HOST RESPONSE
- BASIC CONCEPTS

CONTENTS

- Introduction
- Classification
- Innate immunity
- Acquired immunity
- Cell of the immune system
- Antigens
- Immunoglobulins
- Complement system
- Immune responses
- Cytokines
- References

INTRODUCTION

- ***Host*** can be defined as "the organism from which a parasite obtains its nourishment"
- The immune response is the host reaction to infection/invasion
- Resistance exhibited by the host towards any injury caused by micro-organisms & their products

INTRODUCTION

- The state of periodontal health or disease depends upon the interaction between the resident microbiota and the host response.
- Periodontal pathogens trigger both inflammatory reaction and host immune response.
- The immune system plays a key role in limiting the infections to the gingival crevice.
- It also orchestrates the alterations of the connective tissue in a complex remodeling process involving cycles of destruction and reconstruction

HOST DEFENCE

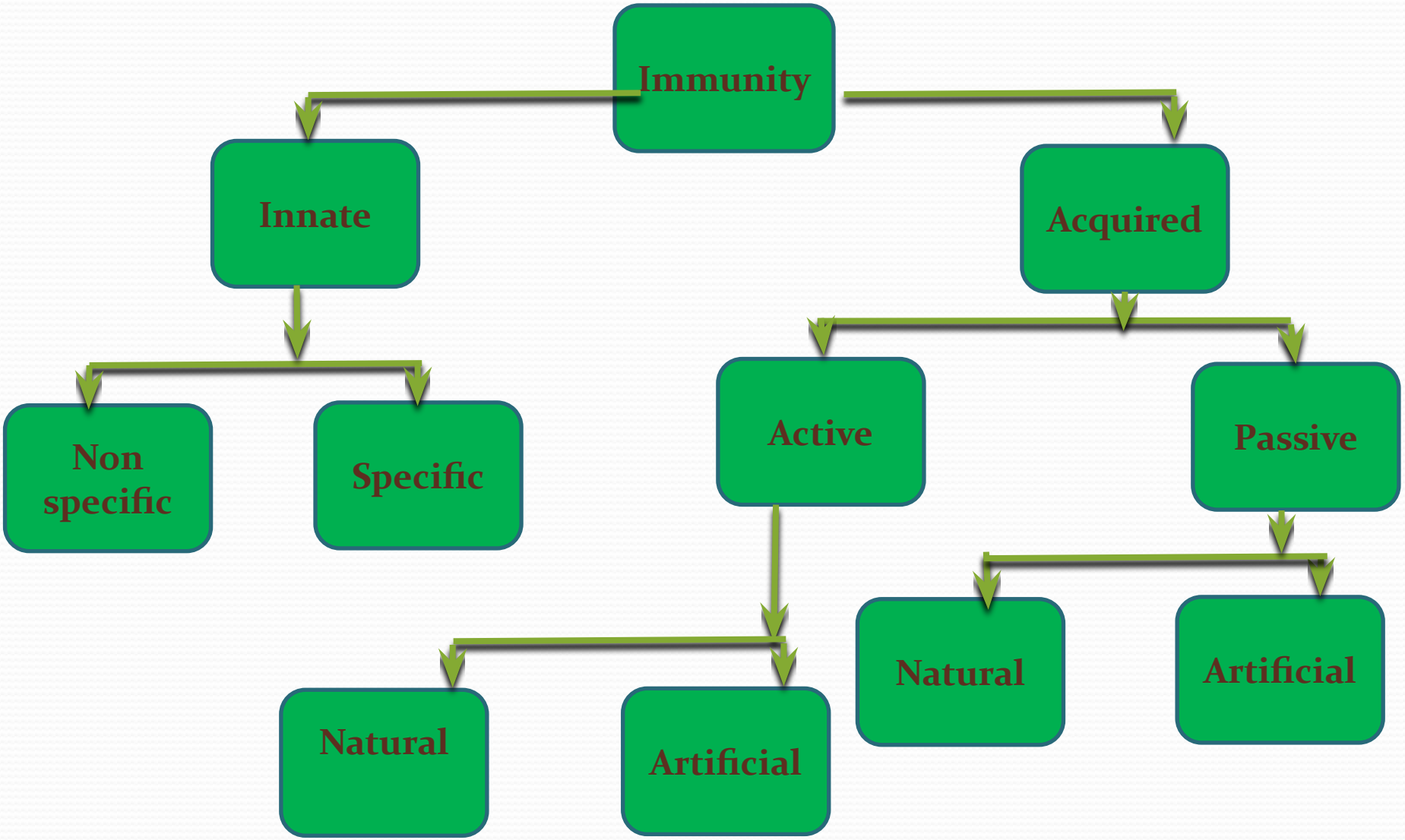
- Pathogen : an infectious agent that causes disease
- The body is under constant attack by microorganisms in the environment
- Infectious disease occurs when a microorganism succeeds in evading or overwhelming host defenses to establish a local site of infection and replication.
- For a pathogen to enter the body it must first overcome the epithelium and then the **innate immune response** and the **adaptive immune response**

TYPES OF IMMUNITY

1. NATURAL / INNATE IMMUNITY

2. ACQUIRED / ADAPTIVE IMMUNITY

CLASSIFICATION



NATURAL OR INNATE (NON SPECIFIC) :

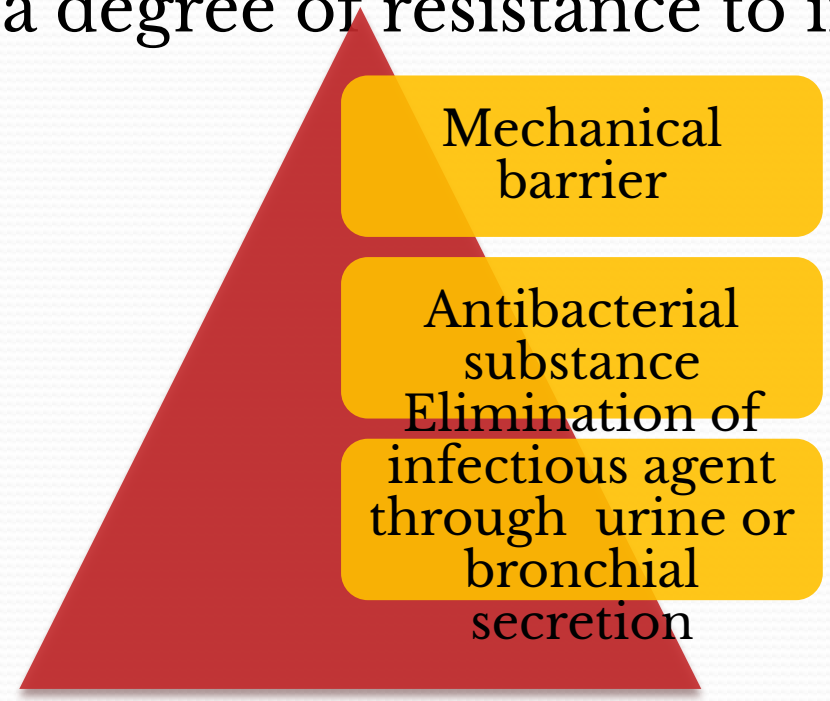
- First line of defense against invasion by microbes.
- Present from birth
- First time a pathogen is encountered
- Does not require prior exposure. System does not distinguish between different pathogens, always gives the same response.
  E.g: Foreign substance entering the skin
- Not modified significantly by repeated exposures.
  Eg: Phagocytosis by leukocytes, natural killer cells, tissue secretion and complement.

Innate immunity

Resistance by virtue of 'genetic' and 'constitutional' make up

a) **Non specific**

indicates a degree of resistance to infections in general



- **Specific**

where resistance to a particular pathogen is

ACQUIRED OR ADAPTIVE IMMUNITY

- Specific
- Resistance that an individual acquires during his life time
- May be weak / absent on first exposure
- Increases with subsequent exposures to same specific pathogen
- Dual system of B and T Lymphocytes

Acquired immunity

- **The resistance that an individual acquires during life.**

A) Active immunity

Resistance develop by an individual as a result of antigenic stimulus .

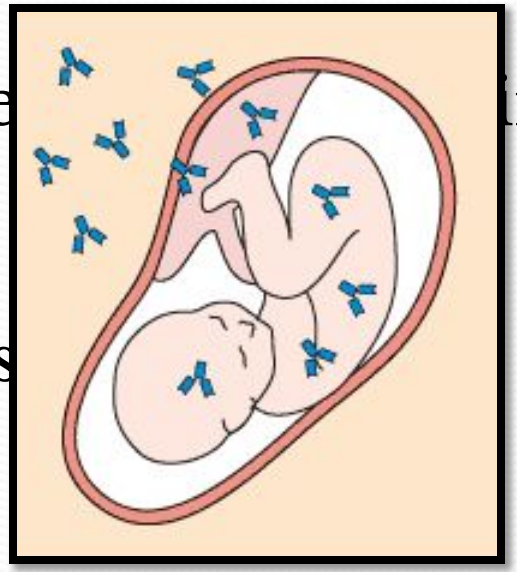
also known as adaptive immunity

B) Passive immunity

The resistance transmitted passive in **READYMADE** form

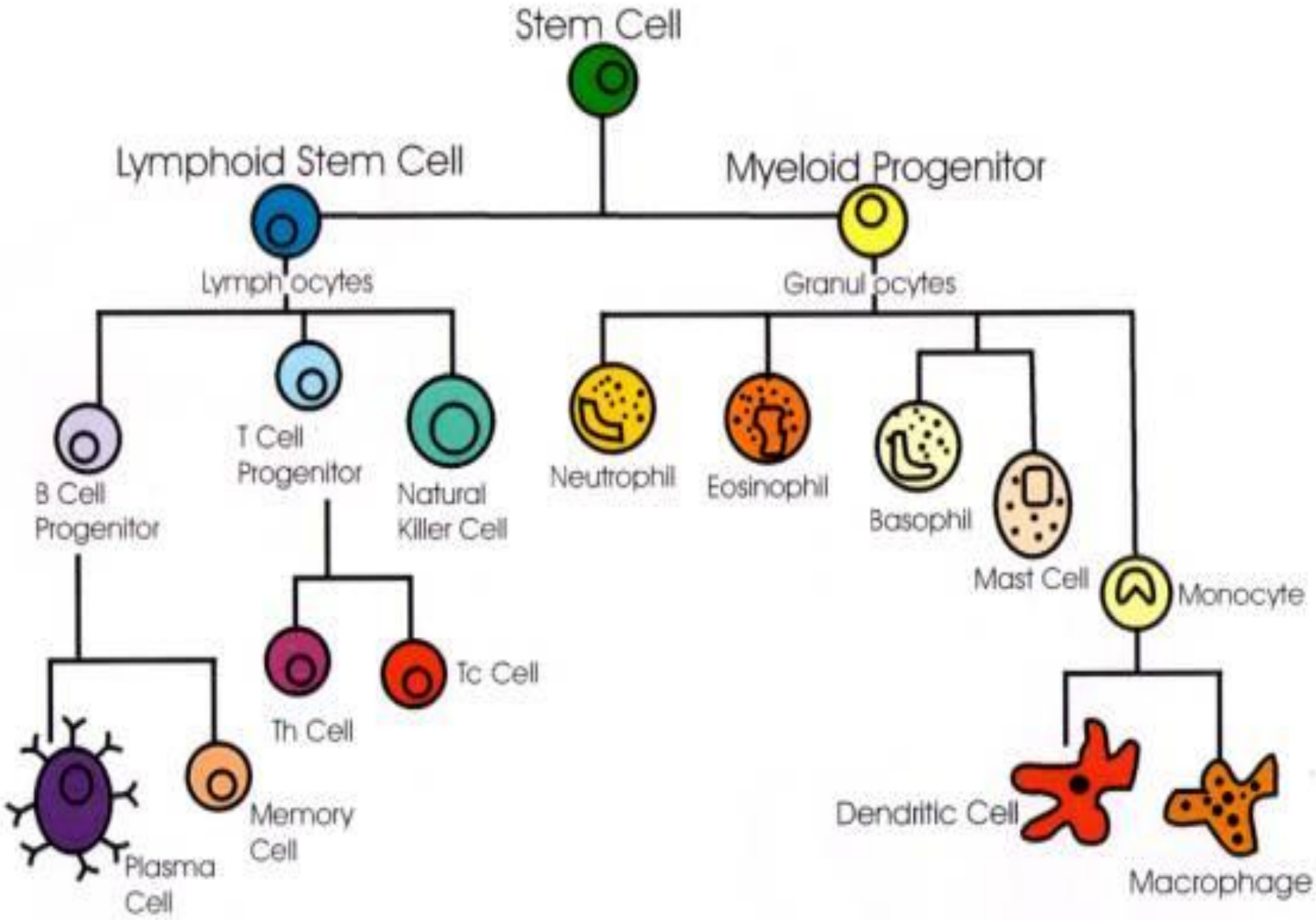
No antigenic stimulus

Preformed antibodies are adminis



CELLS OF THE IMMUNE SYSTEM

Cells of the Immune System



HOST DEFENSE SYSTEM

- FIRST LINE OF DEFENSE:

  Barriers- Physical, Chemical & Genetic.

