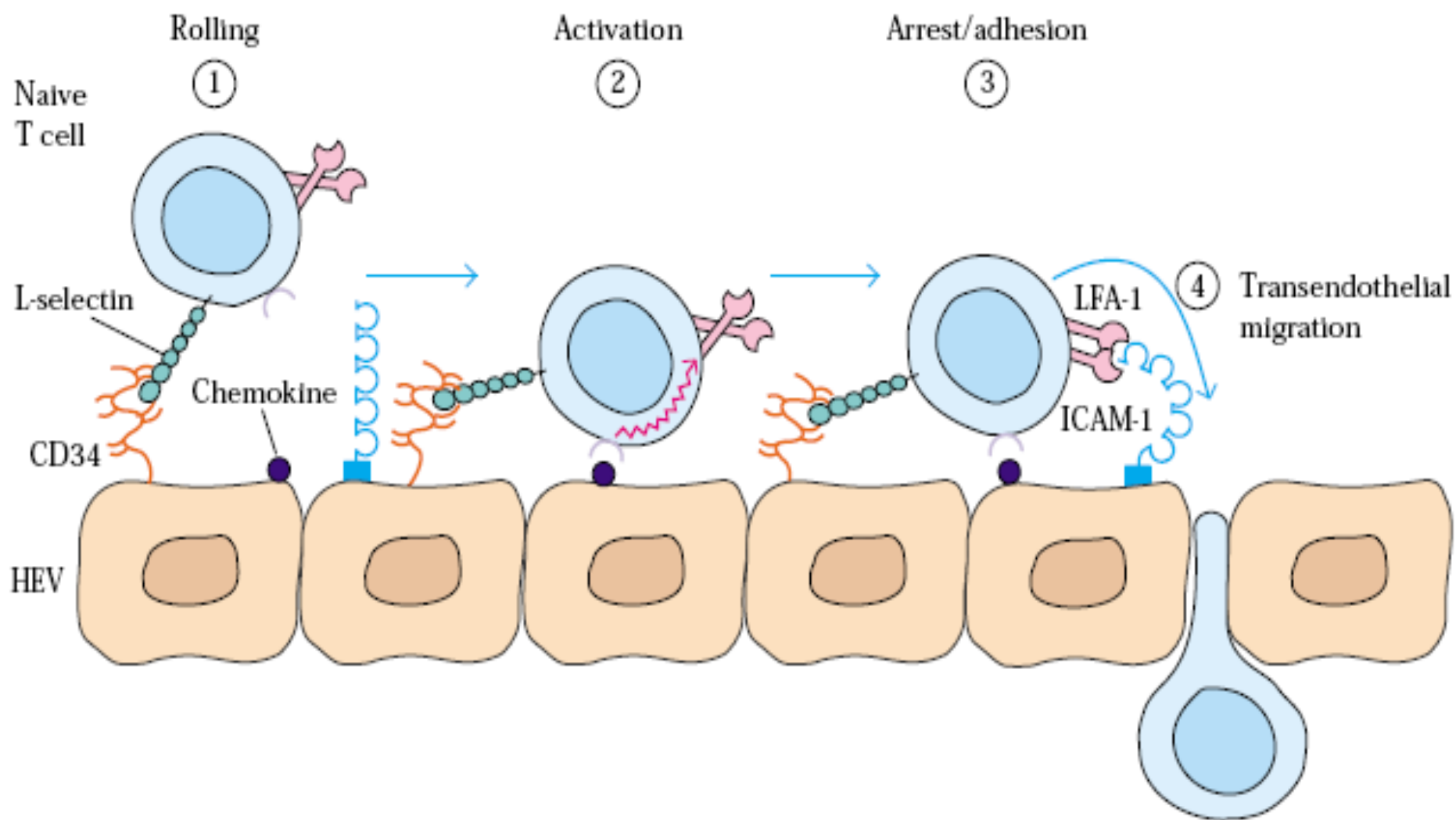
: Chemotaxis

Rolling (loose adherence) to .1
.endothelium

.Activation of cells .2

.Stable adherence to endothelium .3

.Transmigration into tissue spaces .4



:Phagocytic cells

Specialized blood cells internalize (phagocytose), kill and digest whole :microorganisms these cells are

