

MEDIATORS OF INFLAMMATION

The mediators of inflammation are the substances that initiate and regulate inflammatory reactions

Significance

THE MOST IMPORTANT MEDIATORS OF ACUTE INFLAMMATION

Vasoactive amines

Arachidonic acid metabolites

Cytokines

Products of complement activation

OTHER MEDIATORS OF INFLAMMATION

Platelet-Activating Factor (PAF)

Bradykinin

Products of Coagulation

Neuropeptides

VASOACTIVE AMINES

Histamine

Serotonin

SOURCES OF HISTAMINE

Mast cells

Basophils

Platelets

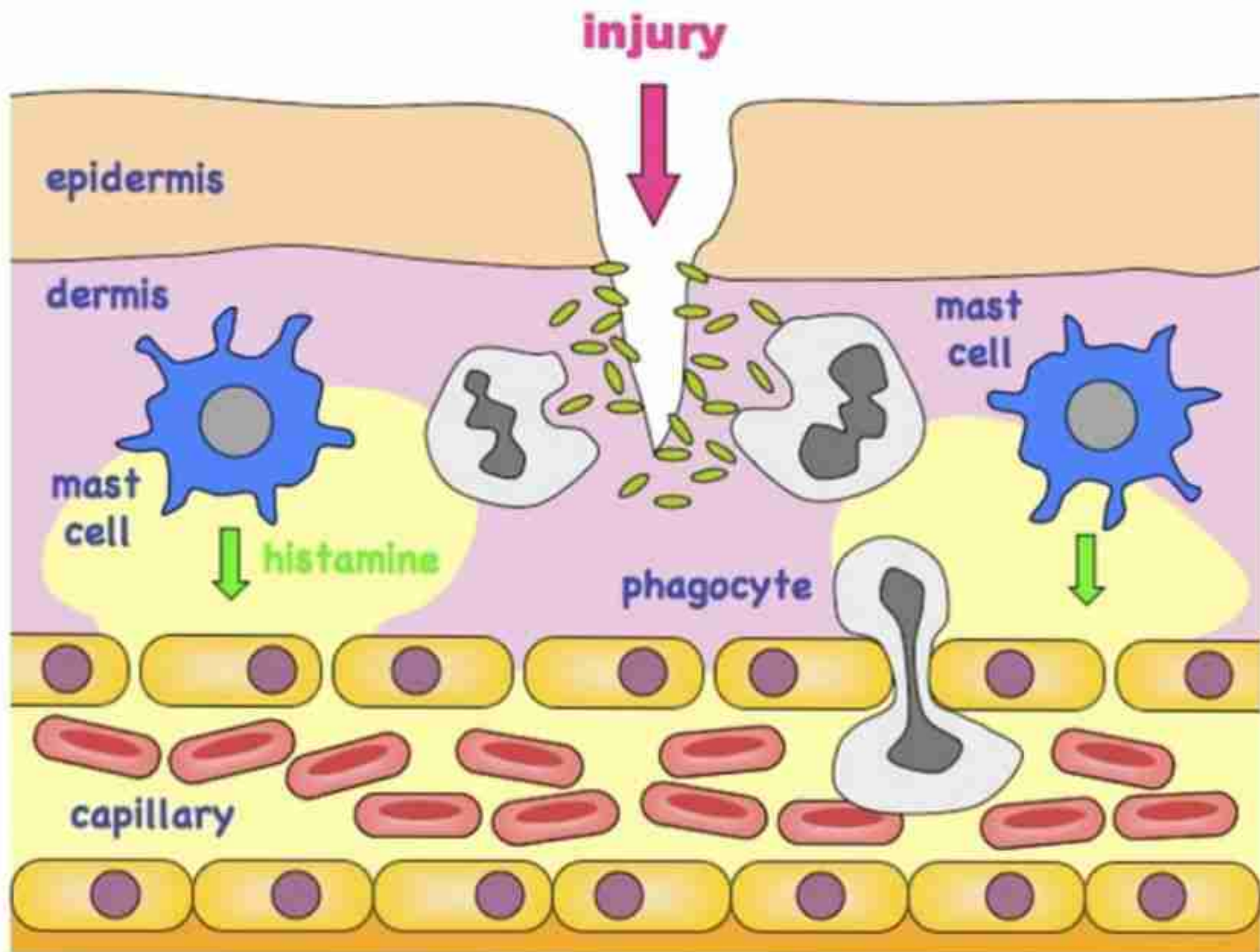
SOURCES OF SEROTONIN

Platelets

ACTIONS OF VASOACTIVE AMINES

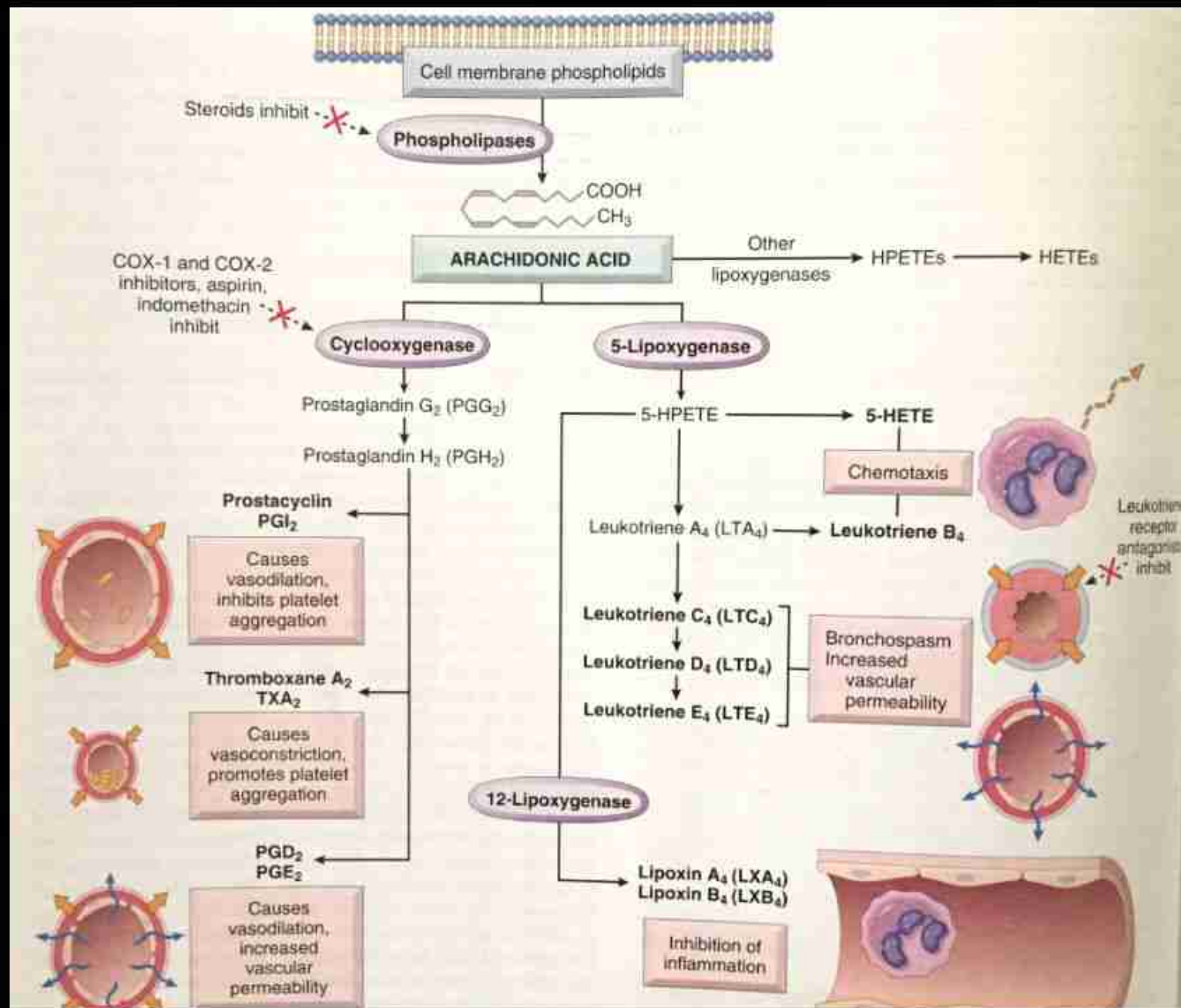
Vasodilatation

Increases vascular permeability



ARACHIDONIC ACID METABOLITES

Prostaglandins
Leukotrienes



ACTIONS OF PROSTAGLANDINS

Prostacyclin (PGI₂): vasodilation

inhibits platelet aggregation

Thromboxane A₂: vasoconstriction

promotes platelet aggregation

PGD₂, PGE₂: vasodilation

Increased vascular permeability

Systemic effects: Pain and fever

ACTIONS OF LEUKOTRIENES

LTB₄: potent chemotactic agent

LTC₄, LTD₄, LTE₄: Increased vascular permeability
Bronchospasm

CYTOKINES

Cytokines are proteins produced by many cell types

Sources: Lymphocytes

- Monocyte/Macrophages

- Dendritic cells

- Endothelial cells

- Epithelial cells

Cytokines produced by activated lymphocytes are called **lymphokines**

Cytokines produced by activated monocytes are called **monokines**

CYTOKINES INVOLVED IN ACUTE INFLAMMATION

Tumor Necrosis Factor (TNF)

Interleukin-1 (IL-1)

Interleukin-6 (IL-6)

