

Classification of Inflammation

- According to duration, inflammation may be peracute, acute, subacute or chronic.

S.N.O.	Properties	Acute inflammation	Chronic inflammation
1.	Duration	Short	Long
2.	Intensity	Severe	Low intensity
3.	Vascular changes	Marked	Less prominent
4.	Exudation	Profuse	Scanty
5.	Consistency	Soft	Firm
6.	Proliferation	No or slight proliferation of connective tissue, blood vessels and epithelium	Proliferation of C.T., Blood vessels and epithelium occurs.
7.	Leucocytes	Neutrophils predominate	Lymphocytes predominate

Acute Inflammation

↓ on the Basis of Exudate

S.N.O.	Type of Inflammation	Type of exudate
1.	Catarrhal or mucous inflam.	Mucus
2.	Serous Inflammation	Plasma
3.	Fibinous "	Fibrin
4.	Suppurative or Purulent "	Pus
5.	Haemorrhagic "	Erythrocyte
6.	Gangrenous "	Necrotic tissue

1. Catechical or Mucous inflammation:

- Principal constituent of the exudate is mucus.

Causes:

- Mild irritants
- Mild irritating chemicals
- Irritating food in the digestive tract
- Cold air, dust
- Bacterial and viral infections

~~Microscopic changes:~~

- There is proliferation of epithelium which is degenerated into exudate.
- Exudate consists of degenerated cells, neutrophils and mucus.
- Mucus stains blue with Haematoxylin.

2. Serous inflammation:

- Principal constituent of the exudate is plasma.

Causes:

- Moderately severe irritants.
- Chemical irritants cause blisters on skin.
- Traumatic injury of rubbing nature
- Second degree burn
- Viral infections such as FMD.

~~Microscopic changes:~~

- It occurs in serous membranes (pericardium, pleura and peritoneum) and in joint spaces.
- Exudate appears as a homogeneous to finely granular material which stains pink with eosin on H&E staining.

3. Fibrinous inflammation:

- Principal constituent of the exudate is fibrin.
- Etiology:
 - viral diseases such as feline enteritis, malignant catarrhal fever
 - bacterial diseases such as salmonellosis, diphtheria
- gross changes:
 - organ is firmer and denser than normal.
 - fibrin is seen as strings, yellowish, net like material on epithelial surfaces.
 - Masses of fibrin on epithelial surface may form

Pseudomembrane
or

Croupous memb.

→ easily peeled away

Diphtheritic memb.

→ firmly attached to underlying tissue

True membrane

False membrane

→ Denuded epithelial cells are present in the mass.

→ epithelial cells not present.

Microscopic changes:

→ fibrin stains dirty pink with eosin.

4. Suppurative or Purulent inflammation:

- Principal constituent of the exudate is pus.
- Etiology:
 - Pyogenic bacteria
 - chemicals - turpentine, zinc chloride, mercuric chloride, croton oil etc.

Microscopic changes:

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→ Neutrophils are mainly present in the exudate.

Definitions in suppurative inflammation:

- a) cellulitis (Phlegmon) → It is diffuse spreading suppurative inflammation of connective tissue.
- b) Abscess → Collection of pus locally within a closed cavity in an organ or tissue.
- c) sinus → It is track in the tissues communicating with an epithelial surface discharging pus from an abscess.
- d) fistula → It is the track that connects two epithelial surfaces: skin and mucous membrane for the discharge of pus from an abscess.
- e) boil or furuncle → small suppurative inflammation of skin which involves hair follicle.
- f) pustule → circumscribed cavity in the epidermis with pus.

5. Haemorrhagic inflammation →

- Principal constituent of exudate is R.B.C. (blood).
- Etiology:

→ Bacterial, viral and protozoal diseases.

gross changes →

- Presence of blood.

Microscopic changes →

- Presence of RBC's

6. Gangrenous inflammation →

- In this type, tissues may become necrotic.

Chronic Inflammation

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Chronic Inflammation is characterized by:

- a) Infiltration by mononuclear cells i.e. lymphocytes, plasma cells and macrophages,
- b) Proliferation of fibroblasts which leads to fibrosis,
- c) Tissue destruction.

Etiology →

Persistence of irritant for a longer duration

→ Granulomatous inflammation is a type of chronic inflammation, characterized by presence of epithelioid cells. These epithelioid cells may fuse together to form Langhans type of giant cells.

