DEFENCE MECHANISMS IN ORAL CAVITY

By-:

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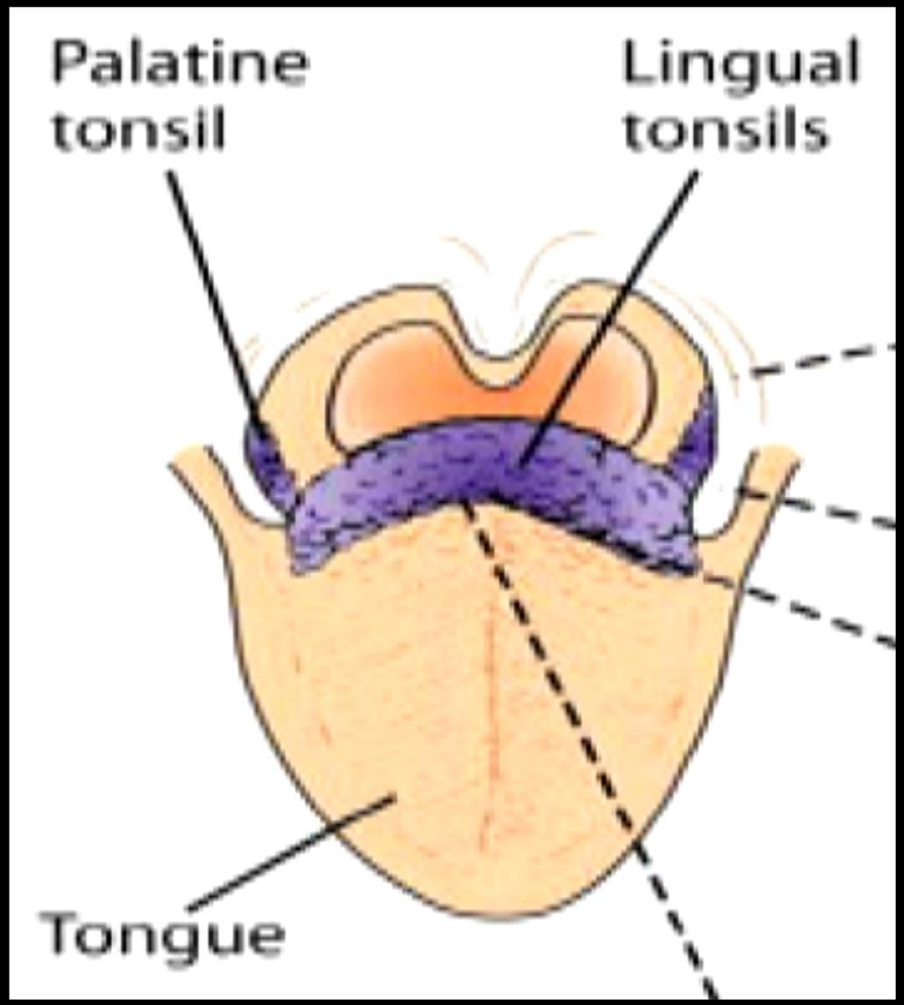
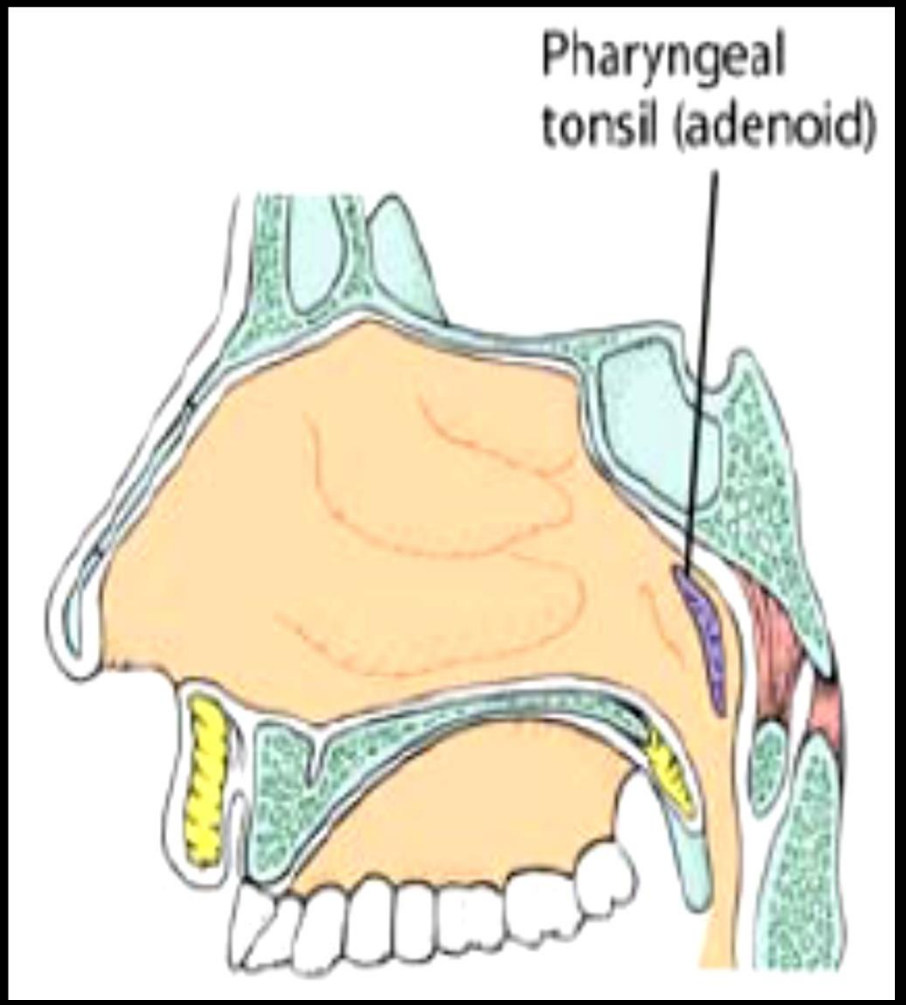
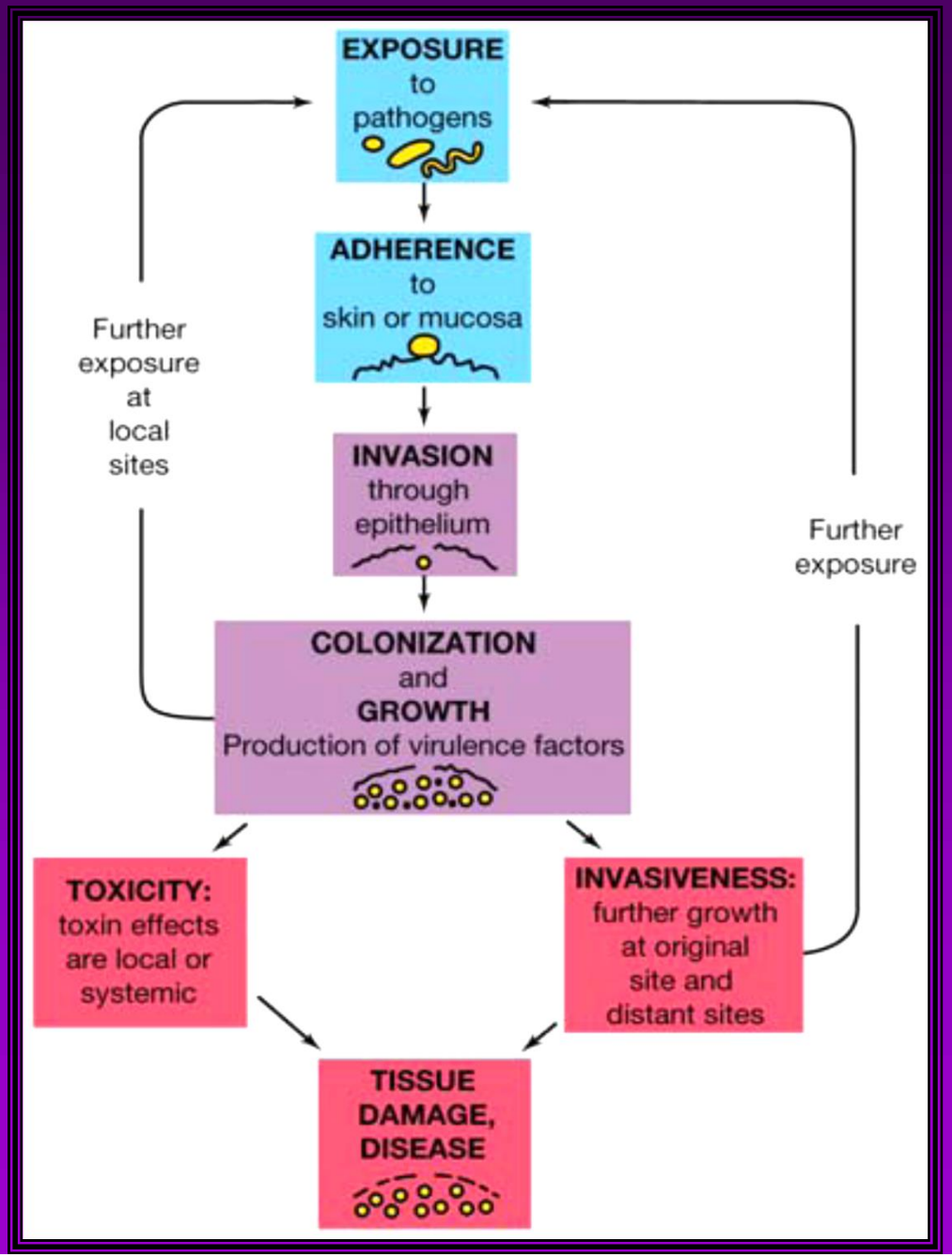
INTRODUCTION

