

INFLAMMATION

L 24 - INFLAMMATORY PROCESS

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Acute inflammation

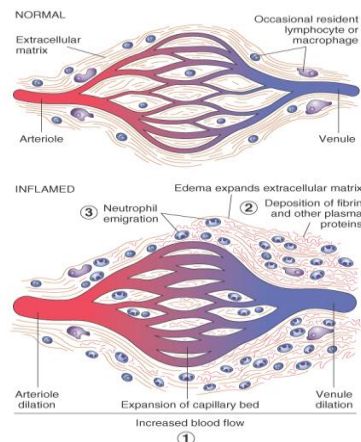
- The immediate and early response to injury
- The point? Get the PMN's to the site as fast as possible
 - Vasodilatation
 - Increased vascular permeability
 - Extravasation of PMN's
- **Two events occur**
 - **Vascular Events**
 - **Cellular Events**

2

1. VASCULAR EVENTS

1. Haemodynamic Changes

- Changes in **microcirculatory bed**
- Under the influence of activated chemotactic factors with transiently initiated by neurogenic mechanisms.
- **Transient vasoconstriction**
- **Dilatation of arterioles**, increased blood flow through the following capillaries and venules. acute local active hyperaemia.
- The resultant overload of drainage causes dilatation of the venules and veins (**Congestion** or Passive Hyperaemia)



3

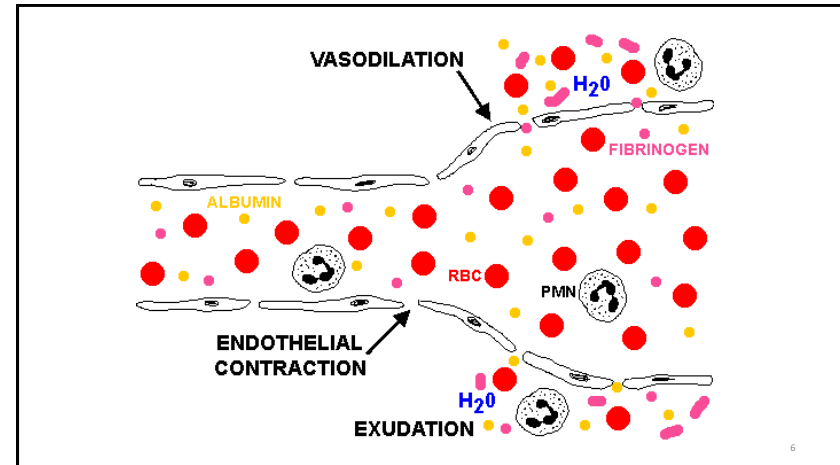
2. Permeability Changes (Capillaries and venules)

- Initially leakage of **watery fluid**
- Later leakage of protein rich fluid, leukocytes and some erythrocytes
- The leakage of the plasma
 - **increased blood hydrostatic pressure**
 - **increase in vessel's permeability**
- The **first phase** of increased permeability appears to be mediated by histamine which is usually transient, lasting for **less than one hour**.
- The **second phase** lasting over the next **3-4 hours** occur, during which the leakage of leukocytes take place, depend on multiple chemical mediators.

4

- The second phase results in migration of fluid between endothelial cells of **venules**.
- Chemical mediators of inflammation work by either not involving or involving **neutrophils**
- **Histamine** has direct effect on endothelial cells
- **C5a and LTB₄** (leukotriene B₄) cause increased permeability by inducing stickiness and paving of neutrophils in the venules and release of chemical mediators from neutrophils.