- SECOND LINE OF DEFENSE

  Inflammation & Phagocytosis

- THIRD LINE OF DEFENSE

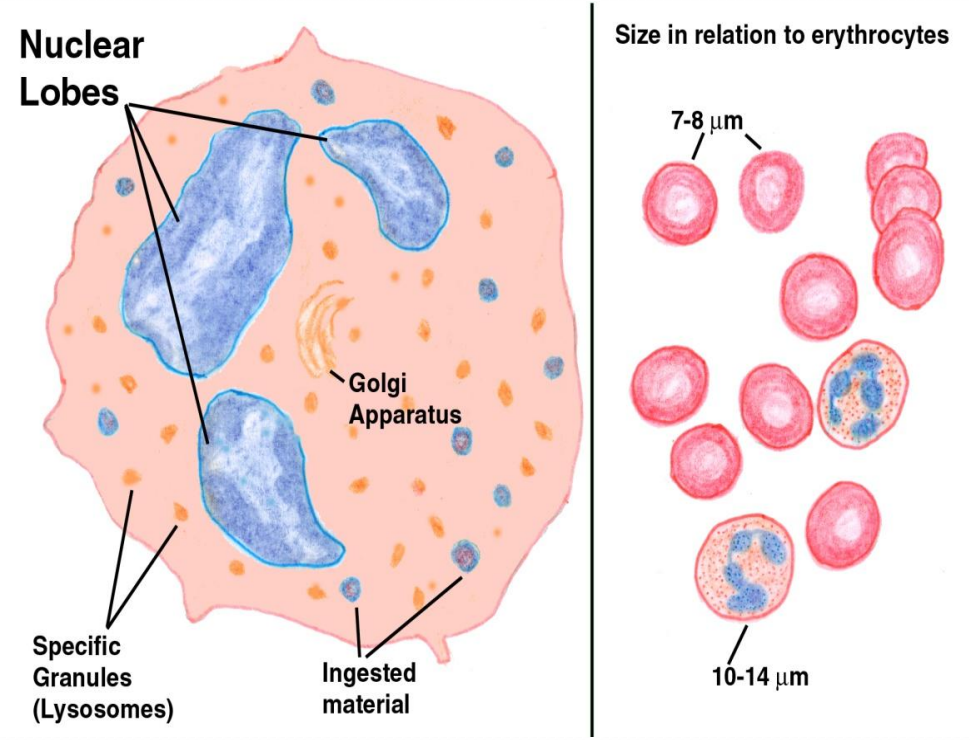
  Cell-mediated Long-term Immunity.

CELLS OF PHAGOCYTOSIS

- **NEUTROPHILS**
- **MACROPHAGES**

NEUTROPHILS (PMNs)

- Considered first line of defense.
- Produced in the bone marrow.
- 55-90 % of circulating WBC
- 4000- 8000 cells/mm^3
- 6-12 hrs in circulation.
- Lifespan of 8 days in tissues

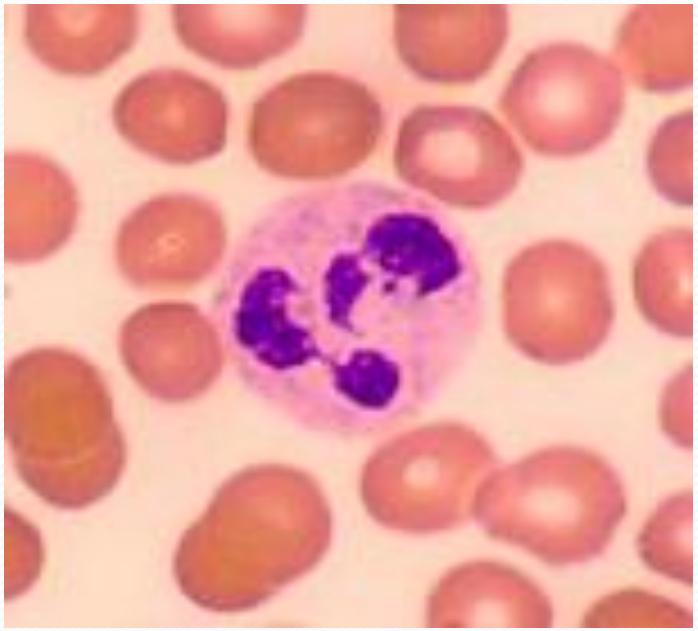


- Newly released cells have a horse-shoe nucleus

- Imp structural components-
  cytoplasmic granules:
  - azurophilic, specific, secretory granules

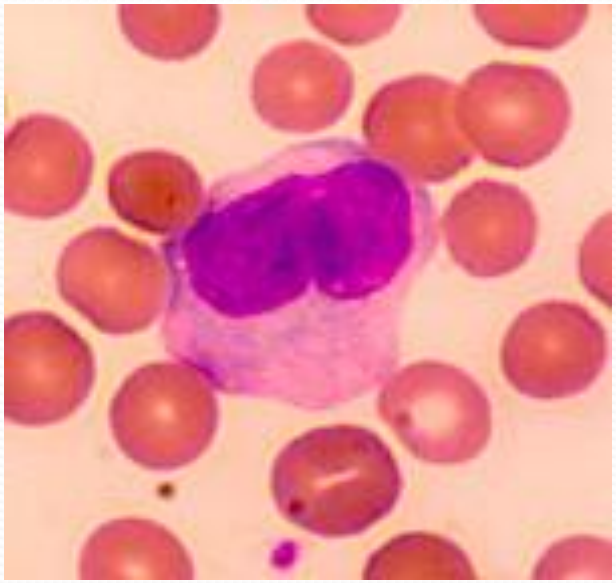
- Cells in inflm'tory lesions

- Chemically attracted to area by chemotaxis, then ingest/ phagocytose & kill the offending agents



MONOCYTES/ MACROPHAGES

- Largest of all WBC's.
- Produced in bone marrow.
- 3 - 7 % of total WBC's.
- Precursor of Macrophage-becomes macrophage within one day of circulation
- Nucleus is oval or kidney-shaped
- Lifespan of 5-16 days



Normal Macrophages includes

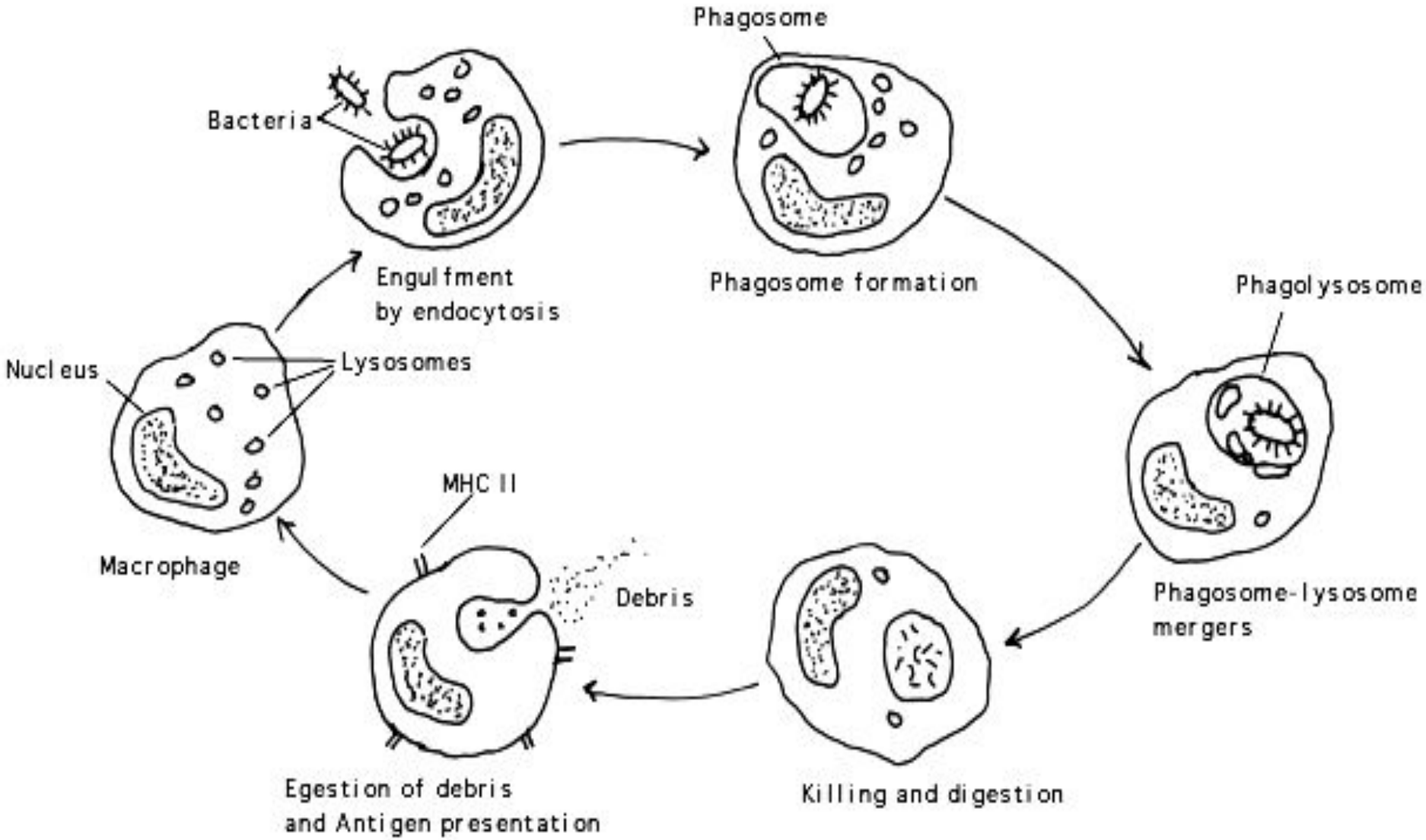
- Connective tissue histiocytes
- Liver Kupffer's cells
- Lung alveolar macrophages
- Lymph nodes free and fixed macrophages
- Spleen splenic macrophages
- Bone marrow fixed macrophages
- Serous fluids pleural and peritoneal macrophages
- Skin histiocytes, Langerhans's cell

Biological Functions of Macrophages

- Most potent nonspecific killer cells (K cells)
- Toxic on dividing extracellular organisms
- Initiate T cell activation by processing and presenting antigen.
- Produce Prostaglandins PGE2 , PGI2 , LT's.
- SRS-A i.e., LTC4 + LTD4 + LTE4.
- Hyaluronidase (spreading factor), elastase, collagenase, and others.

PHAGOCYTOSIS

- Chemotaxis and Ingestion
- Phagolysosome Formation & Killing
- Destructive & Elimination systems



PHAGOCYTOSIS

ANTIGEN PRESENTATION

1. Macrophages engulf the antigen (Ag)
2. Antigen processing (partial degradation of the Ag to expose the epitope)
3. RE-excretion on its surface + Appropriate MHC class
4. To present the Ag to T cell….stimulation of T cell

- If T4…..MHC class I
- If T8…..MHC class II

LYMPHOCYTES

- ***T cells***
- From thymus
- 80 % of circulating
- lymphs in blood
- Long –lived
- TCR (T cell receptor)

- ***B cells***
- Bursa of fabricius *(in birds)*
- 20 % of circulating
- lymphs
- Ig receptor on its surface

- **Natural killer cells**
- Don’t require prior sensitization
- Capable of killing tumor cells, virus infected & other cells

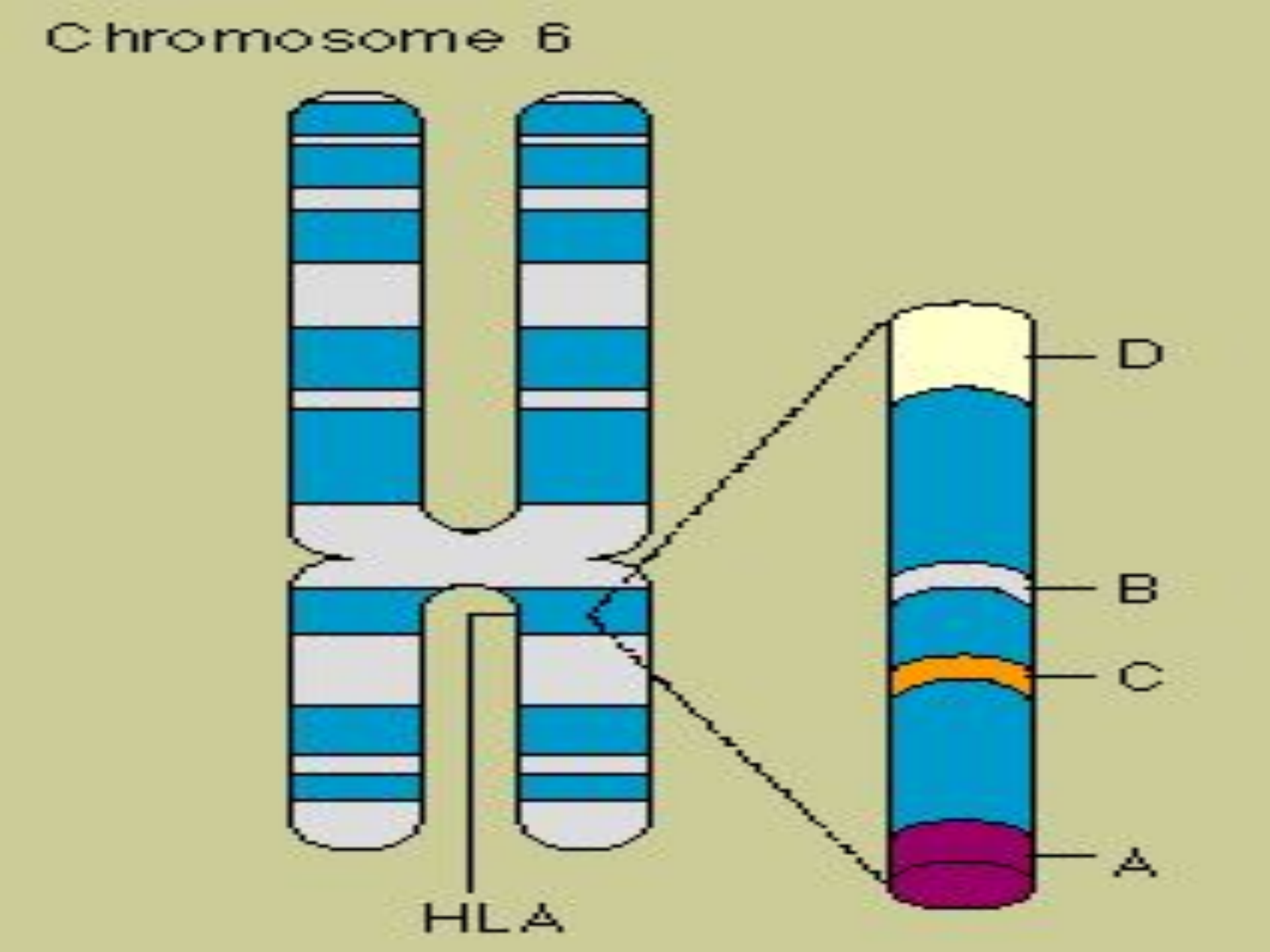
T CELLS

- ***T helper cells***
- T4 / TH
- CD4 + ve
- MHC II restricted

- ***T suppressor /cytotoxic cells***
- T8
- CD8 + ve
- MHC I restricted

Major Histocompatibility Complex (MHC)