- The primary function of defense system of mouth is to protect the teeth, jaws, gingivae & oral mucosa against infection.

- The oral immune system is a part of an extensive & specialized compartmentalized mucosa associated lymphoid tissue (MALT).


Palatine tonsil
Lingual tonsils
Tongue


Pharyngeal tonsil (adenoid)


EXPOSURE
to
pathogens
ADHERENCE
to
skin or mucosa
INVASION
through
epithelium
COLONIZATION
and
GROWTH
Production of virulence factors
TOXICITY:
toxin effects
are local or
systemic
INVASIVENESS:
further growth
at original
site and
distant sites
TISSUE
DAMAGE,
DISEASE
Further
exposure
at
local
sites
Further
exposure

BASICS OF IMMUNOLOGY

Why immunology ?

Infectious diseases

- Mechanisms of infections and diseases
- Management of infections and diseases

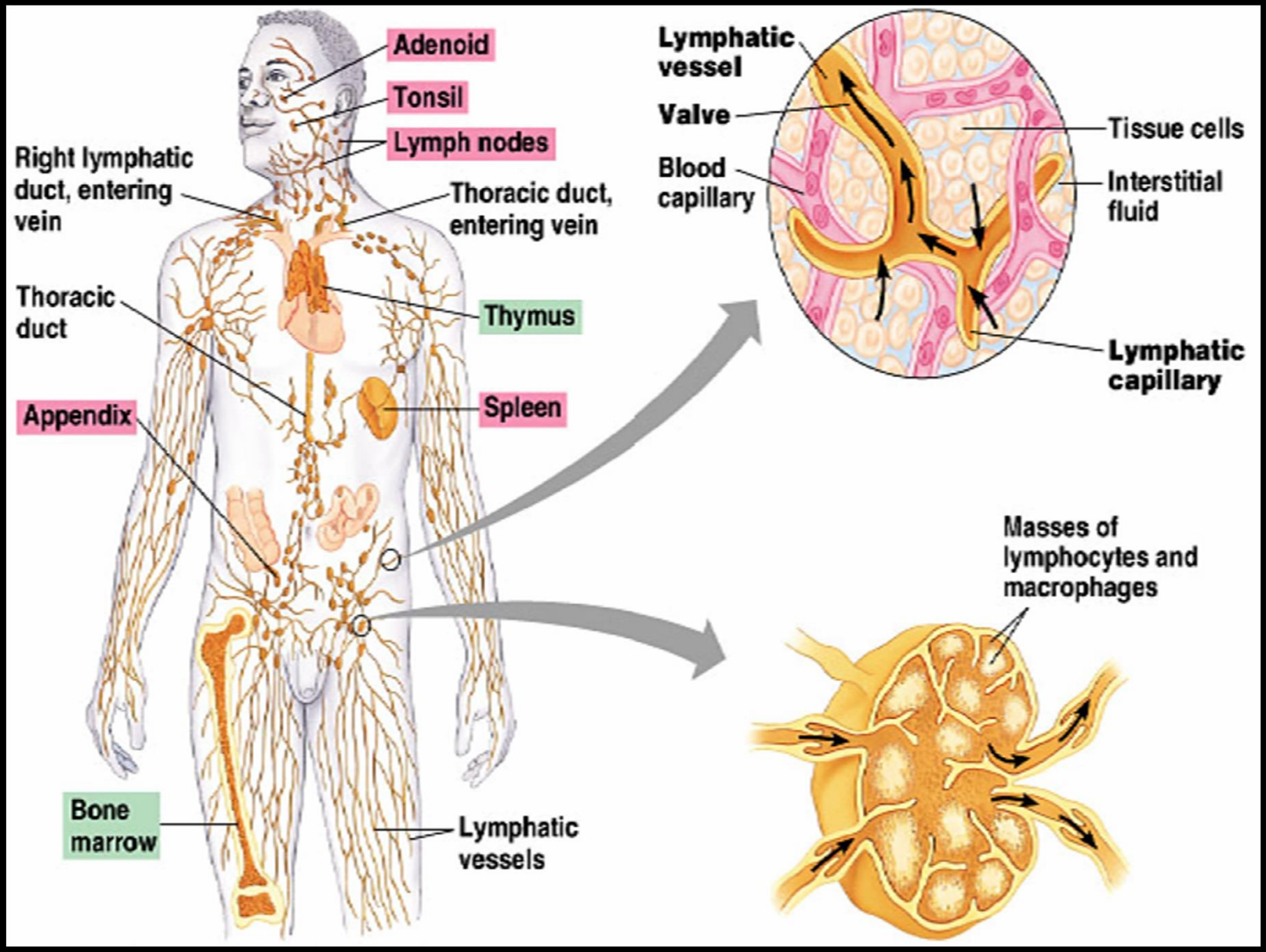
Inflammatory diseases & those caused by abnormal immune response