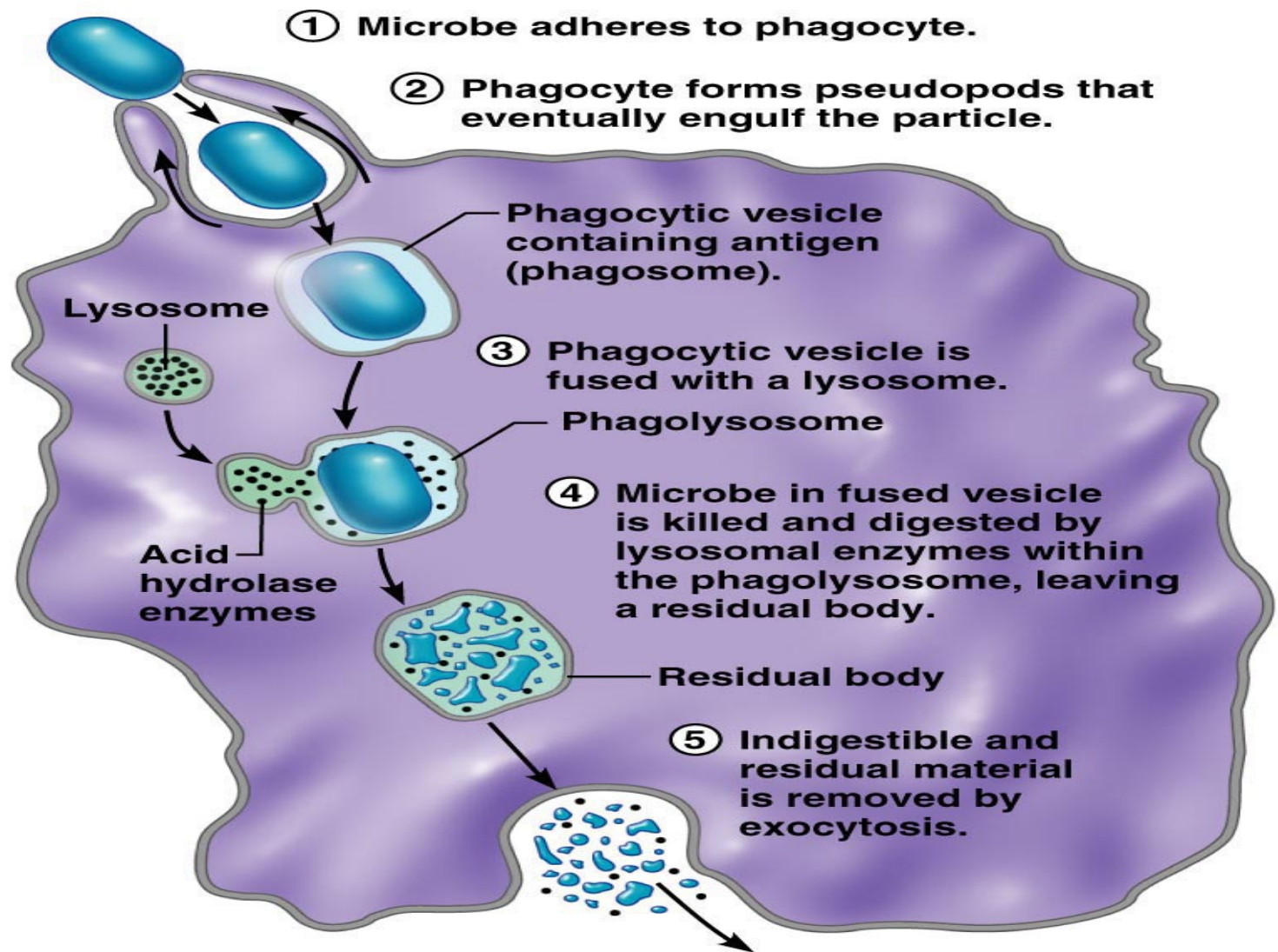
Monocytes -

Neutrophils -

Tissue macrophages -

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:After localization at site of infection, phagocytosis begins