- Play role in intercellular recognition and in descrimination of self and nonself.
- T cells can recognize antigen only when it is combined with an MHC molecule
- The MHC is a collection of genes arrayed within a long continuous stretch of DNA on chromosome 6
- MHC is called HLA Complex in Humans


Chromosome 6
D
B
C
A
HLA

ANTIGEN

- An antigen has been defined as any substance which, when introduced parenterally into the body, stimulates the production of antibody with which it reacts specifically and in an observable manner

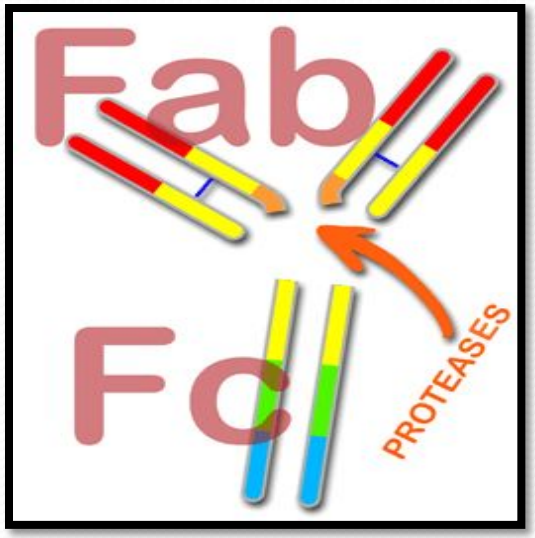
- The word **'specifically'** in the definition is important as specificity is the hallmark of all immunological reactions.
- An antigen introduced into the body reacts only with those particular immunocytes (B or T lymphocytes) which carry the specific marker for that antigen & which produce an antibody or cell complementary to that antigen

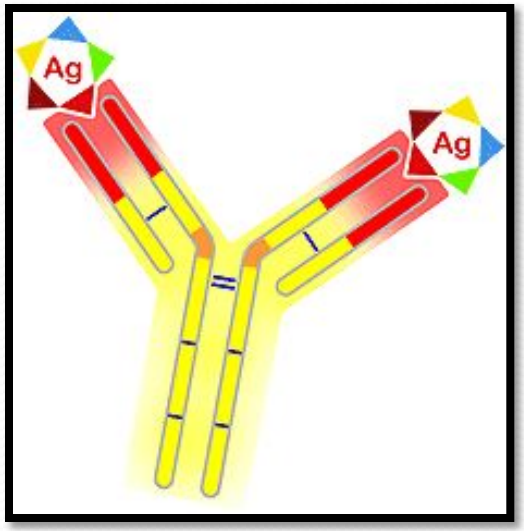
ANTIBODY

- Antibodies are globulin proteins (immunoglobulin's) that react specifically with the antigen that stimulated their production
- Found in blood, tissue fluids and secretions and are the effectors of humoral immunity.
- They are highly specific and sensitive
- The host responds to oral bacteria and their products by plasma cell production of immunoglobulins or antibodies
- All classes and subsets of immunoglobulins have similar structural organizations.

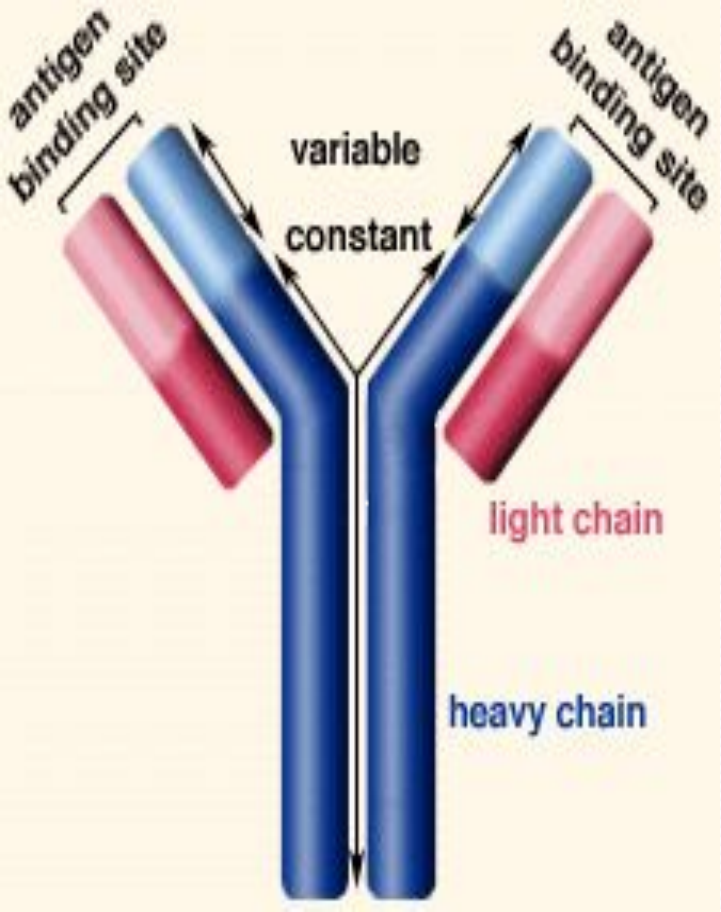
IMMUNOGLOBULIN STRUCTURE

- Each molecule of immunoglobulin is split by papain into three parts ,one Fc and two Fab pieces
  - Fab contains antigen binding site.
  - Fc is the region that determine biological properties of the Ig.

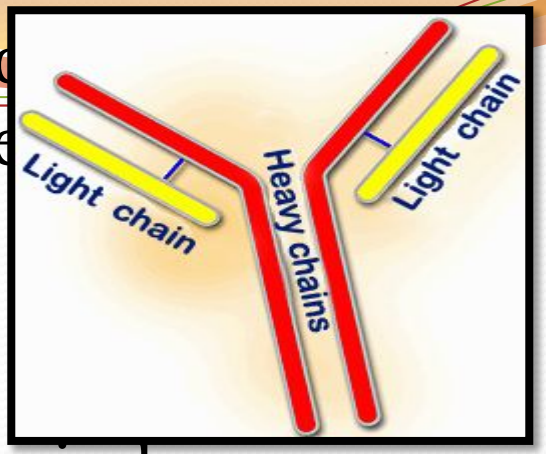




- All the immunoglobulin constant region domains (C) maintain a similar basic structure.
- The variable region domains (V) have a slightly different structure.
- Fab is the antigen binding region of the variable region.
- The polypeptide strand connecting the V and C domains is called the hinge .
- The Fc fragment bears the effector functions of the immunoglobulin molecule.
- Every antibody molecule has a variable region which, allows it to react highly specifically with a particular antigen

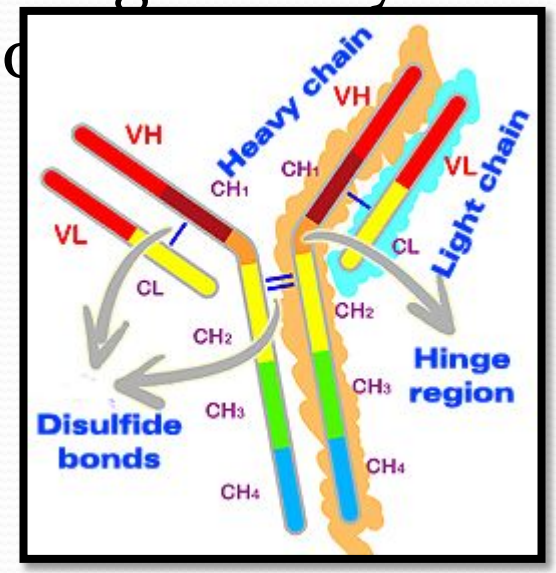


Ig are glycoproteins ,each molecule c
pairs of polypeptide chains of differe
Light chain ….smaller
Heavy chain ….larger



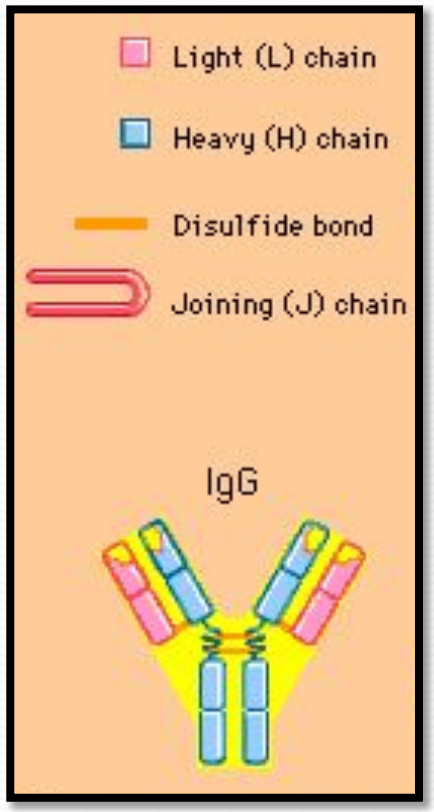
- The L chain is attached to the H chain by a disulphide bonds
- The H chains are structurally and antigenically distinct for each class and designated letter corresponding to the Ig class

IgG …… gamma
IgA ….. Alpha
IgM …..mu
IgD ….delta
IgE…epsilon



IgG

- Most abundant of the immunoglobulinsn in serum -80%
- 154 kd mol wt
- Longest serum half-life of 23days
- Consists of one basic structural unit, i.e. Y-shaped molecule having light chains and Gamma heavy chains.
- 2 antigen binding sites
- Produced in response to a wide variety of antigens, including bacteria, viruses and RBC and WBC
- Four subclasses. IgG1, IgG2, IgG3 and IgG4

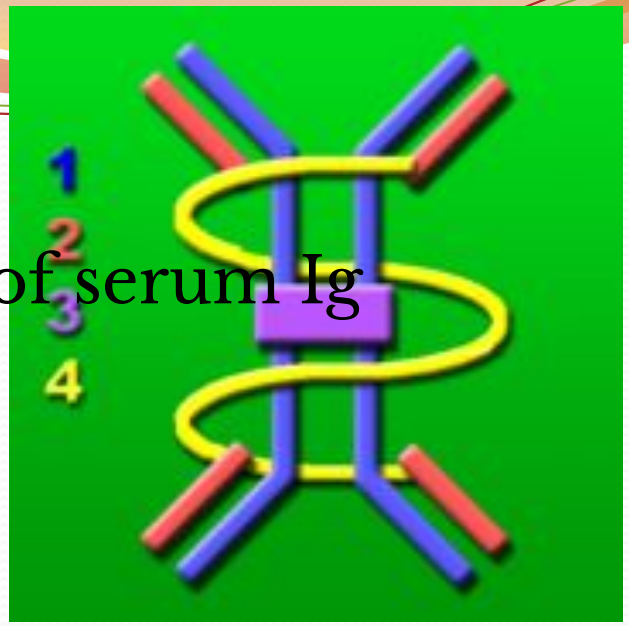


- Through its ***ability to cross the placenta***, maternal IgG provides the major line of defense **against infection for the first few weeks of a baby's life.**
- **It is the predominant antibody produced in the secondary response.**

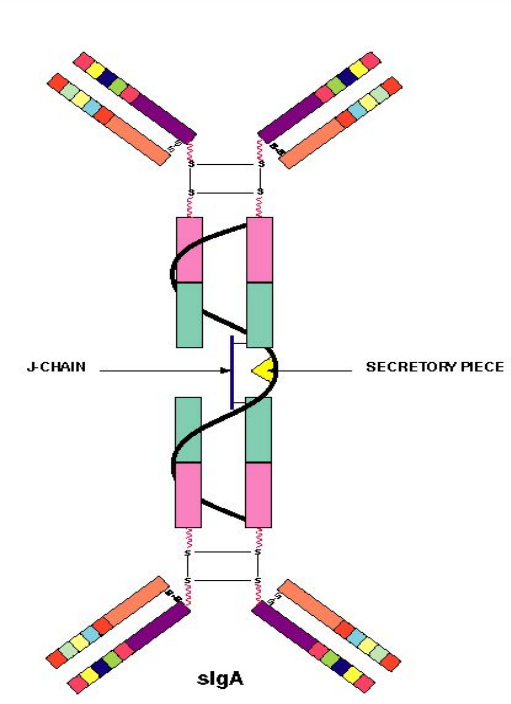
- Functions:

- Acts as opsonin: Coats organisms to enhance phagocytosis by neutrophils and macrophages
- Present on cell surface of B cell
- Fixes complement
- Stimulates chemotaxis