- ALLERGY: Immune responses to innocuous materials e.g. asthma
- AUTOIMMUNITY: Anti-self immunity e.g. multiple sclerosis, sjogren's syndrome

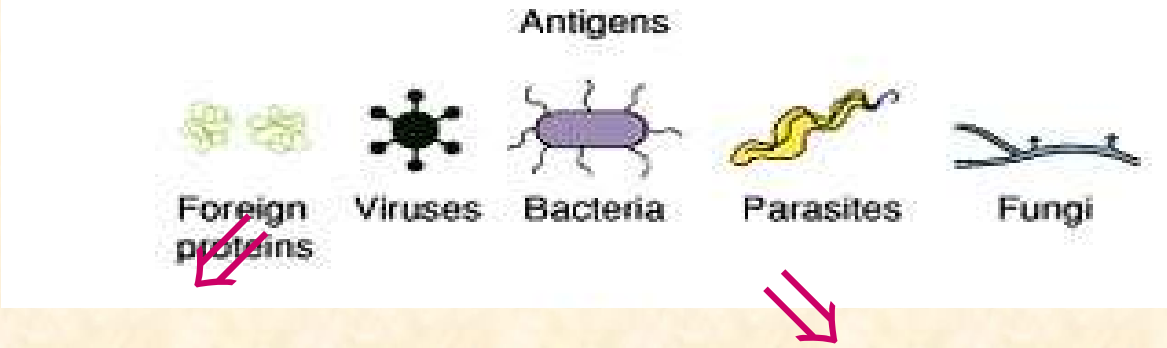
- GRAFT REJECTION: Immune responses to transplanted tissues
- Chronic inflammatory diseases; periodontal disease (gum infiltrated with inflammatory immune cells → bone absorption → teeth loss)

Anti-tumor immunity

- Tumor immunology and anti-tumor vaccine


Adenoid
Tonsil
Lymph nodes
Right lymphatic duct, entering vein
Thoracic duct, entering vein
Thoracic duct
Thymus
Appendix
Spleen
Bone marrow
Lymphatic vessels
Lymphatic vessel
Valve
Blood capillary
Tissue cells
Interstitial fluid
Lymphatic capillary
Masses of lymphocytes and macrophages

IMMUNE DEFENSES

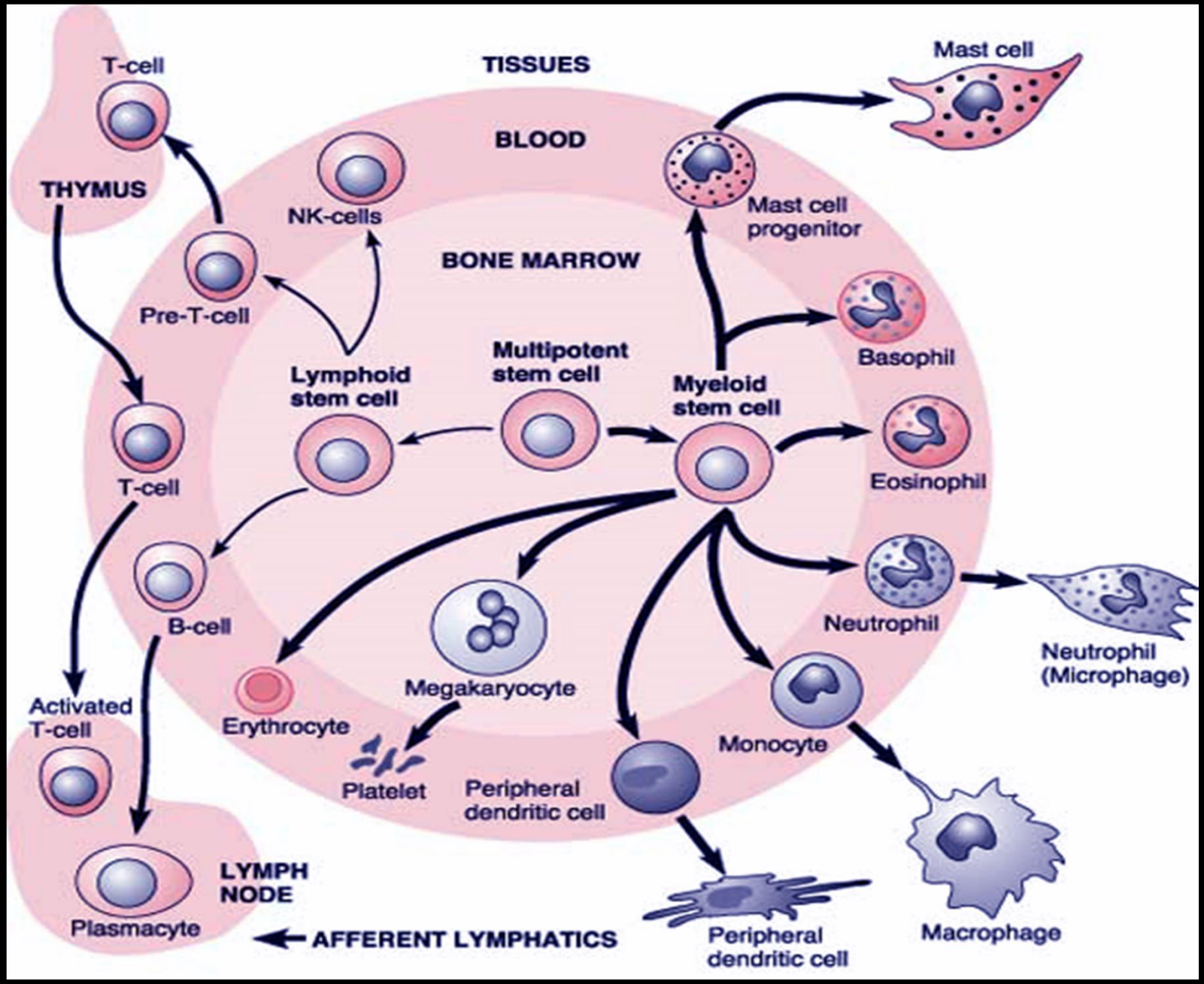


Innate Immunity
- invariant (generalized)
- early, limited specificity
- the first line of defense