5



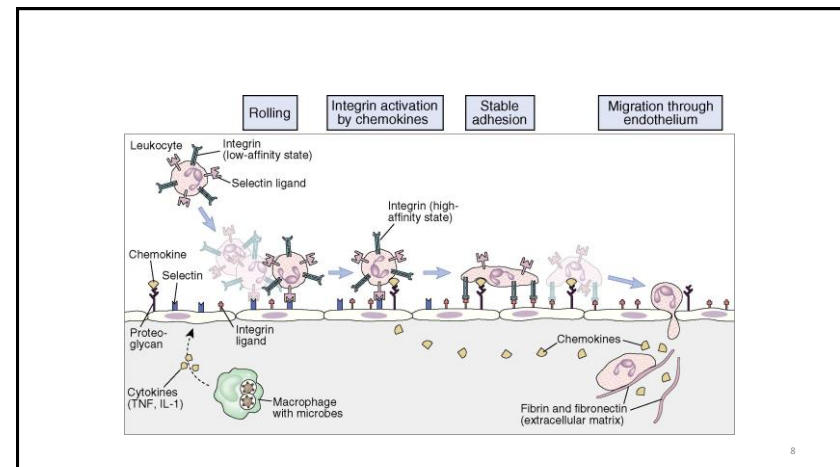
6

2. CELLULAR EVENTS

Margination and Pavementing

- The **margination** and adhesion of the leukocytes to the vessel's endothelium
- Leukocyte's margination occurs due to slowing of the blood flow.
- Leukocytes **crawl** slowly over the inner wall of the blood vessel and **adhere** (adhesion) at some point with the endothelium and also to the other leukocytes (aggregation).
- **Adhesion** and **aggregation** occur under the influence of chemical mediators
- When considerable number of leukocytes (neutrophils) line the endothelium over a considerable distance the process is called **pavementing**.

7



8

ADHESION AND AGGREGATION

- **Cells** **C5a, LTB4**
- **Endothelial cells** **PAF,**

Adhesive Molecules

- Adhesion molecules participate in these events include
 - selectins
 - integrins
 - members of immunoglobulin super-family and
 - cadherins
- **Endothelium** **ELAM-1, ICAM1**
- **Leukocytes** **LeuM5, LFA-1**

9

- **Rolling:** Selectins transiently bind to receptors
- Selectins bind selected sugars
 - Selected + Lectins (sugars) = Selectins
- selectins present on endothelial cells (**E-Selectin**)
- selectins present on leukocytes (**L-Selectin**)
- selectins present on platelets (**P-Selectin**)
- **Adhesion:** Mediated by Integrins ICAM-1 and VCAM-1
- **Transmigration:** Mediated by PECAM-1

10

EMIGRATION (Diapedesis)

- All the leukocytes including neutrophils, eosinophils, basophils, lymphocytes and monocytes use the **same pathways**, i.e., move across the blood vessel between the endothelial cells
- After being adhered to the endothelial surface, these cell throws the **pseudopod** (cytoplasmic extension) in gaps produced between the endothelial cells
- Entire leukocyte then passes quickly, crawls through the basement membrane and pericytes, in to the perivascular area and farther
- While moving between the cells, the **neutrophils** can reduce their diameter to even less than **1 µm**, unlike 10 µm otherwise
- Monocytes and macrophages are less athletic than neutrophils

11

- The process of migration is greater from the **venules**
- The movement of the leukocytes through the **capillaries** suggests that leukocytes secrete certain enzymes capable of **disjoining** (digesting junctions) endothelial cells which perhaps reappear after the passage of the leukocytes.
- The movement through the basement membrane also probably depend on secretion of **collagenase**-type enzymes by the leukocytes.
- Massive migration of the leukocytes allows passive extravasation of the **red blood cells**.
- These leaked RBC's are either digested locally by macrophages or drained by lymphatics to the regional lymph nodes

12

- The emigration of the leukocytes occurs in **wave patterns**.
- The first wave occurs in **30-40 minutes** time with emigration of predominantly **neutrophils** with fewer **monocytes** from the **venules**.
- The second wave occurs **some hours** later at the **venule** and **capillary** level where **monocyte** emigration is higher than the neutrophils.

13

SPREAD HAPPINESS
ELIMINATE ANGER

ONE WORLD
ONE RACE

M. Tariq Javed

14