THE HIGH YELD

margination :During blood stasis more white cells assume a peripheral position along the endothelial surface.
rolling :Activated endothelial cells express adhesion molecules to which the leukocytes attach loosely, then bind and detach
The cells finally come to restat somepoint where they adhere firmly.

The two major families of molecules involved in leukocyte adhesion and migration are the selectins and .integrins

SELECTINS

Mediate the initial weak interactions between leukocytes and endothelium expressedon leukocytesand endothelium

These weakselectin-mediated rolling interactions slow down the leukocytes and give them the chance to recognize additional adhesion molecules on the endothelium.

INTEGRINS

a family of leukocyte surface proteins that mediate the adhesion of leukocytes to endothelium and of various cells to the extracellular matrix.
do not adhere to their specific ligands until the leukocytes are activated by chemokines.
Whentherollingleukocytesactivatedtheiri ntegrinsundergo conformational changes and cluster together, thus converting to a high-affinity form.

TNFandIL-1,activateendothelialcells

LEUKOCYTE MIGRATION THROUGH ENDOTHELIUM

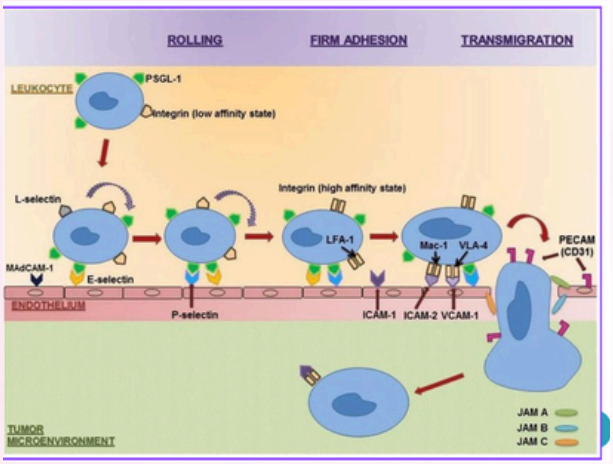
driven by chemokines produced in extravascular tissues squeezing between cells at intercellular junctions.
platelet endothelial cell adhesion molecule-1 (PECAM-1)*

CHEMOTAXIS OF LEUKOCYTES

chemoattractants, including the following:
Bacterial products.
Cytokines, especially those of the chemokine family.
Components of the complement system, particularly C5a .

The leukocyte moves by extending filopodia that pull the back of the cell in the direction of extension, much like the front wheels

In most forms of acute inflammation:
Neutrophils predominate in the inflammatory infiltrate during the first 6 to 24 hours.
Monocyte-derived macrophages over 24 to 48 hours.



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THE HIGH YELD

NEUTROPHILS

More numerous in the blood
more rapidly to chemokines.
more rapidly to chemokines.
After entering tissues, neutrophils are short- lived.

MACROPHAGES

Survive longer.
May proliferate in the tissues.

EXCEPTIONS

Infection with Pseudomonas bacteria, the cellular infiltrate is dominated by neutrophils for several days.
In viral infections, lymphocytes may be the first cells to arrive.
In allergic reactions, eosinophils may be a prominent cell type.

DESTRUCTIVE MECHANISMS:

1. respiratory burst :
Is the rapid release of the reactive oxygen species (ROS), superoxide anion (O2) and hydrogen peroxide (H2O2).
2. Nitric Oxide:
Endothelial (eNOS): maintain vascular tone
Neuronal (nNOS): acts as neurotransmitter.
Inducible (iNOS): involved in microbial killing, expressed when macrophages are activated by cytokines (e.g., IFN-γ) or microbial products.
3. Granule Enzymes: Neutrophils contain granules packed with enzymes and anti-microbial proteins

harmful proteases, however, are normally controlled by a system of anti-proteases in the serum and tissue fluids.
-α1-anti-trypsin, which is the major inhibitor of neutrophil elastase. (A deficiency of these inhibitors may lead to sustained action of leukocyte proteases, as is the case in patients with α1-anti-trypsin deficiency)

LEUKOCYTE ACTIVATION

they must be activated to perform their functions.

The functional responses for destruction of microbes and other offenders are :
Phagocytosis.
Intracellular killing

PHAGOCYTOSIS

1-recognition and attachment
2-engulfment,(phagocytic vacuole).
3-killing or degradation.

TERMINATION OF THE ACUTE INFLAMMATORY RESPONSE

1. Degradation of mediators.
2. Neutrophils apoptosis.
3. Stop signals :

liberationofanti-inflammatorycytokines,including transforming growth factor-β (TGF-β) and IL-10, from macrophages