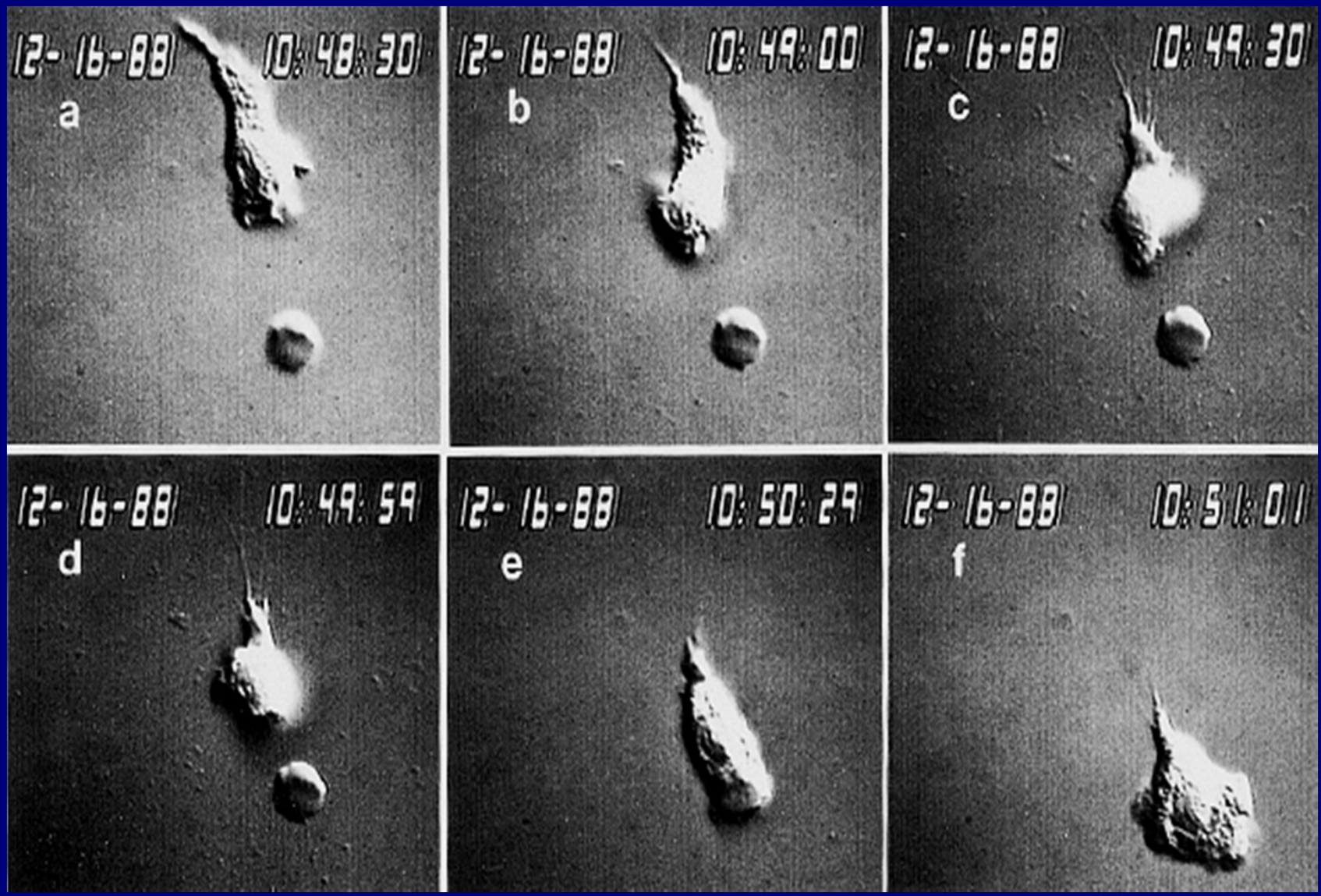
1. Barriers - skin, tears
2. Phagocytes - neutrophils, macrophages
3. NK cells and mast cells
4. Complement and other proteins

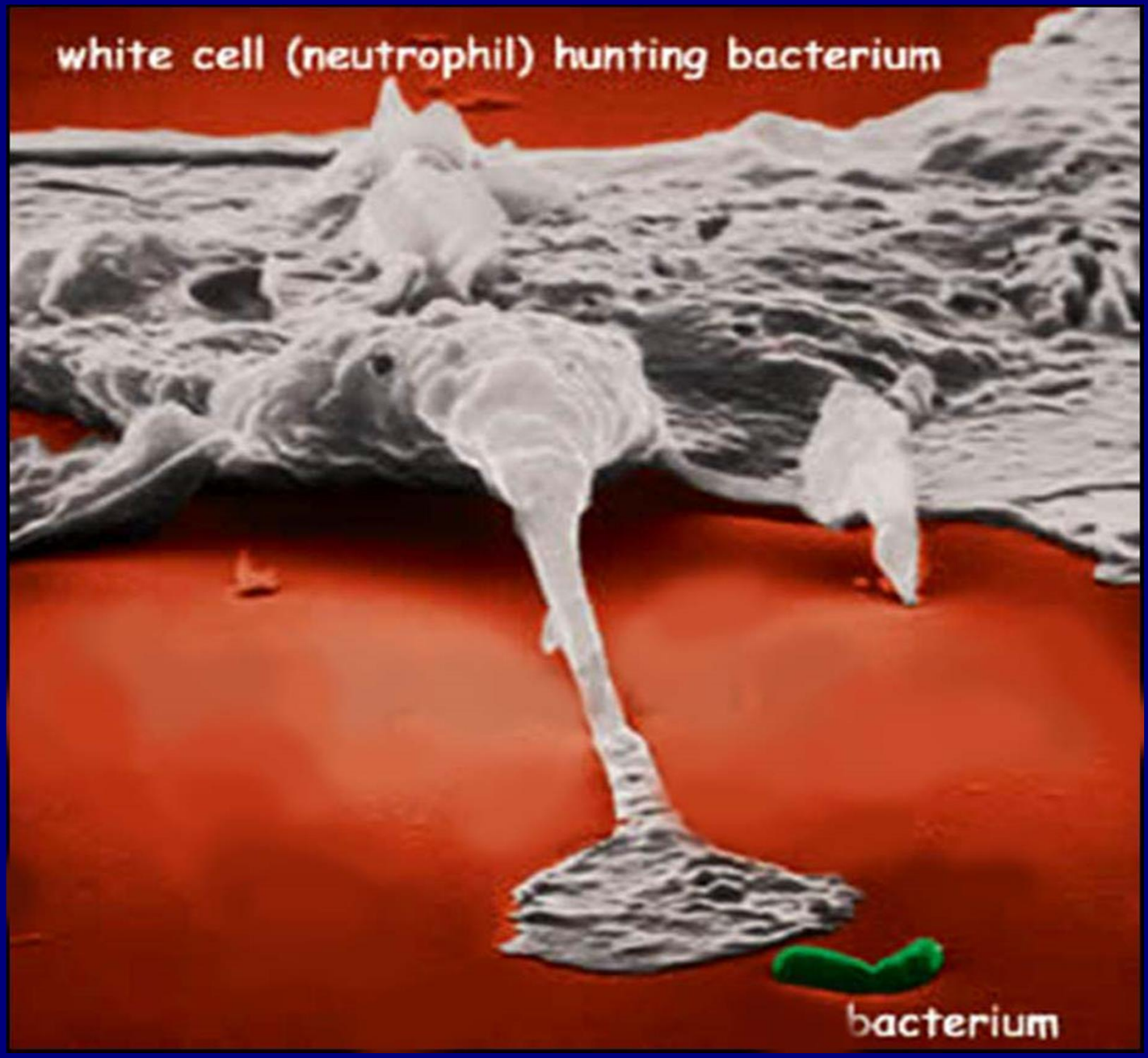
Adaptive Immunity
- variable (custom)
- later, highly specific
- “remembers” infection