Other types of inflammation

1. Allergic inflammation → It occurs when an animal or person previously sensitized to a foreign protein, is injected with the same protein. It causes local inflammatory response as a result of antigen - antibody reaction. There is presence of necrosis due to Ag. - Ab. complex within the cells.
2. Viral inflammation → There is formation of inclusion bodies due to viral infections.
3. Rickettsial inflammation.

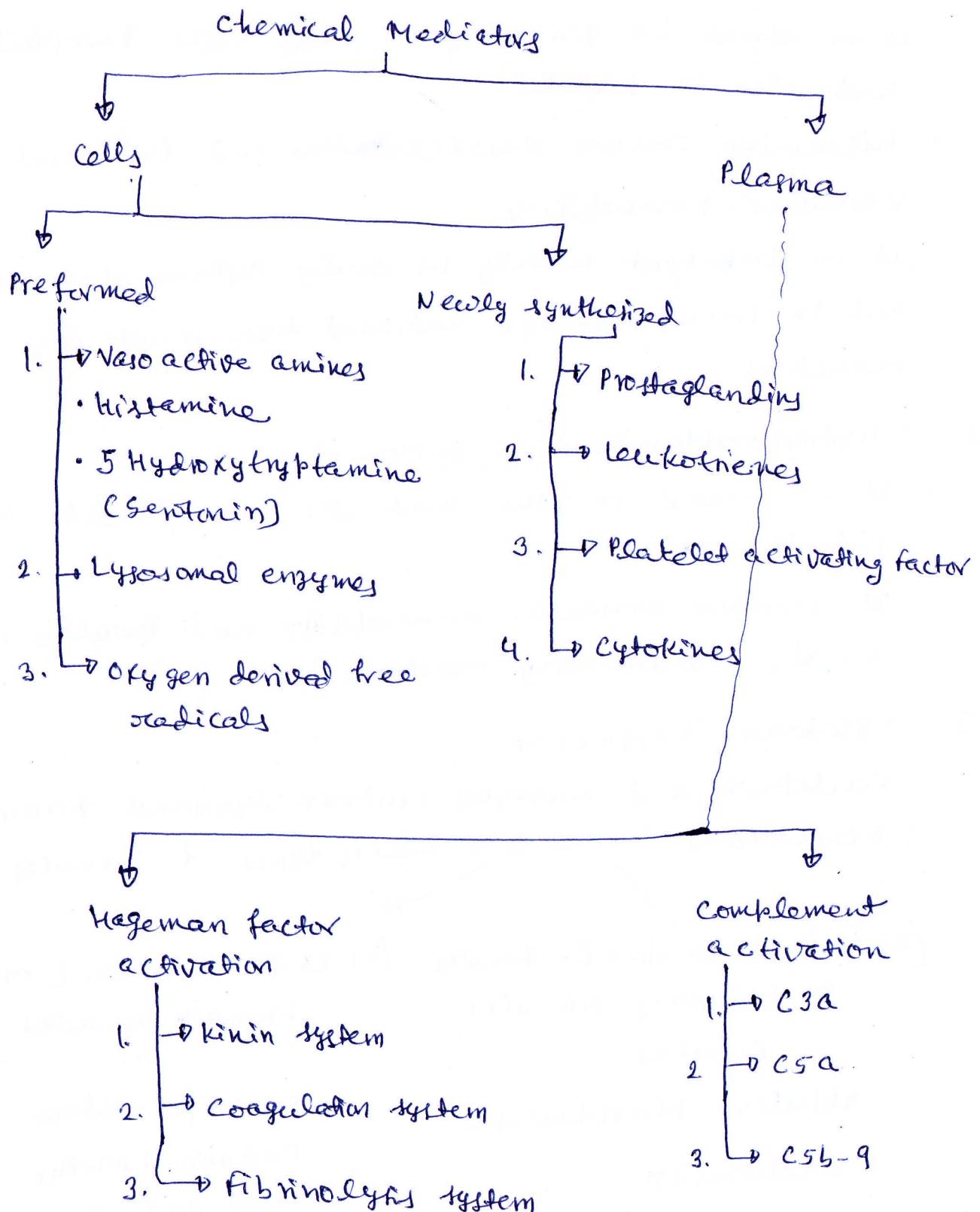
Types of cells in body

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1. The Renewing cell population (labile cells): These cells proliferate throughout the life to replace those lost.
e.g. epithelium of skin and intestinal mucous membrane
2. Expanding cell population (stable cells): These cells normally lie quiescent but have retained their capacity for proliferation. They can multiply when need arises.
e.g. connective tissue cells (fibroblast)
3. Static cell population (permanent cells): These cells lost their capacity to proliferate.
e.g. Nerve and muscle cells.