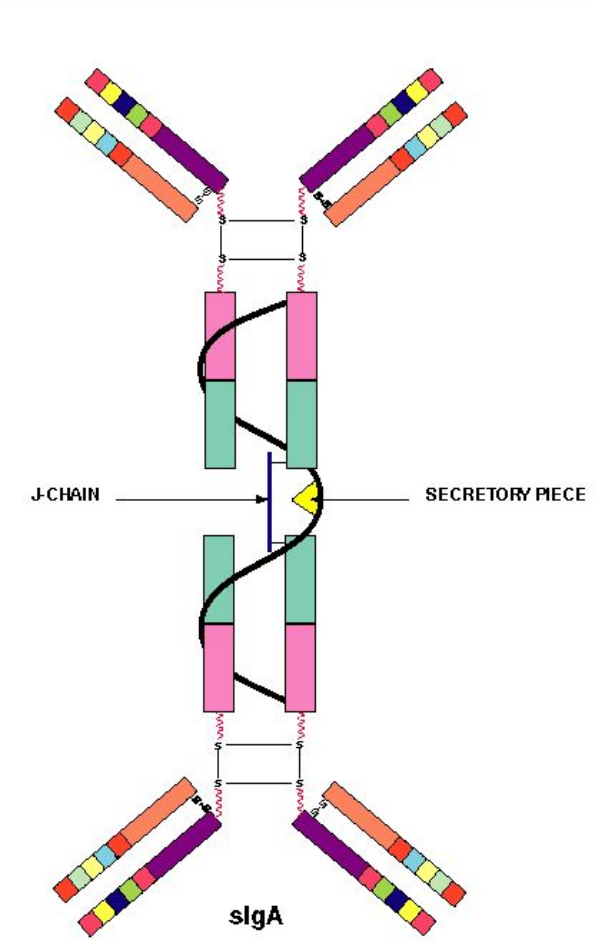
IgA



- Second most abundant ...10-13% of serum Ig
- Serum half life 6-8 days
- 160 kd mol wt
- IgA occur in two form
  -Serum IgA and Secretory IgA
  a single basic structural unit or as
  or three basic units joined togeth
- The dimeric IgA molecule.
  - 1 H-chain,
  - 2 L-chain,
  - 3 J-chain,
  - 4 secretory component
- 2 Subclasses - IgA1 and IgA2



- The IgA present in secretions exists as two basic units (a dimer) attached to another molecule know as **secretory component**.
- **Found in saliva, tears, colostrum and in nasal, bronchial and intestinal secretions**
- Principal site of action is secretions ; promotes release



…IgA

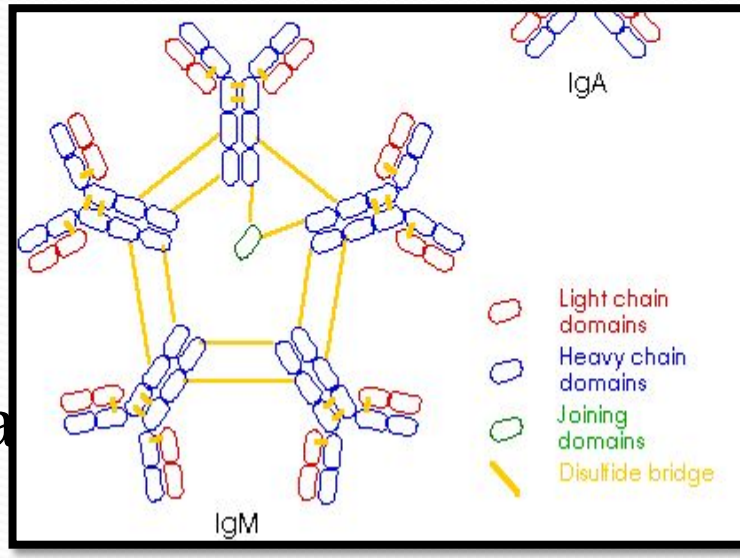
- Plays an important role in protection against respiratory, urinary tract and bowel infections
- Confer important specific local immunity
- **IgA does not cross the placenta**

- **Functions:**

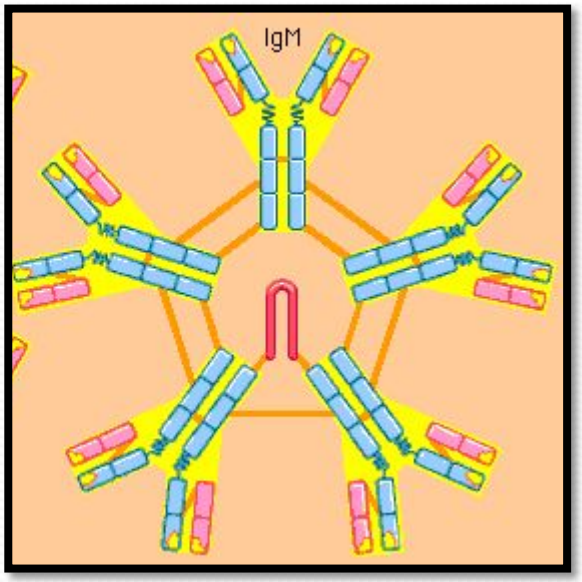
- Aggregated IgA can activate complement via the alternative pathway.

IgM

- **Largest** of all the antibody molecules
- Structure consists of five of the basic units (**pentamer**) joined together by a structure known a **J-chain**.
- Accounts for about 5-10% of the immunoglobulin pool.
- Restricted almost entirely to the intravascular space due to its large size.



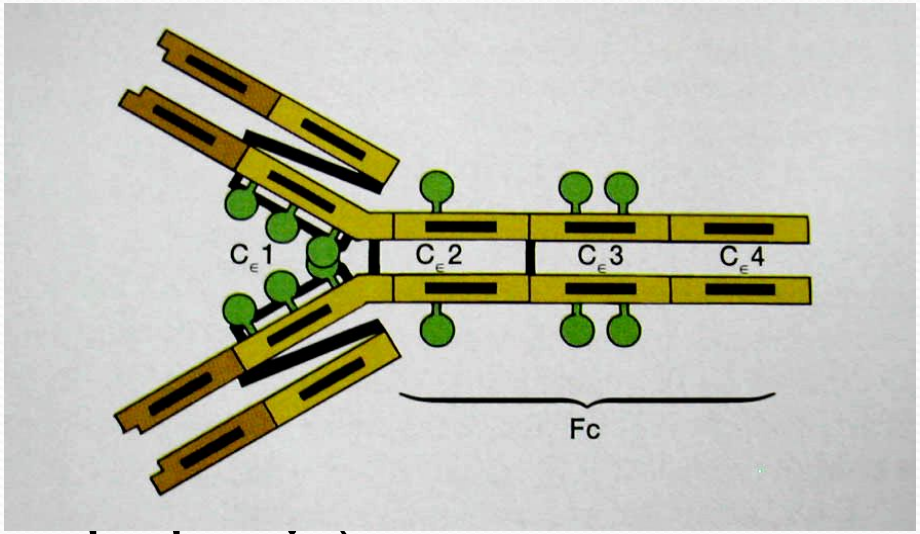
- First antibody to be produced and is of greatest importance in the first few days of a ***primary immune response*** to an infecting organism.
- ***Does not cross the placenta.***
- **Functions:**



- IgM is mot effeicient Ig in *activating complement*
- IgM is 500-1000 times more effective than IgG in opsonisation ,100 times more effective in bactericidal action and about 20

IgE

- 190 kd mol wt
- 2 antigen binding sites
- < 1% -total Immunoglobulin
- Serum half-life 2-3 days



- **Functions:**
  - Mediates immediate (anaphylactic) hypersensitivity
  - It participates in host defence against certain parasites Eg: helminths
- Fc region binds strongly to a receptor on mast cells and basophils and, when antigen is bound it causes the basophil (or mast cell) to release histamines and heparin from these cells, resulting in allergic symptoms.

- Clinical effects of IgE mediated reactions include increased vascular permeability, skin rashes, respiratory tract constriction (wheezing), and increased secretions from epithelium (watery eyes, running nose).
- ***IgE does not fix complement and does not cross the placenta.***

IgD

- Accounts for less than 1% of the total immunoglobulin pool.
- This is primarily a cell membrane immunoglobulin found on the surface of unstimulated B lymphocytes. Functions as an antigen receptor .
- ***Structure is similar to IgG***
- ***IgD does not fix complement and does not cross the placenta.***
- Little is known about the function of this class of

COMPLEMENT SYSTEM

- Set of 20 Serum Proteins
- "Complement " – refers to the ability of these proteins to complement i.e augment , the effects of other components of the immune system Eg: antibody
- Sources- liver hepatocytes, lympocytes and monocytes
- Functions :
  - Lysis of cells – bacteria, allografts & tumor cells
  - Generation of mediators that participate in inflm & attract neutrophils
  - Opsonisation

- C factors numbered C1-C9 in order of their discovery
- Complement components are proenzymes- cleaved to form active enzymes
- Activation by Ag-Ab complexes or by variety of non immunologic molecules eg: endotoxin
- Acts by CLASSICAL OR ALTERNATIVE PATHWAY
- Alternate pathway is more imp the 1st time we get infected

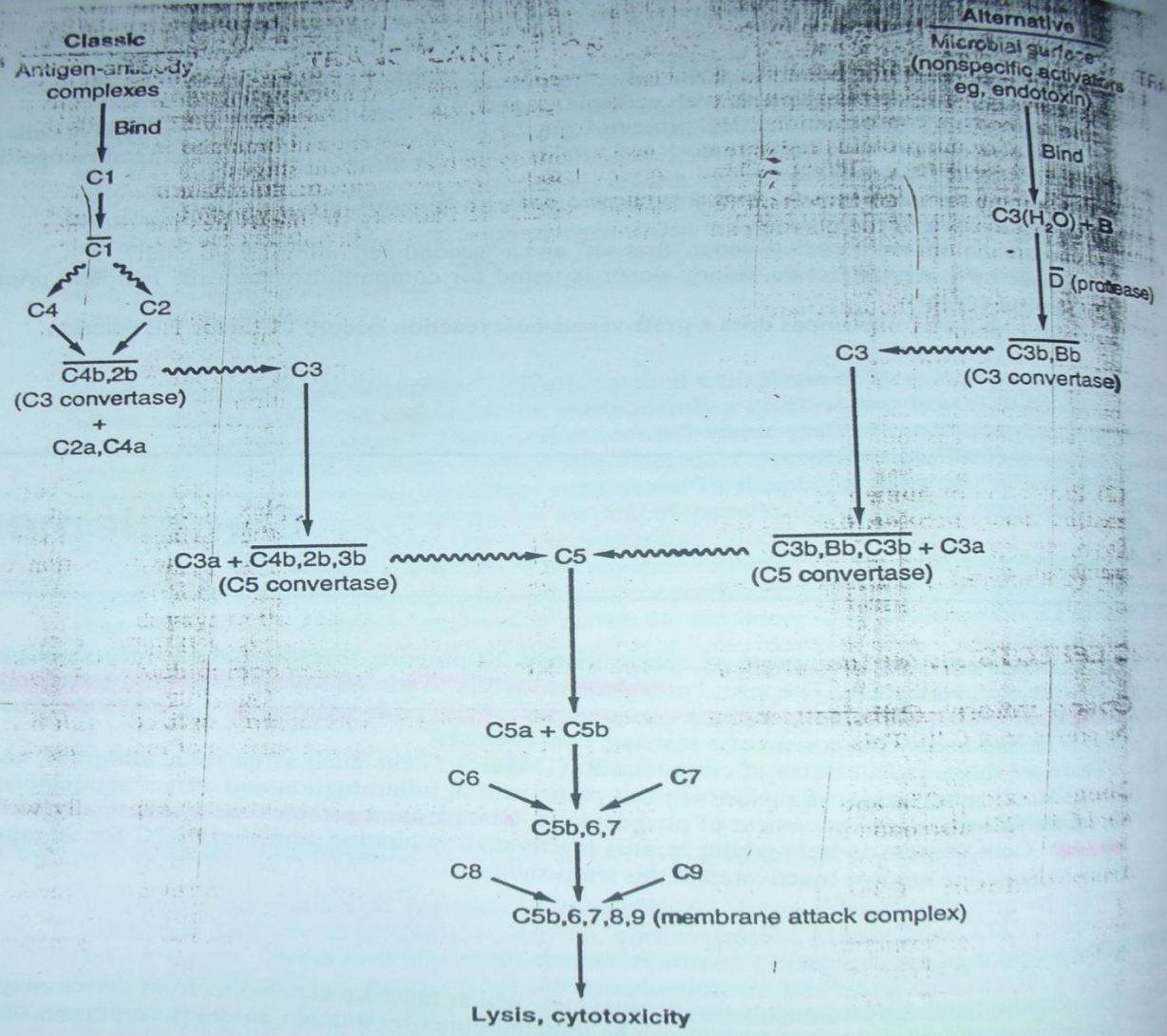


Figure 63–1. The classic and alternative pathways of the complement system. ⇝ indicates that proteolytic cleavage of the molecule at the tip of the arrow has occurred; a line over a complex indicates that it is enzymatically active.

