

Class Act I

PharP 451
Fall 2004

Pain Sources

- Central Nervous System
 - Pain perception
 - Receptors in brain bind with opiates
 - Stimulation of these receptors produces analgesia and pleasure
 - Withdrawal of stimulation produces pain and displeasure
- Peripheral pain – damage to nerve endings with pain impulses sent up the spinal cord
 - Direct damage to nerves
 - Inflammation of nerves
 - Stretching or deformation of nerves
- Inflammatory pain

Classic Signs of Inflammation (Galen)

- Calor – heat
- Rubor – redness
- Tumor – swelling
- Dolor – pain

Inflammation

- Mediated in large part by the production of prostaglandins
 - Arachidonic acid released from damaged tissue – a straight-chain fatty acid
 - Transformed into prostaglandins, which includes a ring structure, by a class of enzymes known as cyclooxygenases (COX)
 - At least 2 types of COX are known: COX-1 and COX-2
 - Drugs that inhibit COX reduce inflammation and the associated pain
- Prostaglandins serve useful functions, particularly in the kidney and stomach
 - Inhibition of COX can produce kidney damage and damage to the stomach lining

Pain Management Drugs

- Analgesics without much effect on inflammation
 - Opioids
 - Acetaminophen
- Analgesics with antiinflammatory activity
 - NSAIDs (non-steroidal antiinflammatory drugs)
 - COX-1 or non-selective COX inhibitors
 - Non-reversible inhibitors (Aspirin)
 - Reversible inhibitors
 - COX-2 selective inhibitors
- Muscle relaxants
- Combinations of the above

Opioids

- Morphine and codeine derivatives
 - Schedule II Drugs (require written Rx)
 - Fentanyl (widely used as a patch)
 - Morphine (mostly used IM or IV or as MS-Contin)
 - Oxycodone (Oxycontin)
 - Schedule III Drugs (Oral Rx, may be refilled)
 - Hydrocodone + acetaminophen or aspirin
 - Codeine + acetaminophen or aspirin
- Synthetic opioids
 - Propoxyphene + acetaminophen or aspirin
 - Darvocet N-100 – no real evidence that it is more effective than aspirin or acetaminophen alone
 - Tramadol, tramadol + acetaminophen
 - A "partial agonist" that is presumably less habit forming with fewer adverse effects.

NSAIDs: Non-selective COX inhibitors

- Propionic acid derivatives (-profen, -proxen)
 - Ibuprofen – dosed 3-4x/day (up to 2400 mg)
 - Generic and available OTC (up to 1200 mg)
 - Naproxen – dosed 1-2x/day
- Indole acetic acids (-ac)
 - Diclofenac – oral watch for liver problems
 - Ketorolac – injectable or oral
 - Because of liver problems with chronic use, has been limited to treatment of acute pain
- Nonacidic
 - Nabumetone

NSAIDs: Non-selective

- Aspirin (salicylate class)
 - Fairly good antiinflammatory effects
 - Irreversibly binds COX in platelets
 - Direct and indirect effects on GI tract
 - Some patients allergic
- Acetaminophen
 - Not much peripheral antiinflammatory effect
 - May be a COX inhibitor in the CNS
 - Good antipyretic and analgesic effects
 - Liver toxicity in overdose – deadly
 - Maximum adult dose 4 g/day (2 g/day in chronic alcoholics)
 - Little or no effect on GI tract

Muscle Relaxants

- Classified as “skeletal muscle relaxants”
- These are largely older drugs that have been on the market since the 50s and 60s and 70s
- Most work through a CNS effect and do not have a direct effect on muscle
- Almost all produce sedation
- Some (carisoprodol, tizanidine) produce withdrawal with chronic use – carisoprodol is popular among drug abusers
- Many have anticholinergic effects that should be avoided in the elderly

Use of Clinical Pharmacology Online

<http://cp.gsm.com/apps/>