Chemical Mediators of Inflammation

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Preformed chemical mediators

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1. Histamine →

- It is stored in granules of mast cells, basophils and also in platelets.
 - Histamine causes vasodilation and increased vascular permeability.
 - It is important mainly in early inflammatory response and in immediate IgE mediated hypersensitivity reactions.

2. 5 Hydroxytryptamine (5 HT, Serotonin) →

- It is present in the mast cells and platelets of rodents (rats).
 - It increases vascular permeability and involved in early inflammatory response.

3. Lysosomal Enzymes →

- Neutrophils and monocytes contain lyosomal granules.
 - Neutrophils have two main types of granules

(a) Smaller or specific granules
or secondary granules
containing

- Alkaline phosphatase
 - lactoferrin
 - lysozyme
 - collagenase

(b) Large agerophil or primary granules

- Myeloperoxidase
 - Cationic proteins
 - Acid hydrolases
 - Neutral proteases

→ Use vascular permeability

→ chemotaxis

→ cause tissue damage

Oxygen derived free Radicals:

These are released from neutrophils and macrophages following phagocytosis and cause endothelial cell damage, resulting in increased vascular permeability.

Newly synthesized chemical mediators

I. Arachidonic acid metabolites: Prostaglandins Leukotrienes

Arachidonic acid is present in large amount in phospholipids of the cell memb. of Neutrophils.

Inflammatory stimuli

Activate Neutrophils.

Cell membrane phospholipids of neutrophils
Act upon phospholipids
Phospholipases enz. released by
lysosomes of activated neutrophils
release Arachidonic acid from
cell membrane

Metabolism of Arachidonic acid occurs
in two ways

Cyclo oxygenase pathway

Prostaglandin α_2 (PG α_2)

PGH $_2$

B

PGI $_2$

Thromboxane A $_2$ (TXA $_2$)

\rightarrow Vasoconstriction

\rightarrow Vasodilation
 \rightarrow Inhibits platelet aggregation

5-lipoxygenase

5-HPE

(hydroperoxy eicosatetraenoic acid)

reduced to

HETE

PGF $_2$

PG E $_2$

PG D $_2$

Von-D $_2$

Leukotriene B $_4$ (LTB $_4$)

Leukotriene C $_4$ (LTC $_4$)

Leukotriene D $_4$ (LTD $_4$)

Leukotriene E $_4$ (LTE $_4$)

Causes aggregation of neutrophils

LTC_4 } \rightarrow Vasoconstriction
 LTD_4 } \rightarrow Bronchoconstriction
 LTE_4 } \rightarrow Increased vascular permeability

$LTB_4 \rightarrow$ Chemotactic causes aggregation of neutrophils.

PGF_2 , } \rightarrow Vaso dilation
 PGE_2 , } \rightarrow Increase vascular permeability
 PGD_2 Oedema
 \rightarrow Pain & fever

\rightarrow Anti inflammatory drugs inhibit biosynthesis of prostaglandins by acting on cyclooxygenase

S.NO.	PGI_2	TXA_2
1.	Vaso dilation	Vaso constriction
2.	Inhibit platelet aggregation	Promotes platelet aggregation

2. Platelet Activating factor (PAF)

\rightarrow PAF is derived from degeneration of membrane phospholipids of basophils mainly and also from neutrophils, endothelium and platelets.

\rightarrow PAF causes increased vascular permeability, \rightarrow vasoconstriction, leucocyte adhesion to endothelium and chemotaxis.

3. Cytokines

\rightarrow Polypeptides secreted from lymphocytes: lymphokines } cytokines
 \rightarrow " " " monocytes: monokines } cytokines

Cytokines are of mainly 3 types: (a) Interleukin-1 (IL-1)

(b) Tumour necrosis factor (TNF) (c) Interleukin-8 (IL-8)

\rightarrow IL-1 & TNF causes expression of adhesion molecules & mediates leucocyte sticking, fever, aggregation & activation of neutrophils.

