**Cellular changes in inflammation:**

The journey of leukocytes from lumen of blood vessels to site of infection is called leukocytes recruitment. This is the major process of cellular changes. Recruited leukocytes eliminate the causative agent of infection. This recruitment of leukocytes rapidly occurs after vascular changes.

**Phases of cellular changes:**

1). During recruitment process, there are also various process occur.

 Some of the events of phase I occurring inside the blood vessels are:-

* Margination
* Rolling
* Adhesion

2). The phase II is movement of leukocytes across the endothelium which is knowm as transmigration.

3). The phase III is the attraction of leukocytes towards the causative agent across the chemical gradient which is also known as chemotaxis.

**Phase I:**

**Margination :** In normal circulation, blood flows in axial manner that has a central stream of red blood cells and white blood cells that is surrounded by plasma proteins. During inflammation, blood flow become slow down. The central stream of blood cells become widen and surrounded plasma proteins become narrow. Ultimately RBCs move faster as compared to WBCs and white blood cells adhere to wall of endothelium. This alteration in axial manner is called margination in which white blood cells adhere to the periphery of blood vessels.

**Rolling:** Rolling is the transient loose attachment and detachment of leukocytes within the endothelium. Firstly leukocytes attached to the endothelium and then detach to the endothelium, ultimately leukocytes roll over the endothelium and this is called rolling. Rolling is mediated by a family of proteins known as selectins .

Selectins are the receptors that are expressed on the surface of leukocytes and endothelium. There are three types of selectins:-

1. E-selectin or CD62E that are expressed on the surface of endothelium
2. L-selectin or CD62L that are expressed on the leukocyte surface
3. P-selectin or CD62P that are expressed on platelet and endothelium surface

**Why this happens?**

During inflammation, tissue macrophages and mast cells release inflammatory mediators i-e TNF-α and IL-1. These mediators act on the endothelial cells and cause their activation. Activated endothelial cells cause expression of selectins on endothelium and these selectins usually expressed within 1-2 hours.

Sometimes selectins are stored inside the intracellular granules e.g in the case of platelets, the selectins are stored inside the granules known as weible-pallady bodies. Release of mediators e.g histamine cause selectins activation and converted into high affinity state due to these mediators. Histamine cause redistribution of selectins.

**Adhesion:** Adhesion is strong attachment of leukocytes within endothelium. This adhesion is mediated by a family of proteins named integrins. Integrins are the glycoproteins that are expressed on surface of leukocytes. Against these integrins, there is specific ligands on surface of endothelium. These are expressed by inflammatory mediators i-e TNF-α and IL-1. These mediators are intercellular adhesion molecule that binds to the integrins e.g leukocyte activated function with antigen-1(LFA-1) or macrophage-1 antigen are also called CD11b/18 and LFA-1 also called CD11a/18. Vascular cell adhesion molecule (VCAM) bind to the very late antigen (VLA-4).

**Phase II or Transmigration:**

Transmigration is the movement of leukocytes across endothelium. It is also called diapedesis. Chemokines participate in transmigration. These chemokines stimulate the movement of leukocytes between endothelial spaces. This movement of leukocytes between endothelial spaces is mediated by adhesion molecule i-e PCAM-1 (Platelet cell adhesion molecule) that facilitate the movement of leukocytes between endothelial cells. Facilitation is by PCAM-1 or CD31. These leukocytes also cause breakdown of basement membrane of endothelium by releasing enzyme known as collagenases that facilitate movement of leukocytes across the endothelium.

After the movement of leukocytes across the endothelium basement membrane again repaired.