



Immunological Regulation of the Inflammatory Response

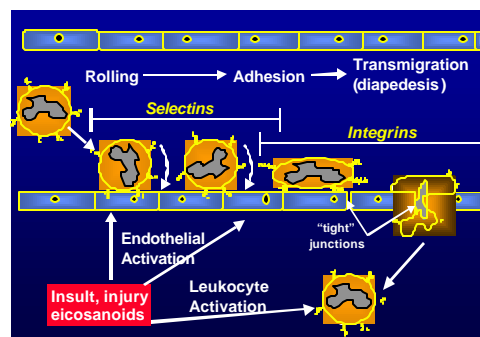
The fundamental functions of the immune system are to rid the body of foreign invaders and to dispose of damaged tissue, allowing healing to occur. Inflammation is involved in both processes. In some situations the inflammatory response appears to do more harm than good. In arthritis, cartilage is damaged by lysosomal enzymes from neutrophils that arrive leading to a vicious cycle of repeated injury and persistent inflammation. Anti-inflammatory drugs are used in arthritis treatment – to interrupt this destructive cycle and to allow healing to occur.

Anti-inflammatory drugs

Inflammation is triggered by both preformed mediators (histamine, serotonin, kinins, etc.), and mediators synthesized by leukocytes (prostaglandins, thromboxanes, leukotrienes, lysosomal enzymes, complement components, etc.) The prostaglandins and other mediators of the arachidonic acid cascade (eicosanoids) have received the most attention. Anti-inflammatory agents in current use act by blocking the synthesis or release of inflammatory mediators that arise in response to injury or infection.

Immunological approach to regulating inflammation

Regardless of the specific cause of inflammation or the mediators called to action, the consequences at the cellular and tissue level are similar. Leukocytes are activated, attracted to the site, and invade the tissue.



Immunological regulation of inflammation involves inhibition of one or more of the steps of leukocyte activation and recruitment:

- Chemoattraction to the site of insult
- Capture and rolling, mediated by leukocyte and endothelial receptors called *selectins*
- Firm adhesion, mediated by receptors called *integrins*
- Transmigration (diapedesis)
 - Block vascular cell adhesion molecules (VCAM) binding or interactions
 - Tighten intercellular spaces (tight junctions)
- Signal transduction among cells (thousands of pathways)