\rightarrow IL-8 is a power chemotactic & activator of neutrophils.

Chemical mediators from Plasma (Plasma Proteases)

I. Hageman factor activation

Inactive Hageman factor (XII)

It gets activated when comes in contact with,
the injured tissues i.e. collagen & vascular
basement membrane

Activated Hageman factor (XII a)

Prekallikrein

Kallikrein

HMWK

(High molecular weight kininogen)

Bradykinin

• It causes pain

• Increased vascular permeability

• Smooth muscle contraction

Plasminogen

XI → XII a

Kallikrein +
Plasminogen activator (PA)

Prothrombin → Thrombin

Fibrinogen → Fibrin

Fibrinopeptides
(IVP, chemotaxis)

It cleaves

Plasminogen → Plasmin

ACF upon

Fibrin

Complement system

Plasmin activates Hageman factor XII

(b) Acts on complement system,
cleaves C3

(c) Degrade fibrin to form fibrin split products
fibrin split products

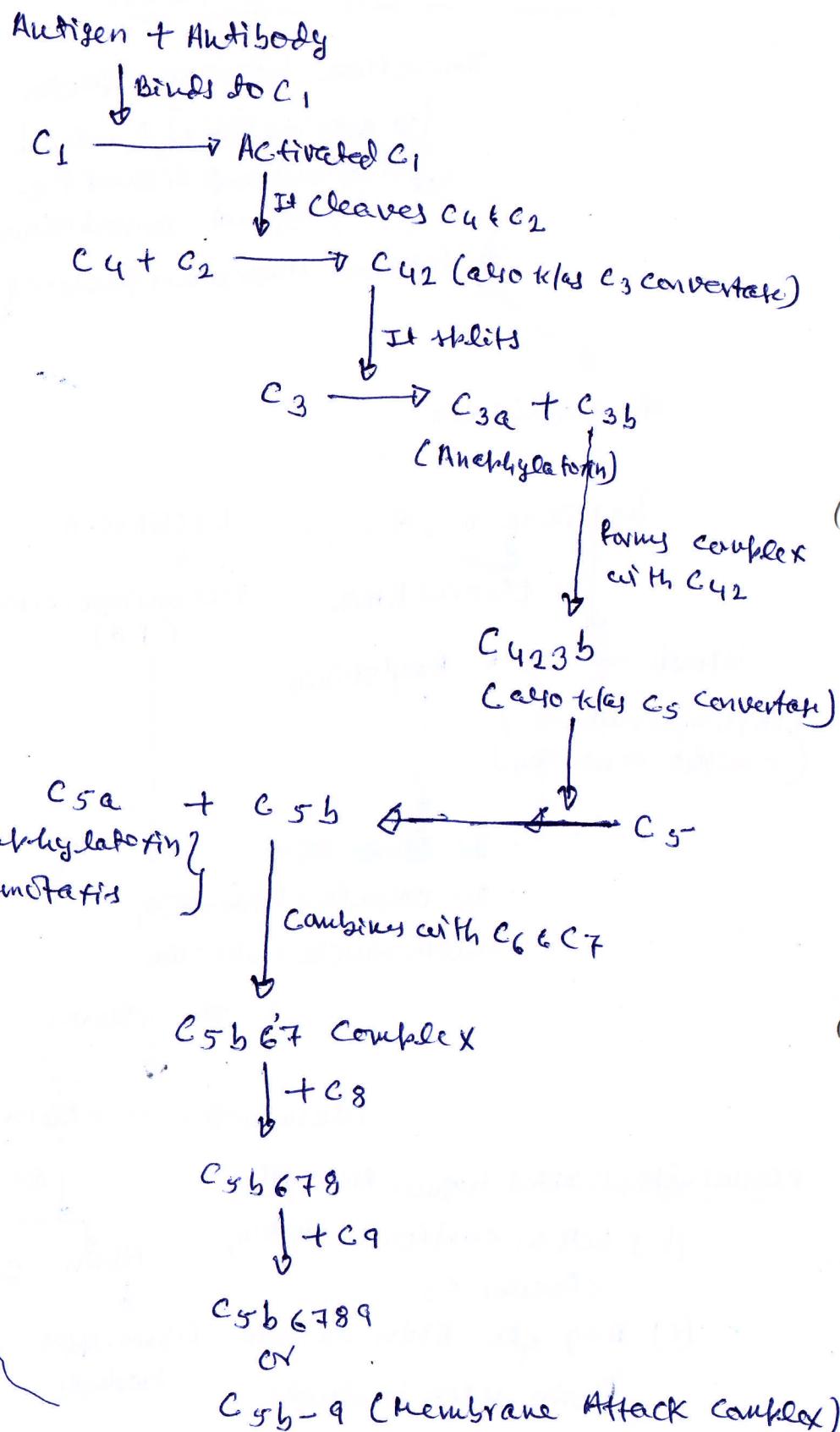
• Causes increased vascular permeability
(IVP)