IMMUNE REACTIONS / RESPONSES

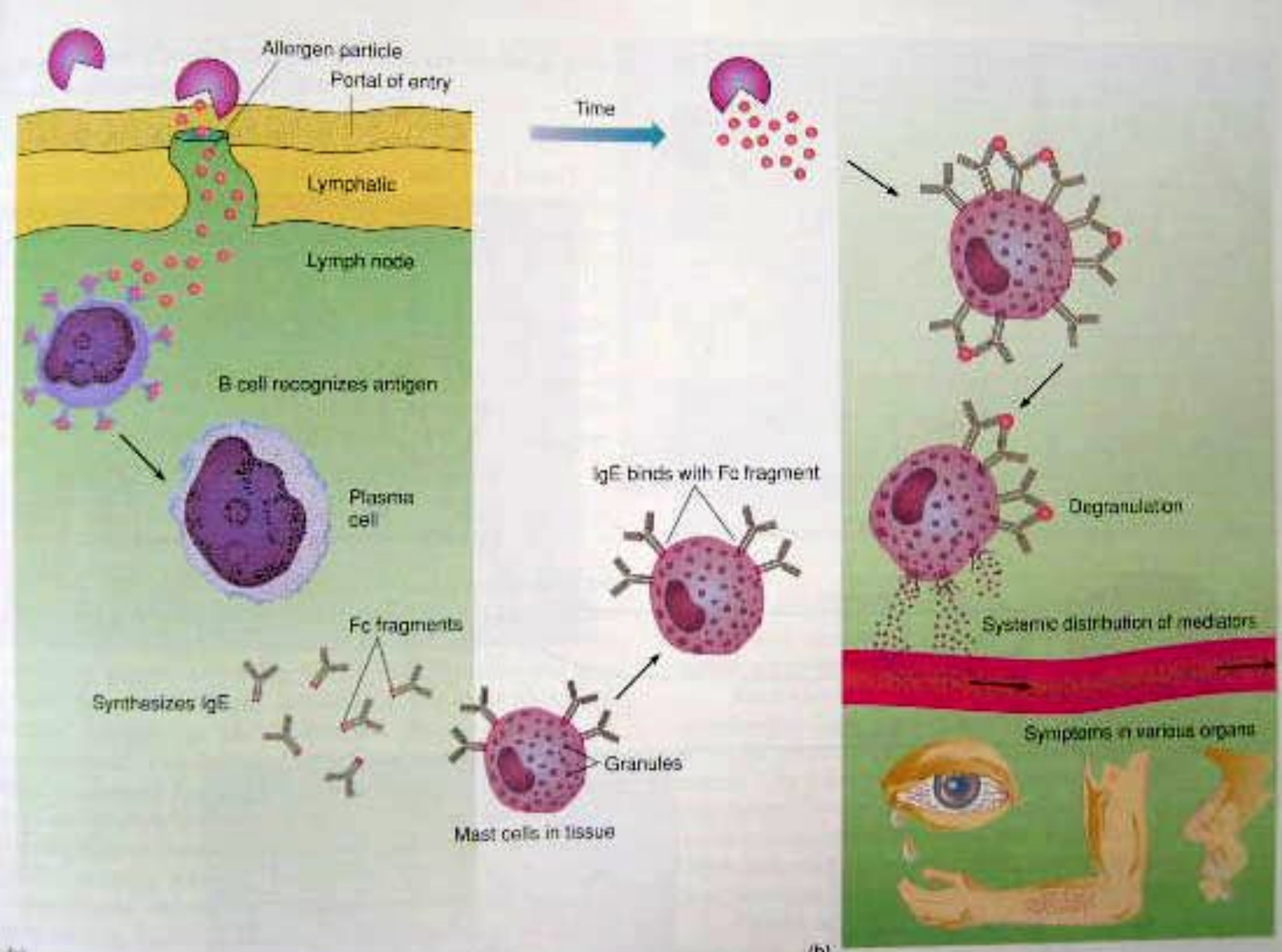
- Hypersensitivity: An immune response resulting in exaggerated/ inappropriate reactions harmful to the host
- Type 1 hypersensitivity
  - Anaphylaxis, Atopy
- Type 2 hypersensitivity
  - Autoimmune reactions
- Type 3 hypersensitivity
  - Immune Complexes
- Type 4 hypersensitivity
  - Cell-mediated delayed reactions(DTH)

TYPE 1 REACTION (ANAPHYLAXIS)

- IgE-mediated allergies
- IgE helps in defending against parasitic infection
- IgE-mediated reactions can occur within minutes.
- The immediate reaction is caused by Histamine, SRSA-A, ECF-A, Serotonin and PG's.

- IgE binds to Fc receptors on Mast cells and thus becomes the cell surface receptor for allergens.

- Cross-linking of this IgE triggers degranulation of Mast cells


Allergen particle
Portal of entry
Lymphatic
Lymph node
B cell recognizes antigen
Plasma cell
Fc fragments
Synthesizes IgE
Time
IgE binds with Fc fragment
Granules
Mast cells in tissue
Degranulation
Systemic distribution of mediators
Symptoms in various organs
(a)
(b)

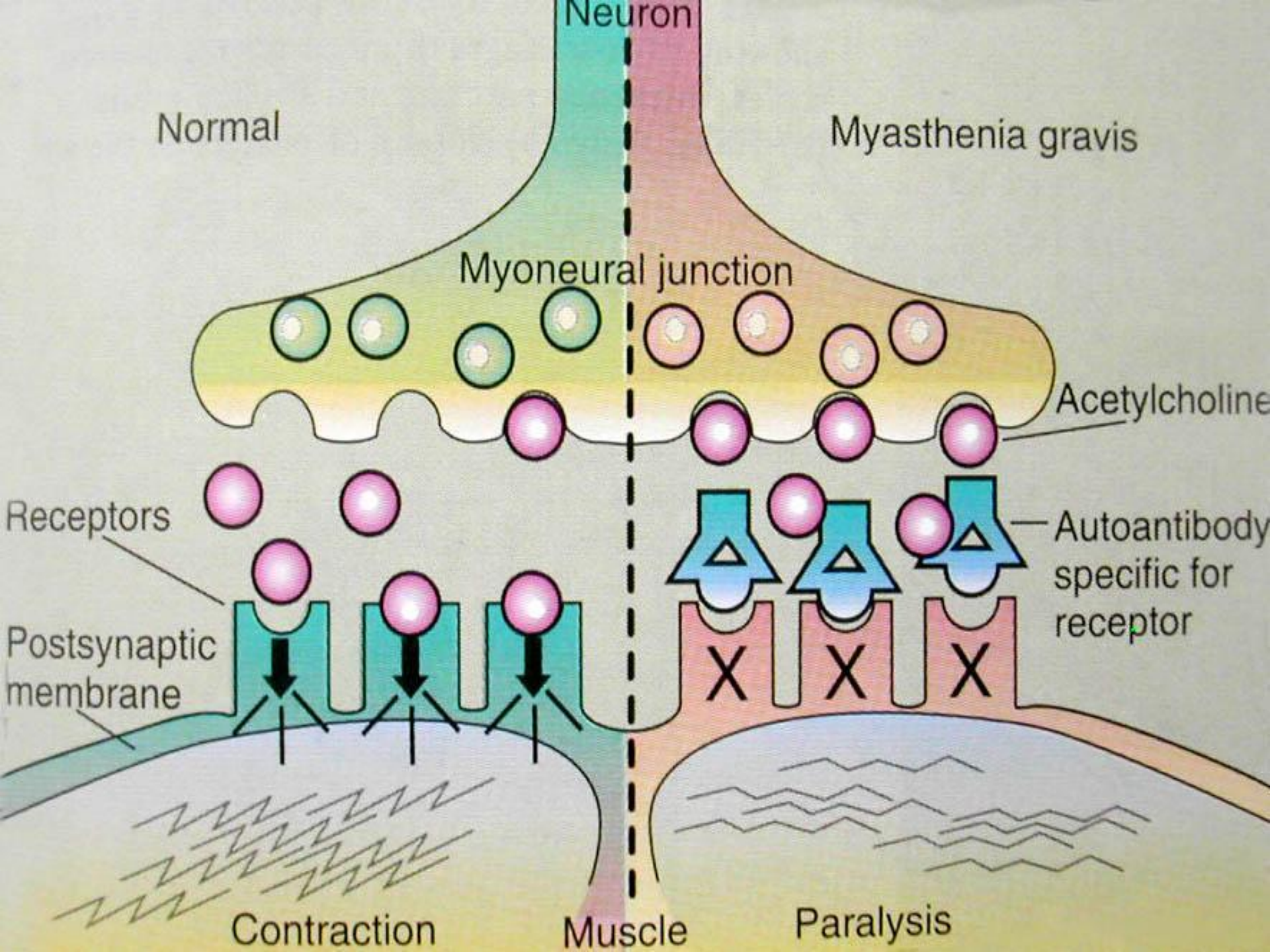
TYPE 2 REACTION (AUTOIMMUNE REACTIONS)

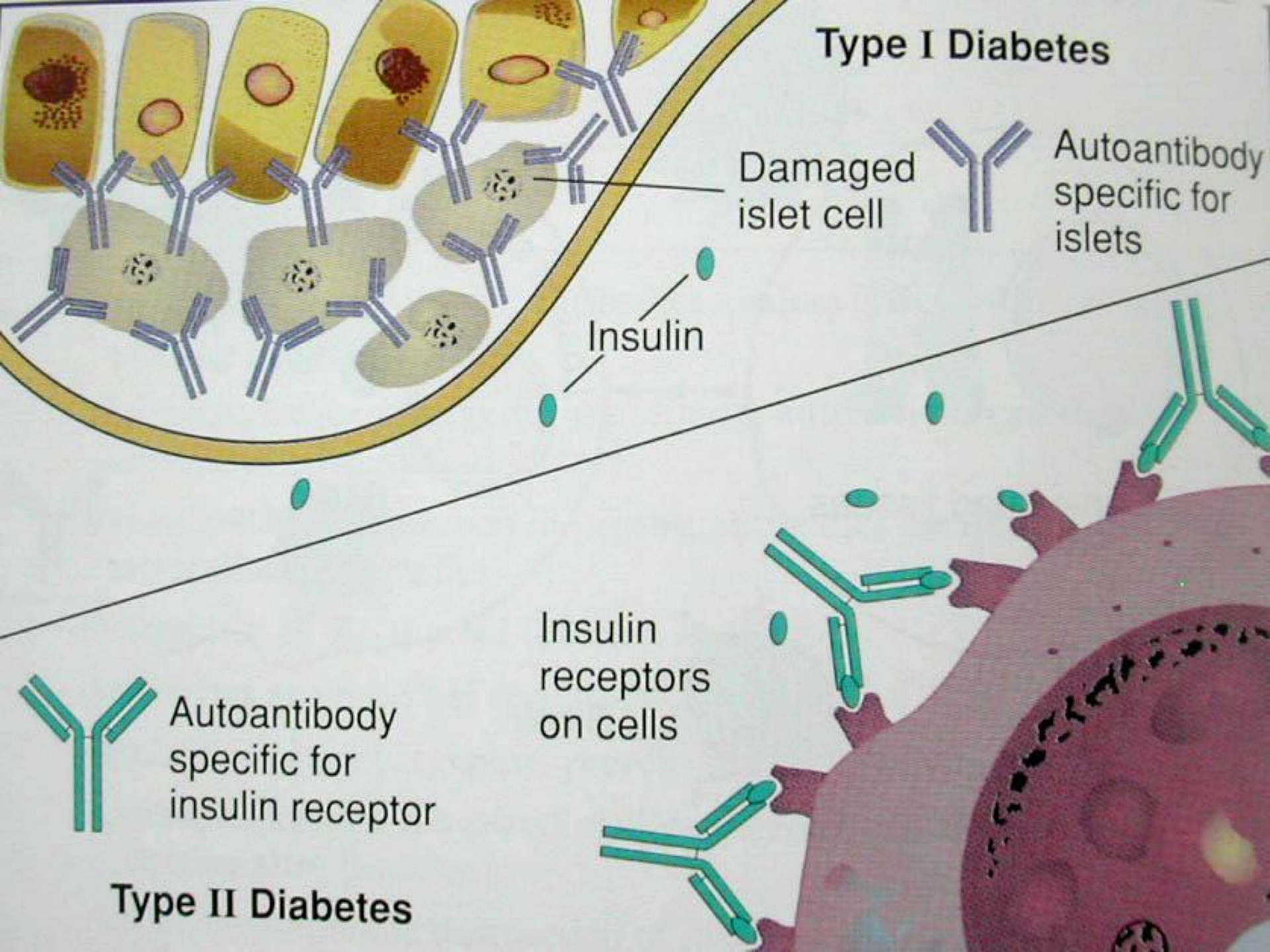
- **Antibody and complement involved**

- Antibody attaches to cell-surface molecules promotes cell lysis either by activating complement or by binding Fc receptors on effector cells.

CLINICAL EXAMPLES

- *Myasthenia gravis*: Ab against Ach receptors
- Type I Diabetes mellitus
- Autoimmune hemolytic anemia
- Rh Incompatibility Reaction.

