Pharmacology

Review of the Inflammatory Process

**Objectives**
- Review the chemical reactions that occur during the inflammatory response
- Discuss the role of prostaglandins in the inflammatory response
- Discuss the role of NSAIDs on prostaglandin synthesis
- Discuss the COX-1 – COX-2 pathway

**Inflammation**
- Localized tissue response to injury or illness
- Produces local sensations
  - swelling
  - redness
  - heat
  - pain

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- Initiated by tissue damage
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- The changes in the interstitial environment trigger the complex process of inflammation

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Inflammation
- Very complex process involving specific integrated steps designed to bring about healing
- From a pharmacology standpoint, we’re most interested in the chemical changes that occur

Arachidonic Acid
- Produced as a by-product of the inflammatory response

Eicosanoids
- Lipids derived from arachidonic acid
- 2 major classes
  - prostaglandins
  - leukotrienes

Arachidonic Acid Pathway

Prostaglandins
- Chemical messengers
- Produced in most bodily tissues
- They work locally
  - they typically do not travel through the circulatory system to reach their target cells
- Referred to as local hormones
- Extremely powerful & effective in small quantities

Prostaglandins
- Released by damaged tissues
  - powerful mediators of the vascular events that occur during the inflammatory process
    - increase vascular permeability
    - increase blood flow through vasodilation
    - produce platelet aggregation
  - stimulate nerve endings to produce the sensation of pain
  - stimulate contraction of smooth muscle (uterus/bronchi)
  - reduce gastric acidity
**Role of NSAIDs in the Inflammatory Process**

- Inhibit the cyclooxygenase enzyme
  - prevent or reduce the synthesis of prostaglandins
  - inhibit or reduce pain
  - inhibit or reduce swelling
  - increase GI acidity
  - decrease platelet aggregation

**Role of NSAIDs in the Inflammatory Process**

- Positive effects produced
  - ↓pain
  - ↓inflammation
- Negative side effects
  - ↑gastric upset
    - Often times antacids are prescribed in conjunction with NSAIDs
  - ↑incidence of ulcers
  - possible ↓wound healing

**The COX-1 COX-2 Pathway**

- **Cyclooxygenase – 1** Housekeeping gene
- **Cyclooxygenase – 2** Inflammatory gene

**Prostaglandins responsible for:**
- GI mucosal integrity
- Platelet aggregation
- Renal function
- Inflammation
- Pain & fever
- Wound healing
- Other functions

**COX-2 Selective NSAIDs**

- Celebrex
- Vioxx

**What questions do you have?**