Fig: Inter-relationships between kinin, clotting, fibrinolytic and complement system

II. Complement system

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I. Classical Pathway:



common (Terminal)
pathway for
both classical &
alternative pathways

Δ C_{3a} & C_{5a} are called anaphylatoxins \leq increases vascular permeability. C_{5a} also causes chemotaxis.

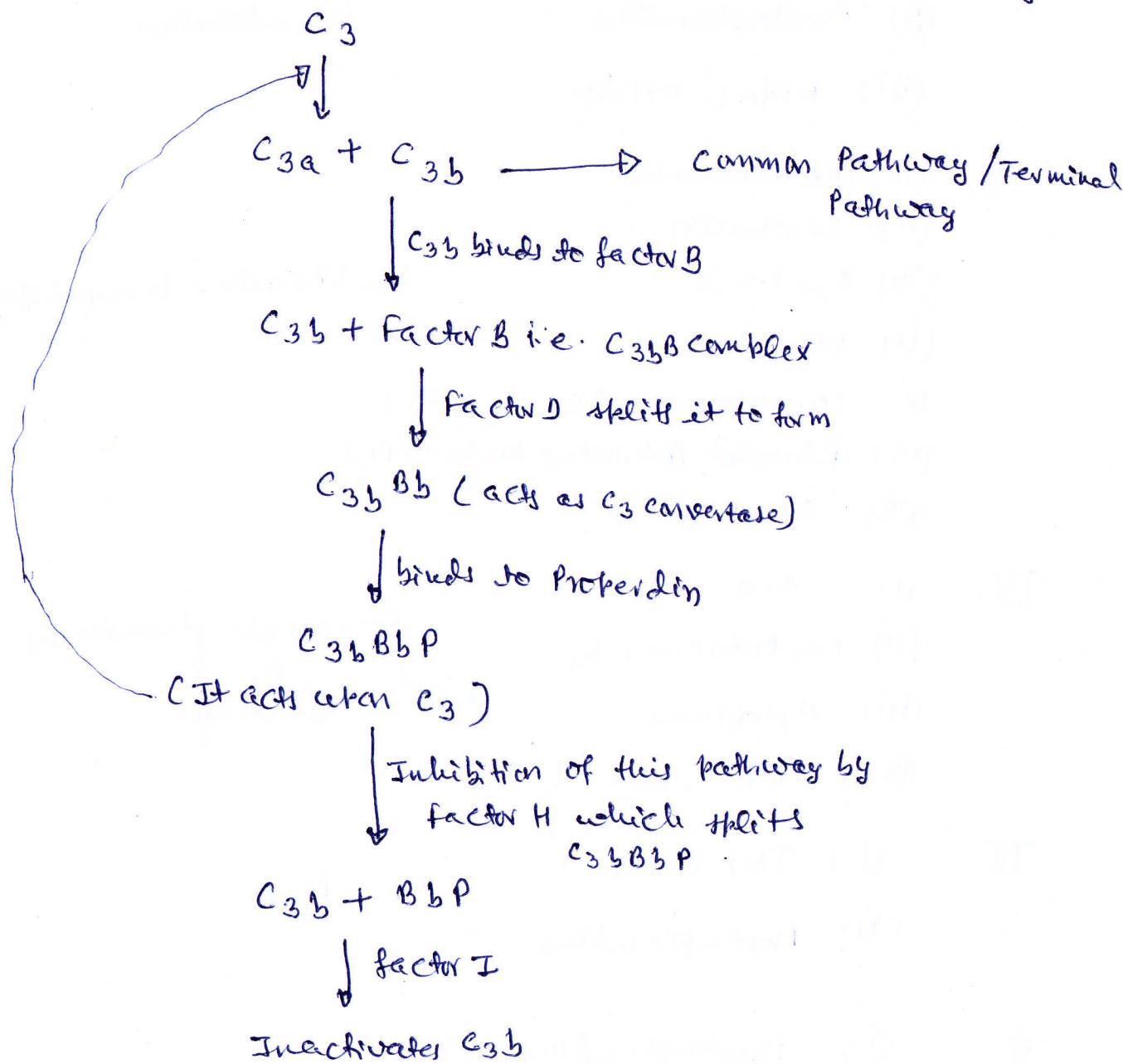
\rightarrow C_{3b} helps in phagocytosis of bacteria.