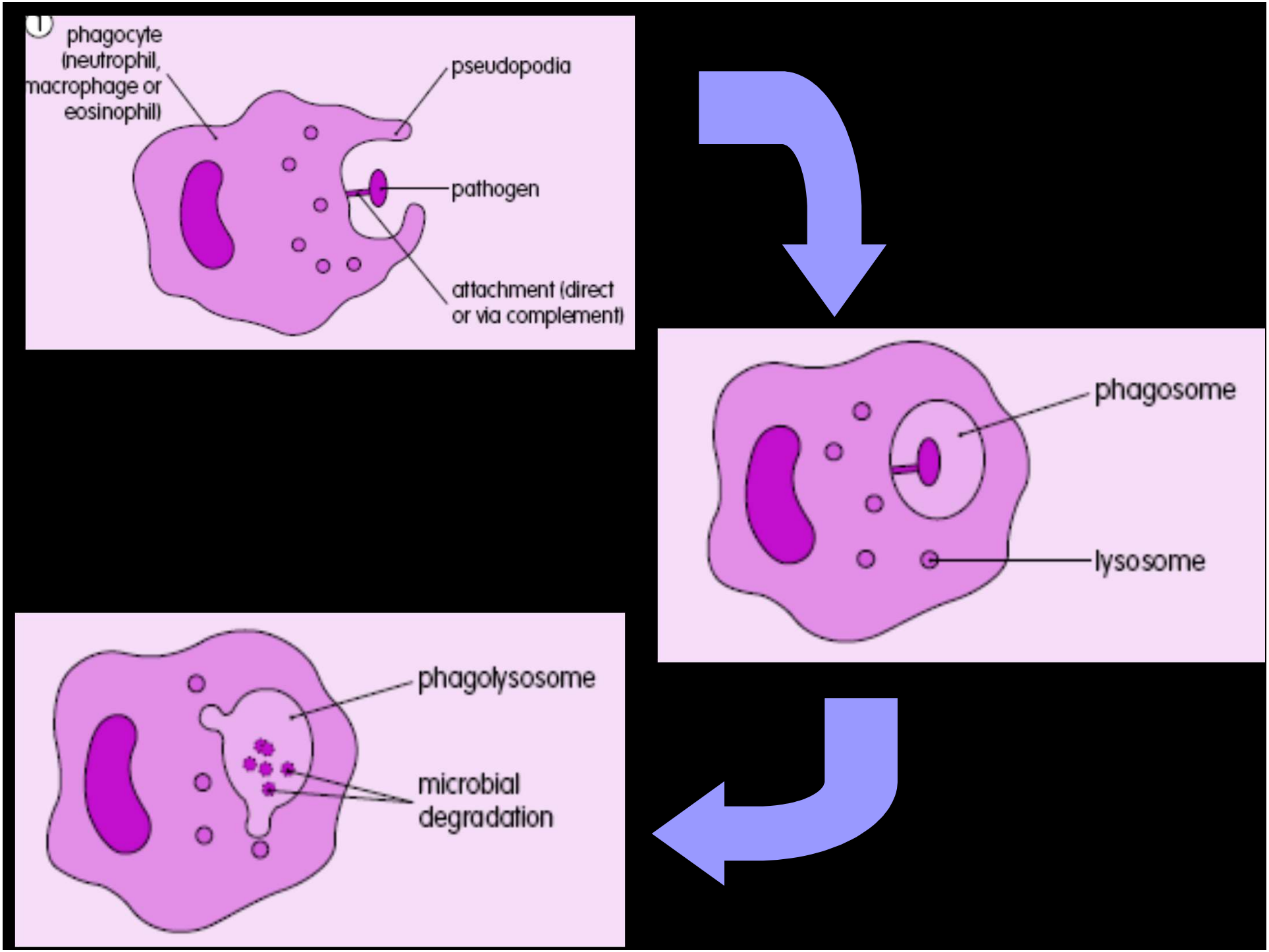
Immune mechanisms	HUMORAL	CELL MEDIATED
INNATE	■Complement ■Neutrophil	■Macrophages ■N.K Cells
ACQUIRED	■B- Cells ■Plasma Cells	■Helper T Cells ■Cytotoxic T Cells


T-cell
TISSUES
Mast cell
BLOOD
THYMUS
NK-cells
Mast cell progenitor
BONE MARROW
Pre-T-cell
Basophil
Multipotent stem cell
Lymphoid stem cell
Myeloid stem cell
T-cell
Eosinophil
B-cell
Neutrophil
Neutrophil (Microphage)
Megakaryocyte
Activated T-cell
Erythrocyte
Monocyte
Platelet
Peripheral dendritic cell
LYMPH NODE
Plasmacyte
AFFERENT LYMPHATICS
Peripheral dendritic cell
Macrophage