ACTIONS OF CYTOKINES

Chemotaxis, leukocyte recruitment and activation

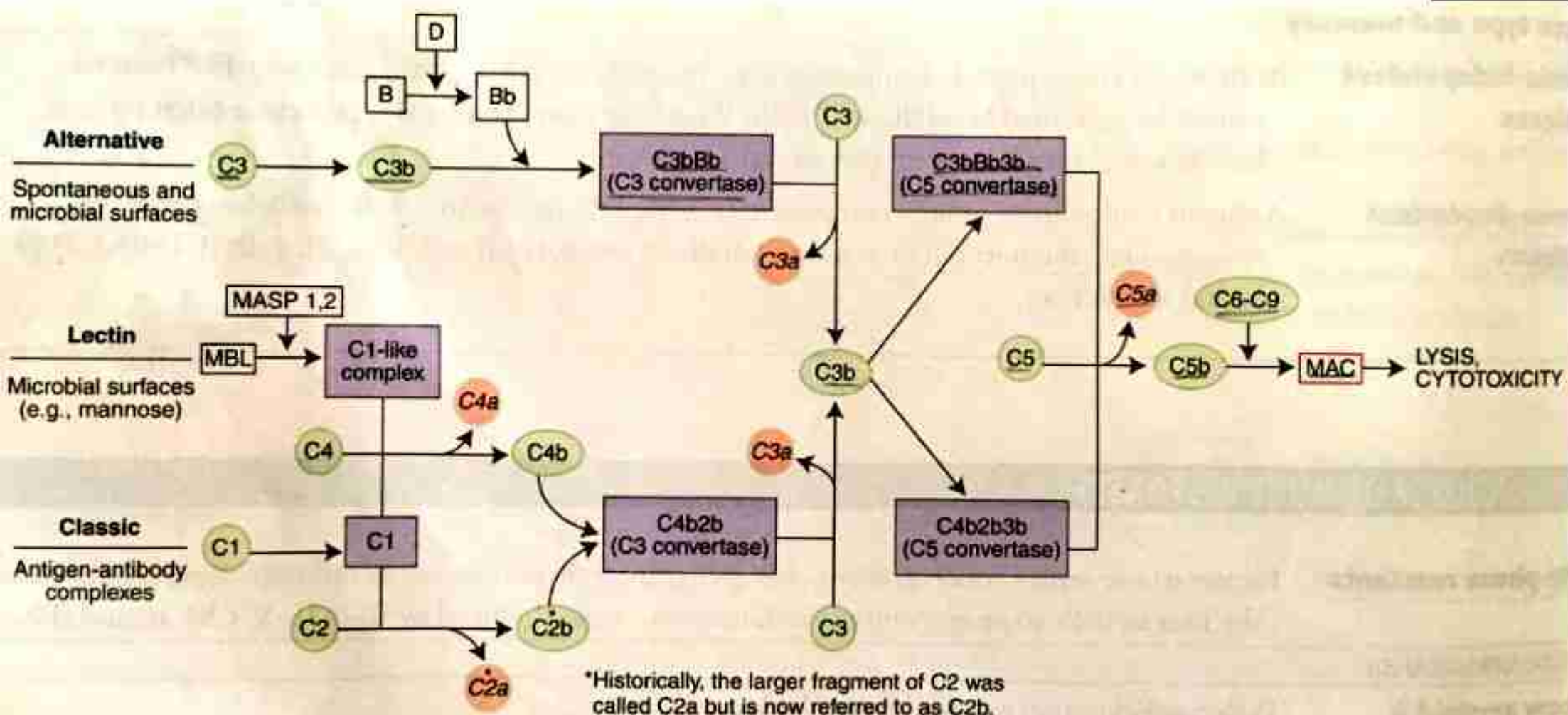
Systemic acute phase response: Fever

COMPLEMENT SYSTEM

System consisting of more than 20 proteins, some of which are numbered C1 through C9.

Complement proteins are present in inactive forms in the plasma.

Activation can occur by one of three pathways



FUNCTIONS OF COMPLEMENT

C3a, C5a: stimulate histamine release from mast cells and thereby increase vascular permeability and cause vasodilation. They are called anaphylatoxins.

Chemotactic agent

C3b act as opsonins

MAC - important for the killing of microbes with thin cell walls, such as *Neisseria* bacteria

PLATELET-ACTIVATING FACTOR (PAF)

Phospholipid-derived mediator

Source: Leukocytes

Mast cells

Platelets

Endothelial cells

ACTIONS OF PLATELET- ACTIVATING FACTOR

Platelet aggregation

increased vascular permeability

low concentrations it induces vasodilation
and vasoconstriction otherwise

Bronchoconstriction

BRADYKININ

Kininogen



Kallikrein

Bradykinin

ACTIONS OF BRADYKININ

Increases vascular permeability

Vasodilatation

Pain

ROLL OF CHEMICAL MEDIATORS IN ACUTE INFLAMMATION

VASODILATION

INCREASED VASCULAR PERMIABILITY

CHEMOTAXIS, LEUKOCYTE ACTIVATION

FEVER

PAIN