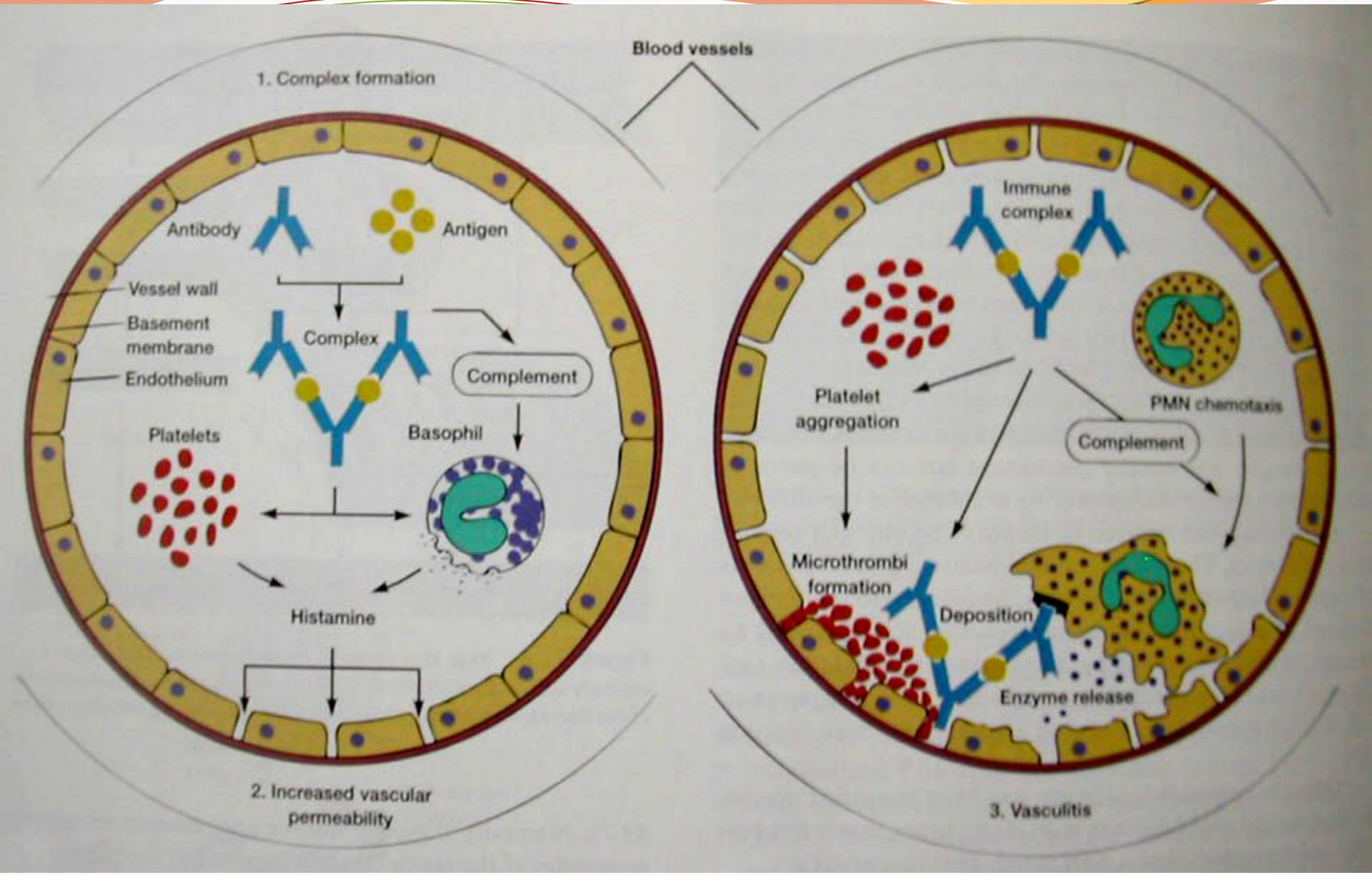

Neuron
Normal
Myasthenia gravis
Myoneural junction
Acetylcholine
Receptors
Autoantibody specific for receptor
Postsynaptic membrane
X
X
X
Contraction
Muscle
Paralysis


Type I Diabetes
Damaged islet cell
Autoantibody specific for islets
Insulin
Insulin receptors on cells
Autoantibody specific for insulin receptor
Type II Diabetes

TYPE 3 REACTION (IMMUNE COMPLEX)

- Immune complexes and complement involved
- Excess soluble antigen in blood binds to antibody, gets trapped in capillaries, especially kidneys and initiates the complement cascade.
- Complement cascade initiates inflammatory reactions.

- Responses occur within **3-6 hrs**.
- Initiators: insect bites; HBV.
- Immune complex diseases
  - **Arthus reaction - skin reaction**
  - **Serum sickness**
  - **Glomerulonephritis**


Blood vessels
1. Complex formation
Antibody
Antigen
Vessel wall
Basement membrane
Endothelium
Complex
Complement
Platelets
Basophil
Histamine
2. Increased vascular permeability
Immune complex
Platelet aggregation
PMN chemotaxis
Complement
Microthrombi formation
Deposition
Enzyme release
3. Vasculitis

TYPE 4 REACTION
(CELL-MEDIATED DELAYED REACTIONS(DTH)

- $CD4^+$ T cell-induced delayed-type hypersensitivity (DTH).
- Essential for controlling fungal infections and intracellular bacteria.
- Examples
  - Contact dermatitis
  - Granulomatous diseases
  - Tuberculin test

HOST MICROBIAL INTERACTIONS

CONTENTS

INTRODUCTION

MICROBIOLOGIC ASPECTS OF HOST-MICROBIAL INTERACTION

- The properties of micro-organisms that enable it to cause disease are referred to as "virulence factors".
- Bacteria must colonize, then destroy. Periodontitis- invasion of bacteria/ bacterial products ⟶ disease

- Virulence properties are categorized into 2 groups:-

1. Factors that enable bacterial species to colonize & invade host tissues
2. Factors that enable bacterial species to cause host tissue damage directly (microbial colonization & proliferation within the tissues) OR indirectly (eliciting the inflammatory response which causes further damage)

MICROBIOLOGIC ASPECTS

- ACTINOBACILLUS ACTINOMYCETEMCOMITANS
- PORPHYROMONAS GINGIVALIS
- FUSOBACTERIUM NUCLEATUM
- TANNERELLA FORSYTHIA
- CAMPYLOBACTER RECTUS
- PREVOTELLA INTERMEDIA

BACTERIAL COLONIZATION & SURVIVAL IN PERIODONTAL REGION

1. BACTERIAL ADHERENCE IN PERIODONTAL ENVIRONMENT

2. HOST TISSUE INVASION

3.BACTERIAL EVASION OF HOST DEFENCE MECHANISM

A) BACTERIAL ADHERENCE IN PERIODONTAL ENVIRONMENT

- Gingival sulcus & Periodontal pocket- GCF
- Bacterial species that colonize must attach to available surfaces to avoid displacement by the fluid flow.
- Therefore adherance – imp virulence factor

- Surfaces available for the attachment are
  i) tooth / root
  ii) tissues
  iii) pre-existing plaque mass.

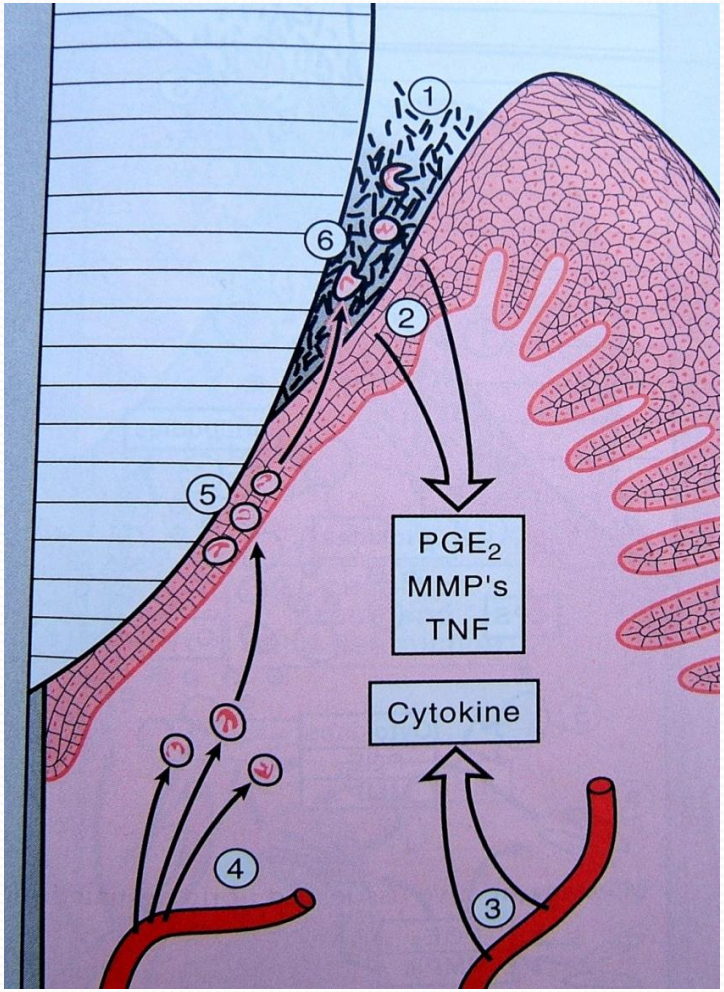
- Bacteria that initially colonize the periodontal environment most likely attach to the pellicle or saliva coated tooth surface.
  Eg: A. viscosus & P.gingivalis – through fimbriae

- Bacterial attachment to pre-existing plaque- adherence between different bacterial strains **(co-aggregation)**
  Eg:- Adherence of A. Viscosus to Streptococcus sanguis.

- Adherence to host tissues- role in colonisazation, critical step in bacterial invasion.

- Ability of *P. Gingivalis* to attach to other bacteria, epithelial cells & connective tissue components like fibrinogen & fibronectin are all likely to be important in the virulence of this micro-organism.

BACTERIAL ACCUMULATION



BACTERIAL ADHESINS & TARGET SUBSTRATES

ATTACHMENT SURFACE	SUBSTRATE	BACTERIA	BACTERIAL ADHESION	SUSTRATE RECEPTOR
1.TOOTH	Saliva coated mineralized surfaces Saliva coated surfaces	A.Viscosus A. Viscosus S. Mitis	Fimbriae Fimbriae	Saliva treated hydroxyapatite Proline- rich proteins
2.TISSUE	Epithelial cells Fibroblasts PMNs CT Components	P. Gingivalis A. Viscosus P. Gingivalis P. intermedia	Fimbriae Surface protein Fimbirae Membrane protein	
3.PRE-EXISTING PLAQUE	S.sanguis A. naeslundii A. israellii	A. Visosus C. ochraceus	Fimbriae Heat sensitive proteins	Repeating heptasaccharide Rhammose, fucose,

B) HOST TISSUE INVASION

- Bacteria may enter host tissues through- ulcerations in epithelium of gingival sulcus / pocket. Another means- direct penetration of bacteria into host epithelial or CT cells.

- Tissue invasive organisms- A.a, P.g, F.nucleatum, T.denticola.

- Clinical significance: Ability to invade tissues is strongly associated with disease & is proposed as the key factor that distinguishes pathogenic from non pathogenic species.

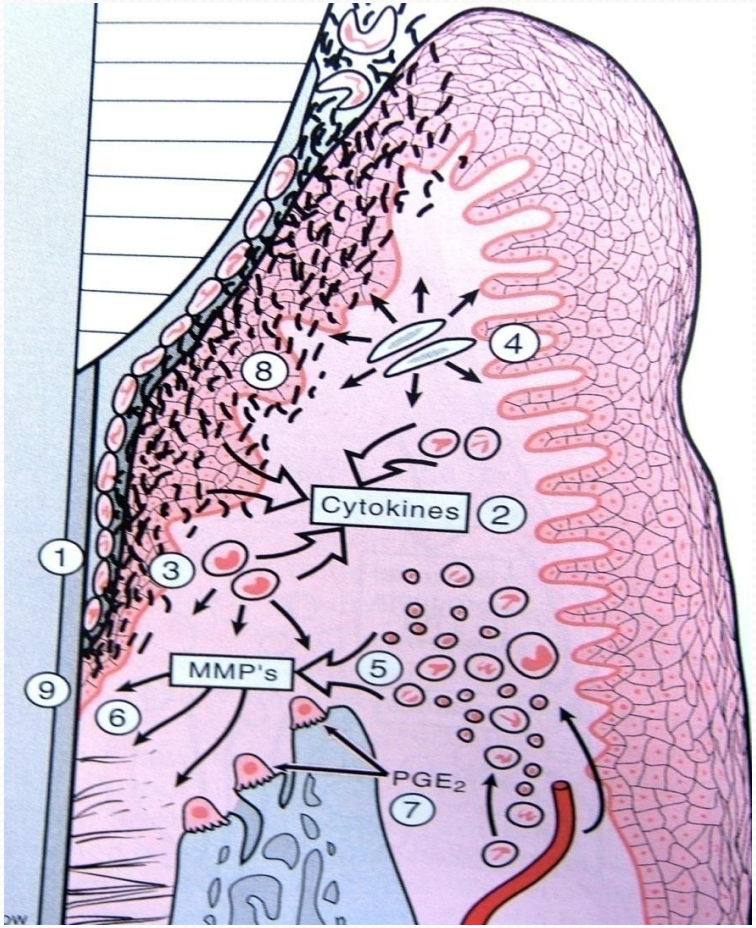
- Localization of bacteria to tissues- provides ideal position to effectively deliver toxic molecules & enzymes to host tissue cells. Thus invasion is an imp virulence factor.

- **"Burst of disease activity"** observed in periodontitis may be related to phases of bacterial invasion of tissues.

- Bacteria in the tissues may enable persistence of that species in the periodontal pocket- provide reservoir for recolonization.

- Eg: Mechanical debridement alone is insufficient & that systemic antibiotics in combination with surgical therapy is required to eliminate A. actinomycetemcomitans *from* lesions with Localized Aggressive Periodontitis (LAP)

TISSUE DESTRUCTION



C) BACTERIAL EVASION OF HOST DEFENSE MECHANISM:

- To survive in periodontal environment, bacteria must neutralize or evade the host mechanisms involved in bacterial clearance & killing.
- The ability to adhere allows bacteria to avoid displacement by host secretions, and eukaryotic cell invasion disrupts the natural barriers formed by host tissue cells.

- Bacterial adherence & invasion- mechanisms

  Eg: Immunoglobulin function- facilitate phagocytosis by opsonization or may block adherence by binding to bacterial cell surface & restricting access to bacterial adhesions.

  So, production of immunoglobulin degrading proteases by specific micro-organisms may counteract these host defences.