\rightarrow C_{5b-9} leads to lysis of bacterial cell membrane.

2. Alternate Pathway

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C₃ is activated directly by stimuli i.e. bacteria, fungi or helminth. It is activated even in absence of antibody.



- Normally factor H is inhibited by presence of activating surfaces of bacterial & fungal cell wall, helminth articles etc.

Action of mediators in Inflammation

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Mediators	Action
I. (i) Histamine	
(ii) Prostaglandins	Vasodilation
(iii) Nitric oxide	
II. (i) Histamine	
(ii) Serotonin	
(iii) C _{3a} & C _{5a}	Increase vascular permeability
(iv) Bradykinin	
(v) Leukotrienes (C ₄ , D ₄ & E ₄)	
(vi) Platelet Activating factor (PAF)	
(vii) Substance P	
III. (i) C _{5a}	Leucocyte chemotaxis
(ii) Leukotrienes B ₄	& Activation
(iii) Cytokines	
(iv) TNF & IL-1	
IV. (i) TNF & IL-1	Fever
(ii) Prostaglandins	
V. (i) Prostaglandins	
(ii) Bradykinin	Pain

Systemic effects of Inflammation

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1. Fever

Def.:-> Fever is a syndrome in which abnormal elevation of central body temperature (Pyrexia) along with various metabolic and functional disturbances such as increased pulse rate, anorexia, nausea, vomiting, constipation, increased thirst, scanty urine and dehydration.

Hyperthermia: It is increase of the body temperature due to heat storage without systemic disturbances.

Etiology of fever:-

- (i) Endotoxins of gram negative bacteria
- (ii) Gram positive bacteria
- (iii) Viruses
- (iv) Protozoa, fungi & Rickettsiae
- (v) Hypersensitivity
- (vi) Mechanical injuries
- (vii) Vascular disorders
- (viii) Neoplasms

* Heat regulating centre located in the hypothalamus.

Pathogenesis of fever

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Infectious agents, immune complex in hypersensitivity,
Neoplasm etc. causes



IL-1, TNF (Tumour necrosis factor) i.e. IL-6
(Interleukins) EPF
Production by leucocytes from the tissues of host



stimulates thermo-regulatory centre of
hypothalamus



Production of Prostaglandin - E



reaches at Vaso motor centre



Stimulation of sympathetic nerves



Vaso constriction of skin vessels



Decreased heat dissipation



Fever

Stages of fever: →

- a) The cold stage or period of rising temperature: The temperature starts to rise but the person feels cold and shiver occur due to contraction of cutaneous blood vessels.
- Also known as initial stage or stage of shivering.
- b) The hot stage (Fasigium): The temperature remains high and reaches the maximum.
- The person feels hot as cutaneous vessels are dilated.
- c) The sweating stage: The temperature begins to fall and patient sweats profusely.

Functions of fever: →

- (i) Increased Phagocytosis due to increased ^{number} activity of neutrophils.
- (ii) Distribution of leucocytes is accelerated due to increased velocity of blood.
- (iii) Increased & faster formation of antibodies
- (iv) Fever is bactericostatic because bacteria cannot thrive at high temperature.
- (v) Antigen - Antibody reactions occur more rapidly.

2. Acute Phase Reactions

Systemic manifestations of inflammation collectively known as acute phase reactions.

- It includes decreased appetite, increased sleep, increased degradation of proteins, hypotension and other haemodynamic changes.

3. Changes in Peripheral Blood Leucocytes

Leucocytosis i.e. increase in number of leucocytes is a common feature of inflammation.