MOTILE NEUTROPHILS




white cell (neutrophil) hunting bacterium
bacterium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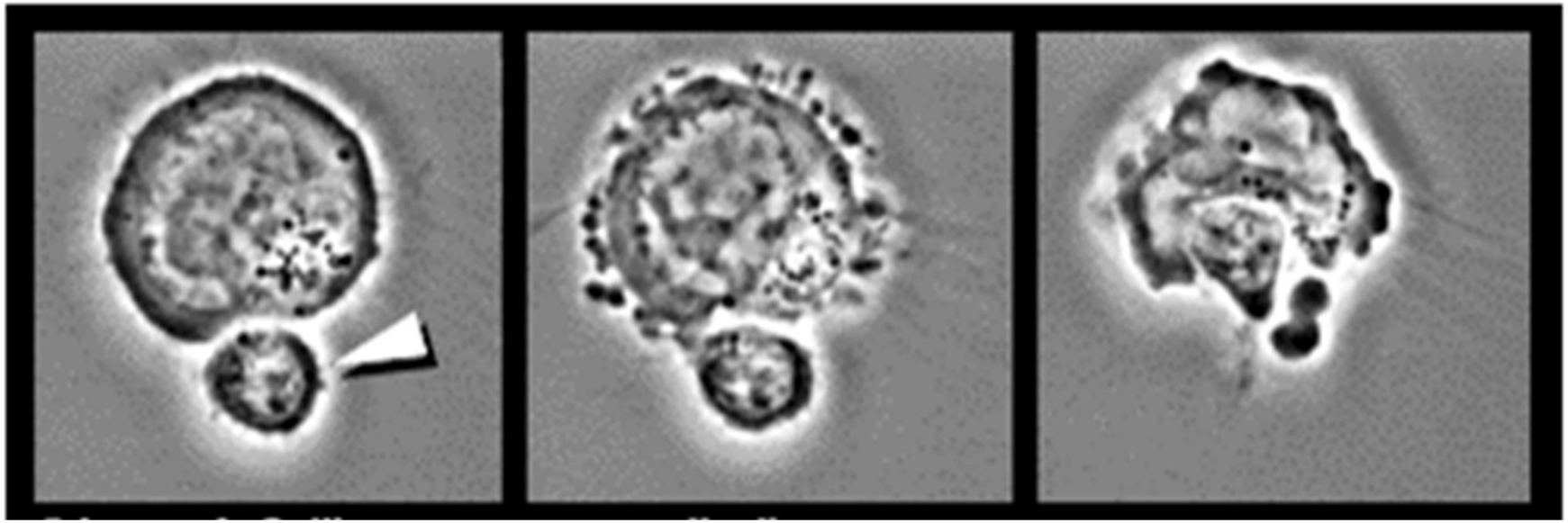
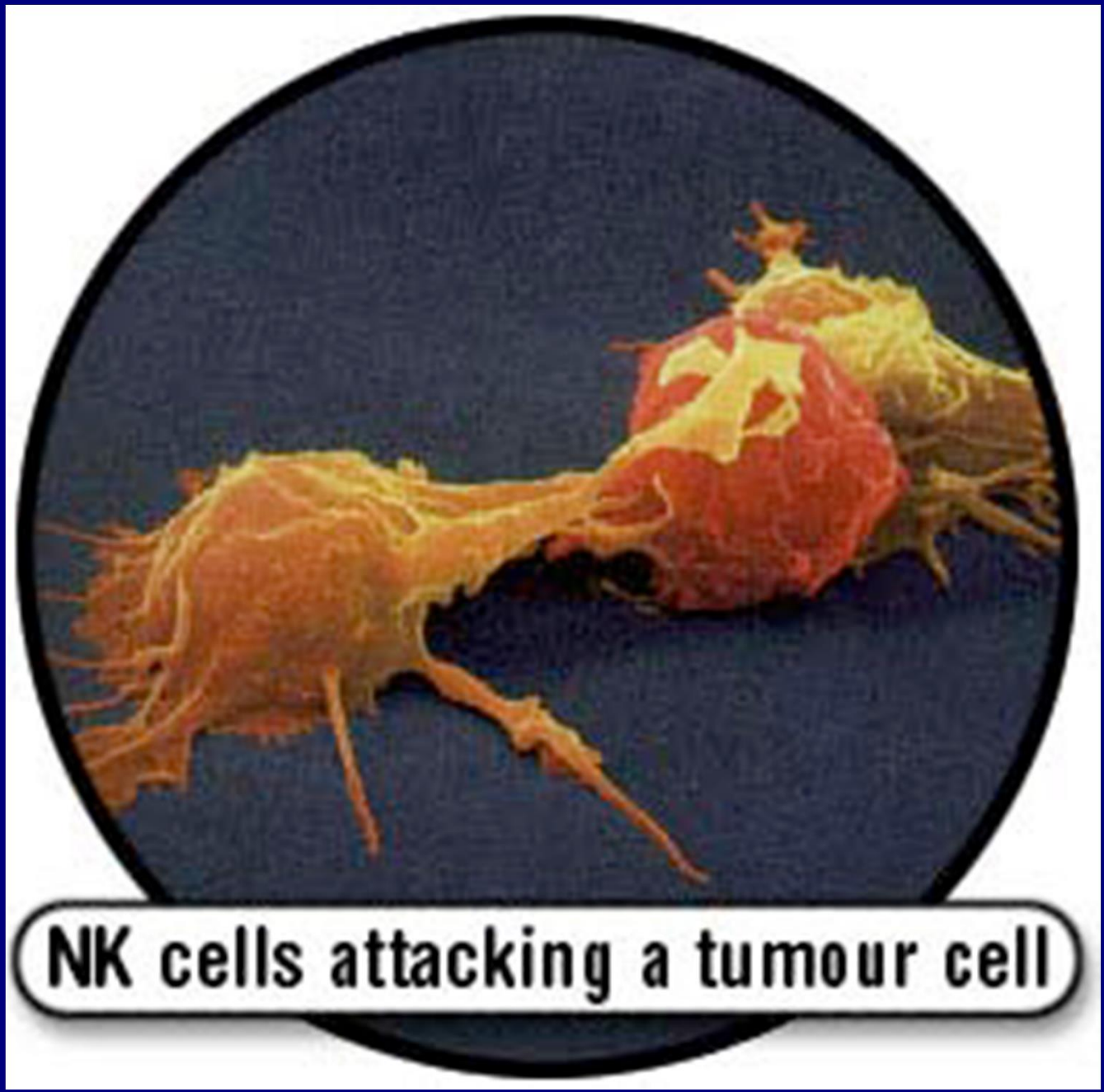
phagocyte (neutrophil, macrophage or eosinophil)
pseudopodia
pathogen
attachment (direct or via complement)
phagosome
lysosome
phagolysosome
microbial degradation

A Cytotoxic T Cell Attacking and Killing a Virus-Infected Target Cell



Here, the smaller cytotoxic T cell or T_c (arrow) is attacking and killing a much larger virus-infected cell. The T cell will survive while the infected cell is destroyed.