BACTERIAL PROPERTIES INVOLVED IN HOST DEFENCE EVASION

HOST DEFENCE	BACTERIA	BACTERIAL PROPERTY	BIOLOGIC EFFECTS
1. SPECIFIC ANTIBODIES	P. Gingivalis P. Intermedia Capnocytophaga	IgA & IgG DEGRADING PROTEASES	DEGRADATION OF SPECIFIC ANTIBODY
2.PMNs	A.actinomycetemcomitans F. Nucleatum P. Gingivalis T. denticola	LEUKOTOXIN HEAT SENSITIVE SURFACE PROTEIN CAPSULE INHIBITION OF SUPEROXIDE PRODUCTION	INHIBITION OF PMN FUNCTION APOPTOSIS OF PMN FUNCTION INHIBITION OF PHAGOCYTOSIS DEC BACTERIAL KILLING
3.LYMPHOCYTES	A.actinomycetemcomitans F. Nucleatum T. denticola	LEUKOTOXIN CYTOLETHAL DISTENDING TOXIN SUPRESSION	KILLS MATURE B & T CELLS IMPAIRMENT OF FUNCTION DEC RESPONSE TO Ag & MITOGENS.
4. RELEASE OF IL- 8	P. Gingivalis	INHIBITION OF IL 8 PRODUCTION BY EPITHELIAL CELLS	IMPAIRMENT OF PMN RESPONSE TO BACTERIA

MICROBIAL MECHANISMS OF HOST TISSUE DAMAGE

- Properties of bacteria related to the destruction of host tissues broadly categorized as-

1. Those resulting directly in degradation of host tissues, &
2. Those causing the release of biologic mediators from host tissue cells that lead to host tissue destruction.

- Eg: - Some bacterial products inhibit growth / alter the metabolism of host cells- ammmonia etc

  - Bacterial enzymes

  - Host tissue proteinases- MMPs, elastase

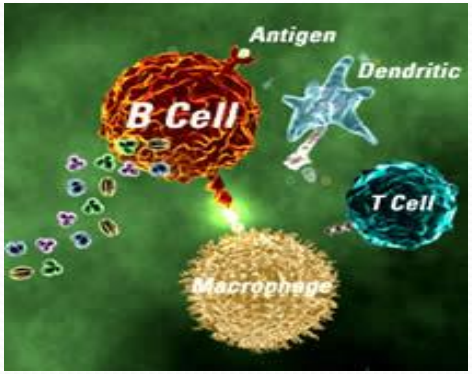
  - Disruption of regulatory molecules- IL 1, TNF- bone resorption.

BACTERIAL ENZYMES CAPABLE OF DEGRADING HOST TISSUE

ENZYME	BACTERIA
1. COLLAGENASE	P.GINGIVALIS
2. TRYPSIN LIKE ENZYME	P.GINGIVALIS
	T.DENTICOLA
3. ARYLSULFATASE	C.RECTUS
4. NEURAMINIDASE	P.GINGIVALIS
	T.FORSYTHIA
	P.MELANINGENICA
5. FIBRONECTIN DEGRADING ENZYME	P.GINGIVALIS
	P.INTERMEDIA
6.PHOSPHOLIPASE A	P.MELANINGENICA
	P.INTERMEDIA

IMMUNOLOGIC CONCEPTS OF HOST MICROBIAL INTERACTION

Paradigm for the role of the immune system in periodontal pathogenesis include:

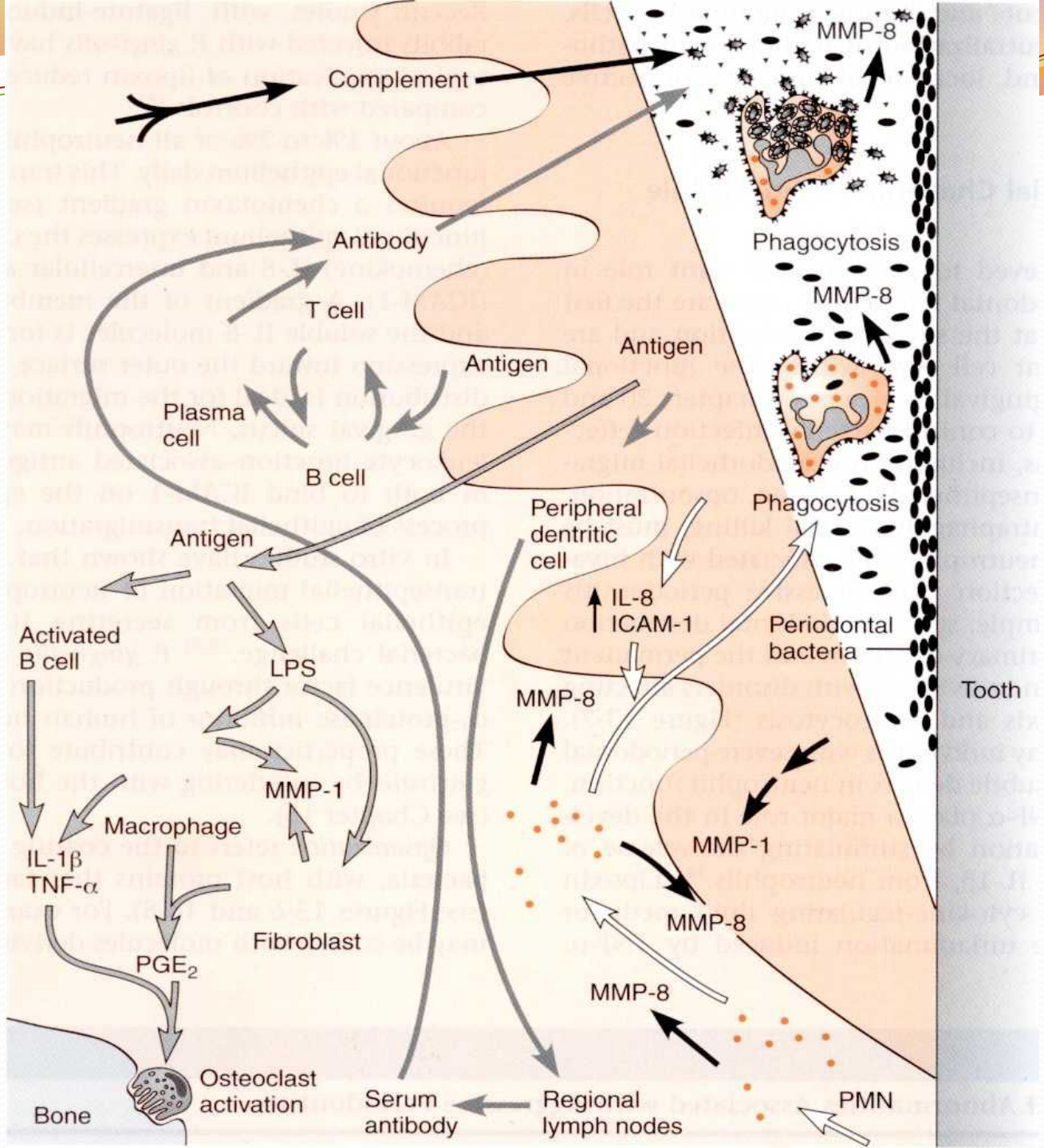


1. Innate factors such as complement, resident leukocytes & especially mast cells play an important role in signalling endothelium, thus initiating inflammation

2. Acute inflammatory cells (i.e. Neutrophils) protect local tissues by controlling the periodontal microbiota gingival crevice & junctional epithelium

3. Chronic inflammatory cells, macrophages & lymphocytes protect the entire host from within the subjacent connective tissue & do all that is necessary to prevent local infection from becoming systemic life threatening, including the sacrifice of local tissues.

HOSTBACTERIALINTERACTION



CONNECTIVE TISSUE ALTERATIONS :TISSUE DESTRUCTION IN PERIODONTITIS

- The fundamental event in transition from gingivitis to periodontitis is loss of attachment & subsequent loss of alveolar bone.

- Mediators of host response that contribute to tissue destruction:
  - PROTEINASES
  - CYTOKINES
  - PROSTAGLANDINS

PROTEINASES

- MMPs are primary proteinases- degrade extracellular matrix molecules such as gelatin, collagen & elastin.
- They are secreted in latent form ; they are activated by proteolytic cleavage of portion of enzyme.
- They are inactivated by α macroglobulin, TIMPs found in serum and GCF also by tetracycline.

CYTOKINES

- Pro inflammatory cytokines such as IL-1, IL-6, TNF have central role in tissue destruction.
- IL in 2 main forms IL-a IL-b which are main constituents of "OSTEOCLAST ACTIVATING FACTORS".
- IL-6 has bone remodeling effect.
- TNF α & β stimulate bone resorption.

PROSTAGLANDINS

- Arachidonic acid metabolites produced by cyclo – oxygenase pathway (COX 1 & 2)

- COX-2 is upregulated by IL1β,TNF α & bacterial LPS for generating the prostaglandin (PGE2) associated with inflammation.

- Primary cells responsible for PGE2, production in the periodontium are macrophages & fibroblasts.

- PGE2 is increased in periodontal sites demonstrating inflammation and attachment loss. In gingivitis & periodontitis, particularly in active disease.

- PGE2 -Induction of MMPs & osteoclastic bone resorption in periodontitis. Thus diagnostic marker.

- NSAIDS- inhibitor of prostaglandin synthesis.

CONNECTIVE TISSUE ALTERATIONS : HEALING PROCESSES IN PERIODONTITIS

- Periodontal "healing" cycle
- Periodontal repair occurs in overlapping phase of inflammation shut down, angiogenesis & fibrogenesis.

POST INFLAMMATORY HEALING PROCESS:

- First shut down of inflammatory processes
- Then, initiation of post inflammatory healing is orchestrated by leukocytes
- Important anti-inflammatory signals generated by leukocytes are IL-1a(macrophages), TGF-b(mast cells), IL-4, IL-10, IL-11.

ANGIOGENESIS & FIBROGENESIS

- Cytokines like IL-1β &TNF-β help induce these processes

- IL-1α & IL-1β - indirectly involved in inducing fibroblast proliferation & collagen synthesis by stimulating production of PGE2 or release of secondary cytokines like PDGF & TGF- β

- PDGF- 5 isoform & produced by numerous cells & tissues including endothelium,vascular smooth muscles & monocytes/ macrophages & induced by anti-inflammatory factors like TGF-β

- TGF- β - stimulates osteoblasts & fibroblasts
  - Inhibit osteoclasts, epithelial cells & immune cells
  - Activation requires acidic conditions

- Other fibrogenic cytokines-

  Basic Fibroblast Growth Factor (bFGF) -produced by endothelium & PDL cells)

  TNF-α (by monocytes)

  TGF-α (by monocytes)

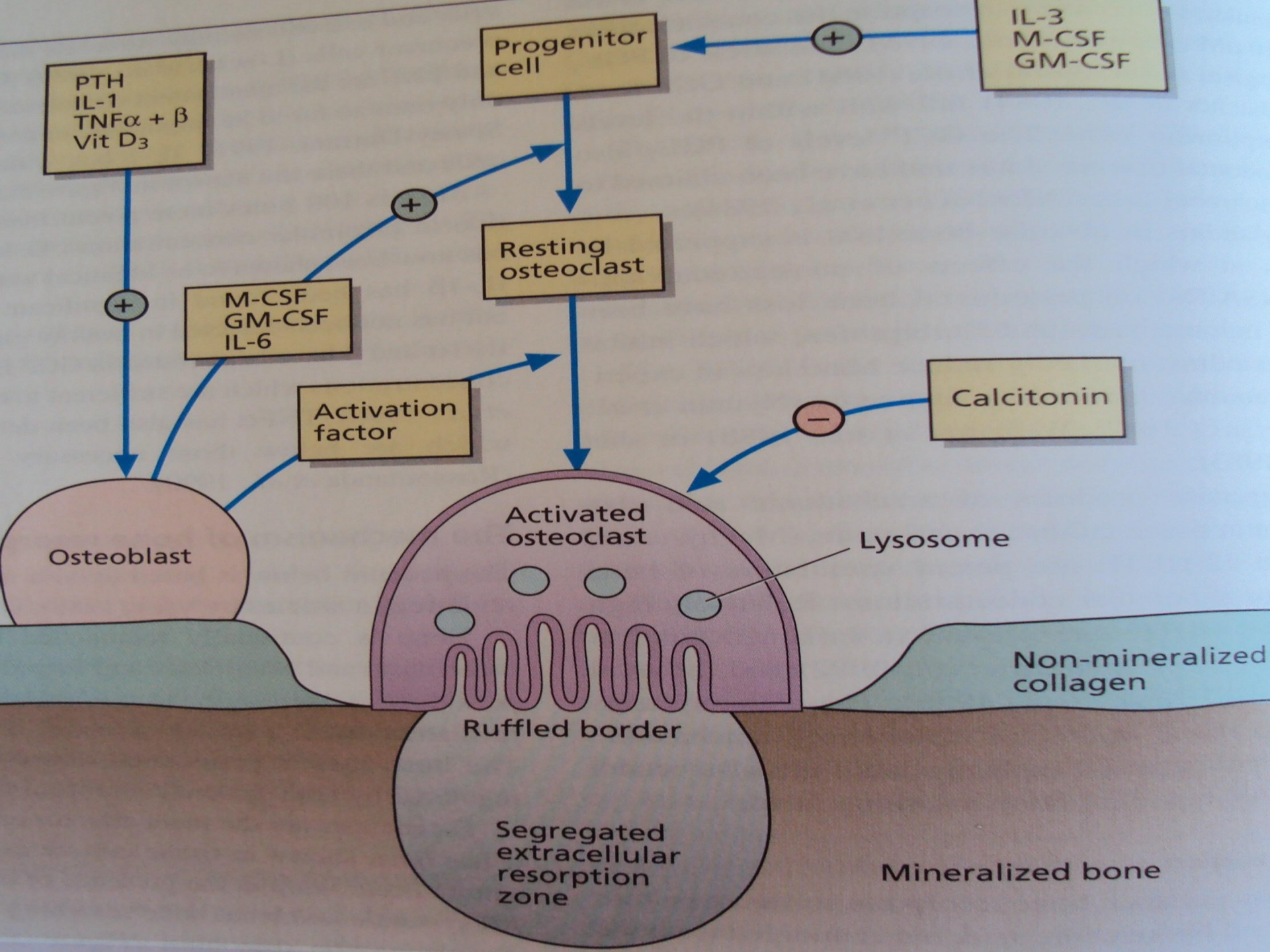
- In healing of alveolar bone, regeneration of bone within the defect occur.
- Immune system can induce regenerative bone healing by preventing osteoclast formation & by activating osteoblasts.