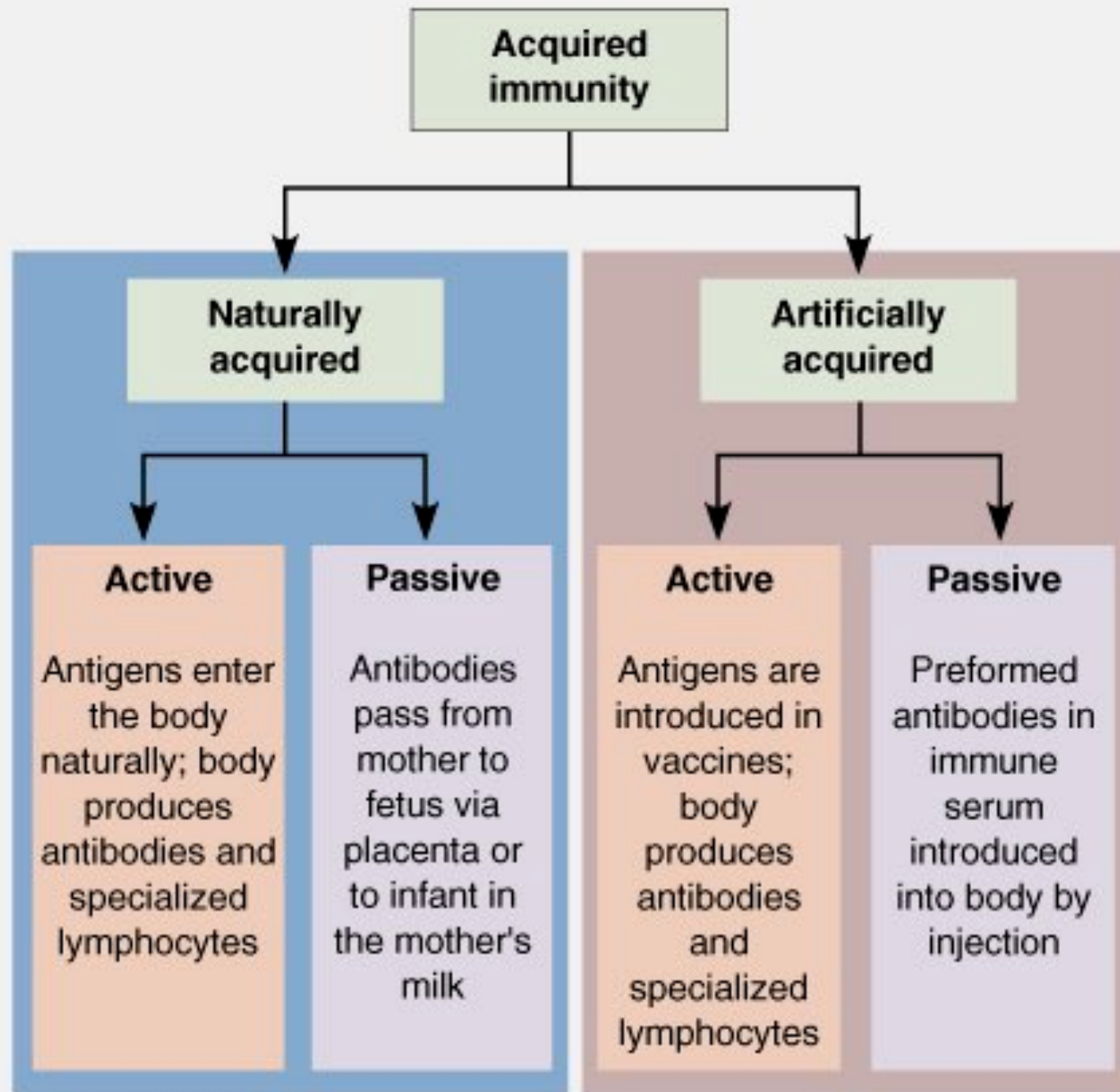


(b)

Acquired
Immunity

Humoral
Immune
Response

Antibody
Mediated



:Sequence of action of defense mechanisms

NONSPECIFIC DEFENSE MECHANISMS		SPECIFIC DEFENSE MECHANISMS (IMMUNE SYSTEM)
First line of defense	Second line of defense	Third line of defense
• Skin • Mucous membranes • Secretions of skin and mucous membranes	• Phagocytic white blood cells • Antimicrobial proteins • The inflammatory response	• Lymphocytes • Antibodies

Thank you