NK cells attacking a tumour cell

Cytokine	Main sources	Main actions
IL-1	Macrophages	Fever T-cell and macrophage activation
IL-2	T helper 1 cells	Growth of T cells Stimulates growth of B cells and NK cells
IL-3	T helper cells	Growth factor for progenitor haemopoietic cells
IL-4	T helper 2 cells	Activation and growth of B cells IgG1, IgE and MHC class II induction of B cells Growth and survival of T cells
IL-6	Macrophages	Lymphocyte activation Increased antibody production Fever, induces acute phase proteins
IL-8	Macrophages	Chemotactic factor for neutrophils Activates neutrophils

IL-10	T helper 2 cells Macrophages	Inhibits immune function
IL-12	Macrophages	Activates NK cells Causes CD4 T cells to differentiate into T helper 1 cells
IFN-γ	T helper 1 cells NK cells	Activation of macrophages and NK cells Produces antiviral state in neighbouring cells Increases expression of MHC class I and II molecules Inhibits T helper 2 cells
TNF-α	T helper cells Macrophages	Activates macrophages and induces nitric oxide production Proinflammatory Fever and shock
TNF-β	T helper 1 cells	Activates macrophages and neutrophils Induces nitric oxide production Kills T cells, fibroblasts and tumour cells

DEFENSE MECHANISMS IN ORAL CAVITY

(ORAL MUCOSAL IMMUNE MECHANISMS)

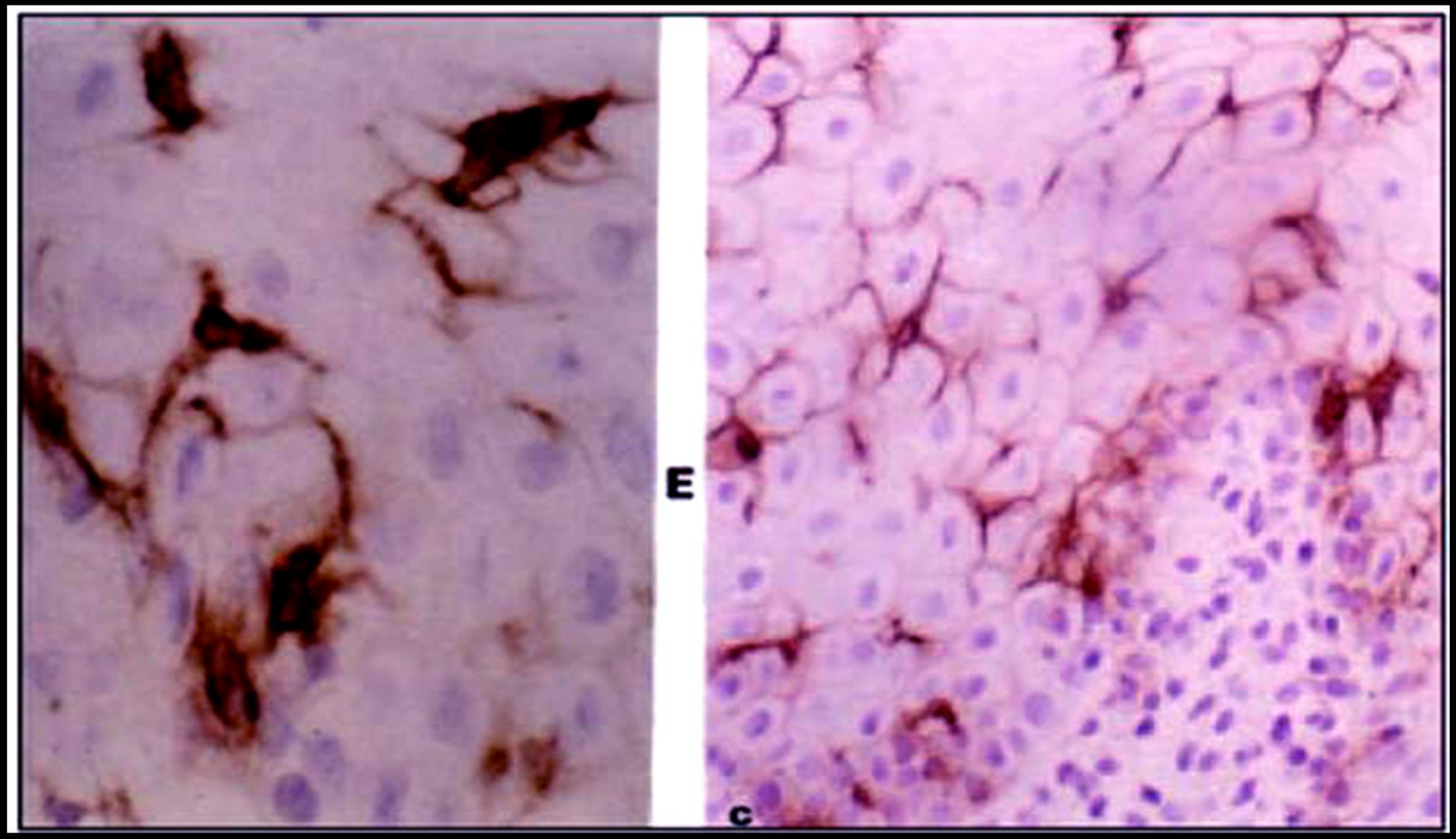
- The host defense against infection vary in the different oral microenvironments or domains represented by the -:
  - **ORAL MUCOSA**
  - **SALIVARY GLANDS & SALIVA**
  - **GINGIVAL CREVICE**