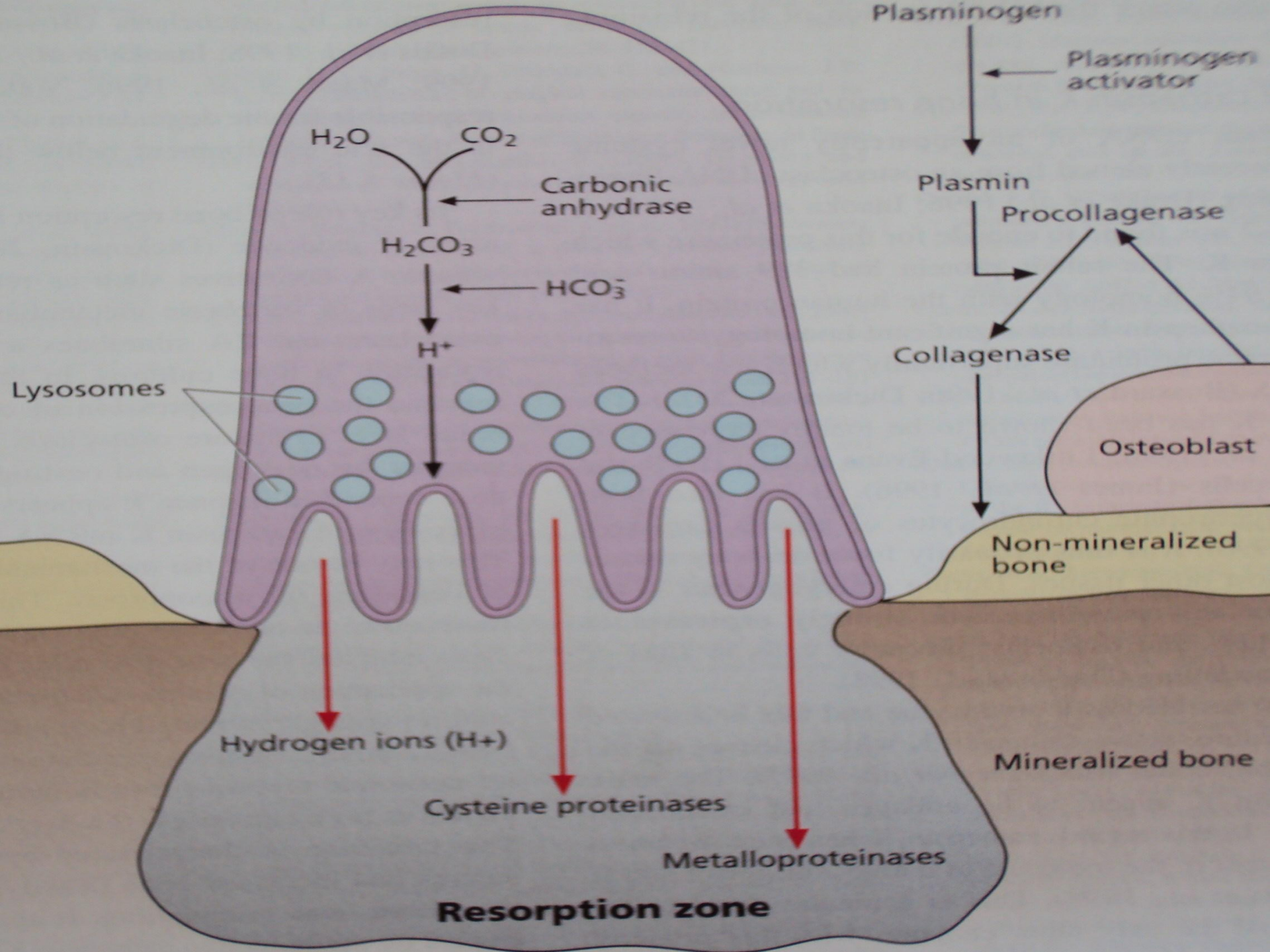
- IFN-γ inhibit osteoclast differentiation produced by natural killer cells, Th-1 T cells & macrophages.
  - It also inhibits IL-1 & TNF- a induced osteoclast activation.

- Insulin like Growth Factor(IGF) & PDGF induce or augment periodontal tissue repair.

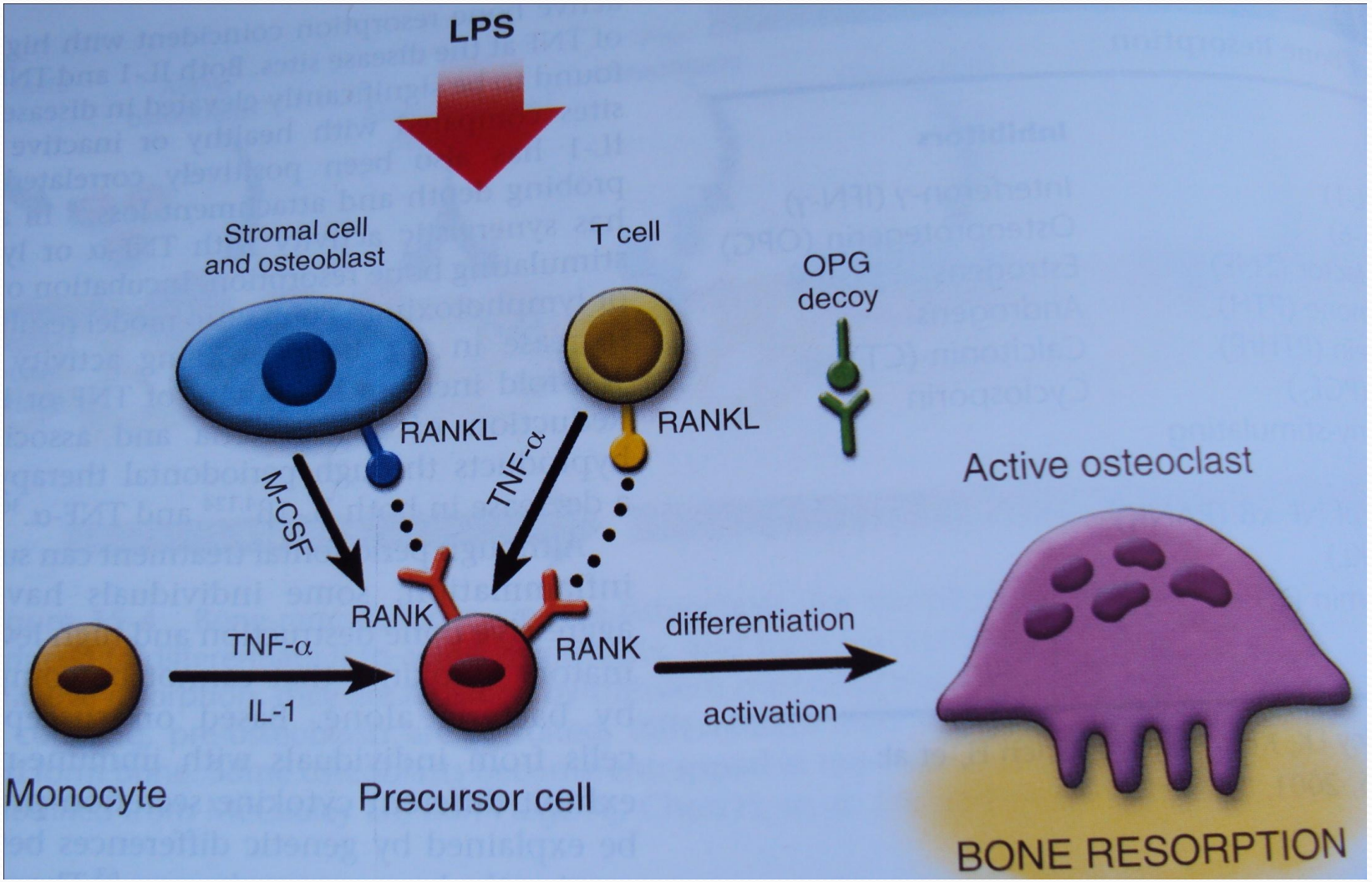
  IGF-1 induce growth, differentiation & synthesis of collagen

PATHOBIOLOGY OF BONE DESTRUCTION

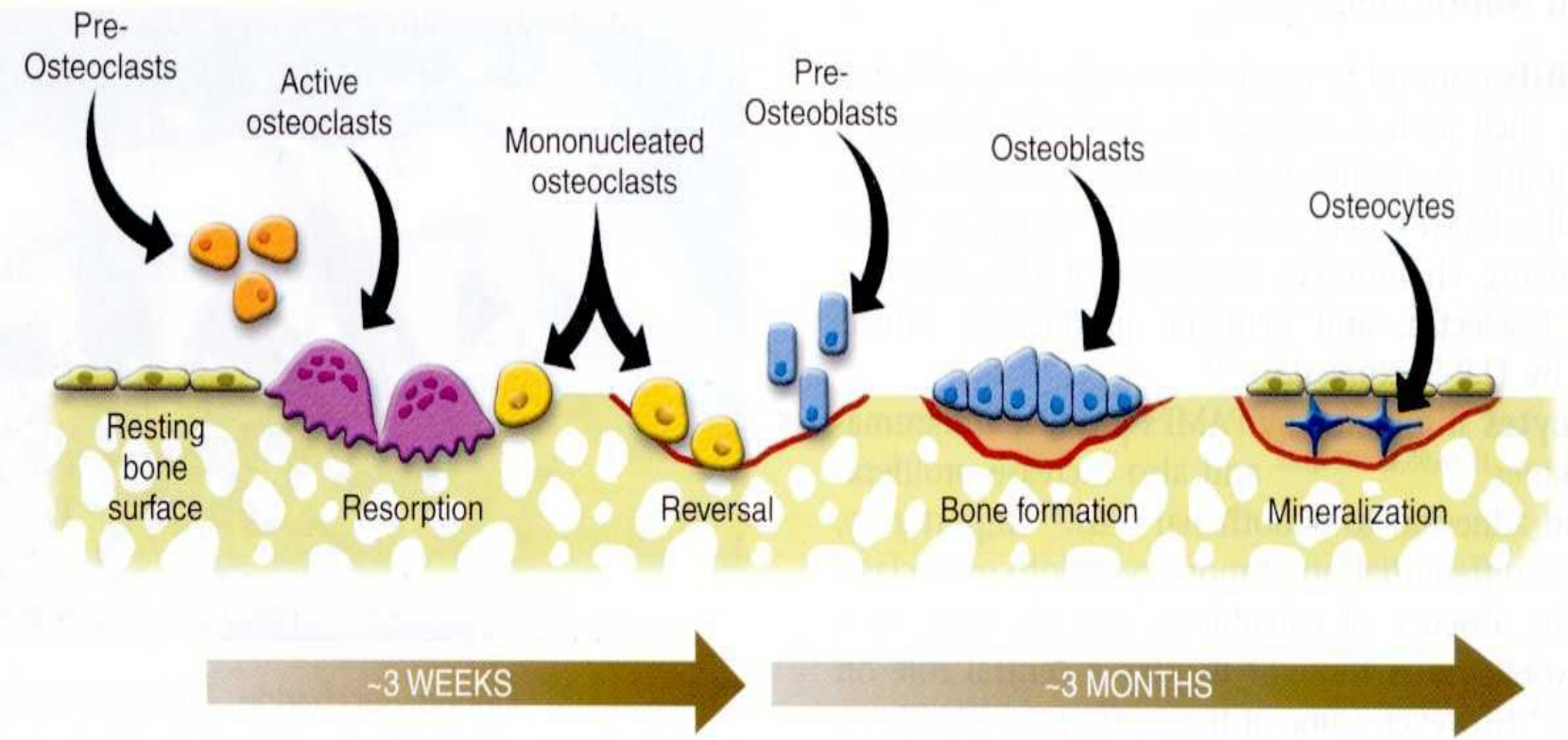

Progenitor cell
IL-3
M-CSF
GM-CSF
PTH
IL-1
TNFα + β
Vit D3
Resting osteoclast
M-CSF
GM-CSF
IL-6
Activation factor
Calcitonin
Osteoblast
Activated osteoclast
Lysosome
Non-mineralized collagen
Ruffled border
Segregated extracellular resorption zone
Mineralized bone


Plasminogen
Plasminogen activator
Plasmin
Procollagenase
Collagenase
Osteoblast
Non-mineralized bone
Mineralized bone
H_2O
CO_2
Carbonic anhydrase
H_2CO_3
HCO_3^-
H^+
Lysosomes
Hydrogen ions (H+)
Cysteine proteinases
Metalloproteinases
Resorption zone

Stimuli Factors Regulating Osteoclast Formation & Function



BONE COUPLING



CONCLUSION

- Pathogenesis of periodontal destruction involves a complex interplay between bacterial pathogens & host tissues. “Not all dental plaque is equal”
- In process of effectively limiting bacterial assault, host defence mechanisms contribute to the destruction of tissues locally
- Not all strains of a specific microbial species are equal in their capacity to cause disease, & not all hosts are equal in their susceptibility to disease

THANK YOU

QUESTIONS

- LONG ESSAY /SHORT ESSAY:

1. Immunity & inflammation
2. Microbial interactions with the host in periodontal disease
3. Molecular biology of host-microbe interaction in periodontal disease

- SHORT ESSAYS:

1. Cytokines?
2. Mast cells in periodontal disease?
3. Role of macrophages in periodontal disease?

- SHORT NOTES:

1. Type I hypersensitivity?
2. Cytokines?
3. Neutrophils?
4. Lymphocytes?
5. Prostaglandins?
6. Lyphokines?