ROLE OF ORAL MUCOSA

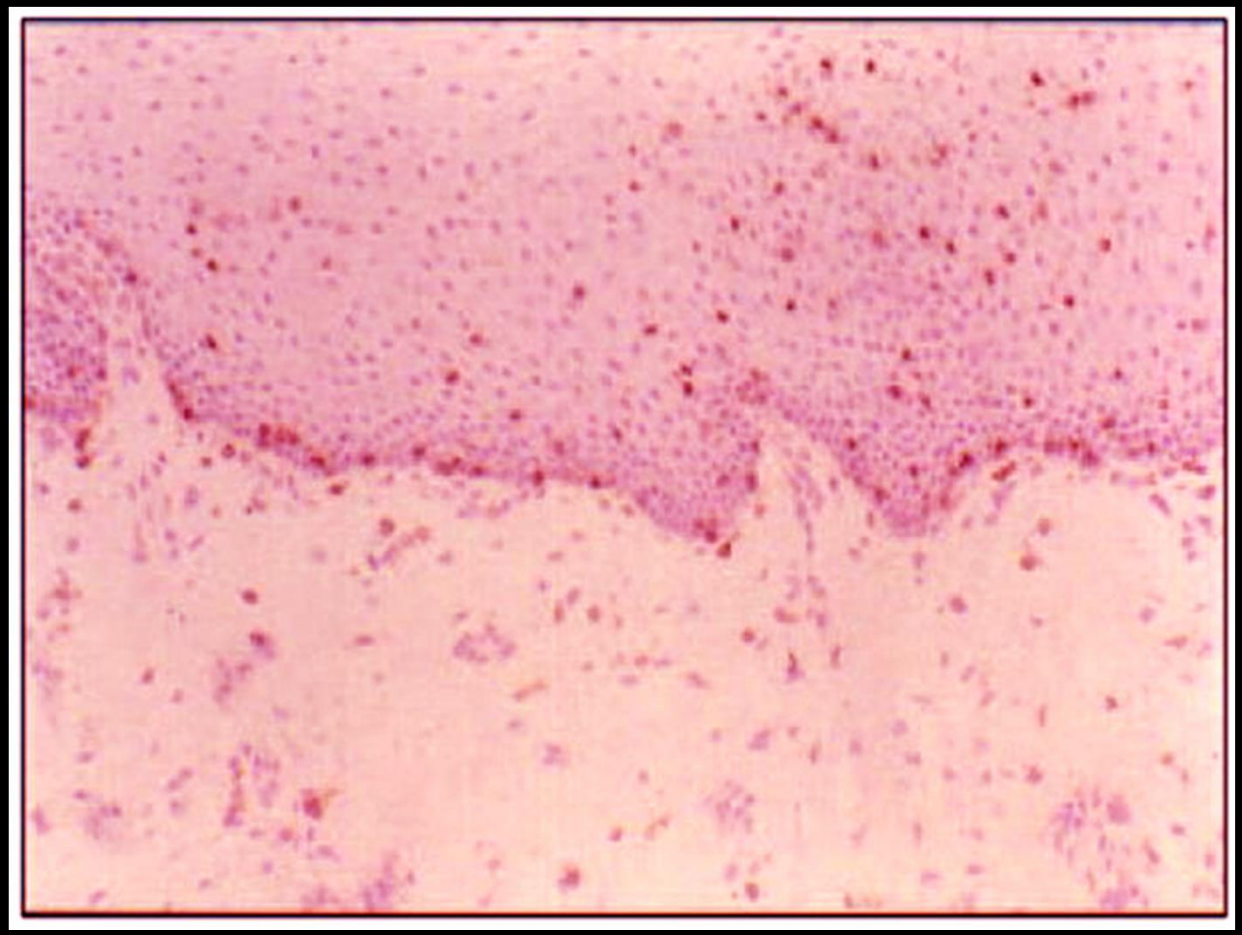
- Mechanical barrier to oral microorganisms.
- Continuous shedding by exfoliation of epithelial squames limits microbial colonization of surface.

- Membrane coating granules discharged extracellularly in granular layer, transudation of antibody through the mucosa and the barrier presented by basement membrane contribute to mucosal defenses.

- Intraepithelial dendritic langerhans cells are also available for antigen presentation and immune response.



Section of normal mildly inflamed oral mucosa showing the distribution of Langerhans cells (left x50, right x20). Note that the interdigitating processes appear to go around epithelial cells.



CD4-positive cells within the epithelium in normal oral mucosa. Note that these are mainly intra-epithelial, with few cells in the connective tissue.

- Oral epithelial cells also produce a range of cytokines including IL-1 beta, IL-6, TNF-alpha, GM-CSF, TGF-beta, IL-8 and their receptors.

- Cytokines can also be secreted by macrophages, fibroblasts, dendritic cells, mast cells and intra epithelial lymphocytes in oral mucosa.

ROLE OF SALIVA & SALIVARY GLANDS

- Flow of saliva has mechanical effect, flushing micro-organisms from tooth and tooth surfaces.
- Saliva also contains important anti-microbial agents and patients with a significant xerostomia are prone to dental caries and candida infections.

Table 1. Antimicrobial Properties of Saliva

Antimicrobial agent	Activity
Secretory IgA (also s-IgG, s-IgM)	Inhibits adherence. Agglutinates bacteria.Virus neutralisation. IgA is the major antibody in saliva.
Lactoferrin	Iron-binding. Bacteriostatic.
Lysozyme	Effective against *S. mutans*.
Agglutinins	Glycoproteins, mucins, fibronectin, 2-microglobulin, histatins, proline-rich proteins.
Myeloperoxidase system	Bactericidal in presence of thiocyanate/halide-H_20_2.
Salivary peroxidase system	(enzyme-thioycyanate-H_20_2)
Complement (trace amounts)	C3 probably largely derived from gingival crevice fluid.
Leukocytes	>98% are neutrophils, but up to 50% may not be capable of phagocytosis.

- Secretory IgA, the major antibody in saliva synthesized by plasma cells associated with salivary glands.IgA-2 subclass predominates in salivary secretion.

- Secretory IgA can also opsonize bacteria for phagocytosis by polymorphs, activate complement by alternate pathway, and directly neutralize some viruses.

ROLE OF GINGIVAL CREVICE

- The fluid present within the gingival sulcus is known as Gingival Crevicular Fluid (G.C.F).
- The components of GCF includes specific antibodies, antigens, and cellular components which include leukocytes (PMNs, monocytes/ macrophages).
- Even in healthy gingiva, there is a continuous traffic of neutrophils from gingival capillaries into the gingival sulcus attracted by bacterial

peptides from the biofilm of dental plaque and IL-8 from gingival epithelium.

- Most of the neutrophils entering the gingival sulcus are functionally active and capable of phagocytosis and the killing of micro-organisms.

- Drugs which are excreted through GCF may be used advantageously in periodontal therapy eg. Tetracyclines and metronidazole

TABLE 1 - Role of Mucosal Immunity in Prevention of HIV Transmission

- Block HIV entry; prevention of mucosal contact
- Prevent initial infection of target cells
  - Block attachment of virus to epithelial cells
  - Block attachment of infected cells to EC
- Interception of virus during epithelial transport
- Neutralization of virus in mucosae
- Elimination of locally infected cells by ADCC

SUMMARY

- Oral mucous membrane act as a barrier and serve as the 1st line of defense against pathogens.
- Innate immune cells function as the 2nd line of defense; pre-formed and fully active, can function immediately upon the entry of pathogens, not specific, PMN ingest and destroy many different bacteria.
- Adaptive (acquired) immunity, the 3rd line of defense, play major roles in immune clearance of pathogens after infection.


Thank You