DEPARTMENT OF PHARMACOLOGY

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18.7.2013

PHARMACOTHERAPY OF PAIN

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1. Pathophysiology of pain	:	M.Akhilesh Kumar
2. Types of pain- treatment overview:		A. Charan Chand.
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Pain is the most common symptom of disease. The International Association for the Study of Pain has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage."Pain is the end perceptual consequence of the neural processing of particular sensory information. The initial stimulus usually arises in the periphery and is transferred under multiple controls through sensory relays in the central nervous system to the cortex.

Pathophysiology of pain:

The physiological process by which pain is perceived is known as nociception. Pain is transmitted from all over the body by nociceptive neurons known as nociceptors, which are of two types. Aδ fibers are myelinated ad have fast conduction velocities; carrying information about brief, sharp pain. C-fibres are unmyelinated neurons and therefore have slower conduction velocities. Activation of C-fibres result in a sensation of blunt, throbbing pain often longer lasting compared to pain transmitted by Aδ fibers. Both fiber types project to the dorsal horn of the spinal cord where the nociceptive signal is conveyed and projected up to cerebral regions of the central nervous system.

The mechanisms involved in pain pathology are

1. Peripheral sensitization- result in allodynia and hyperalgesia. The major known effectors are the inflammatory mediators.

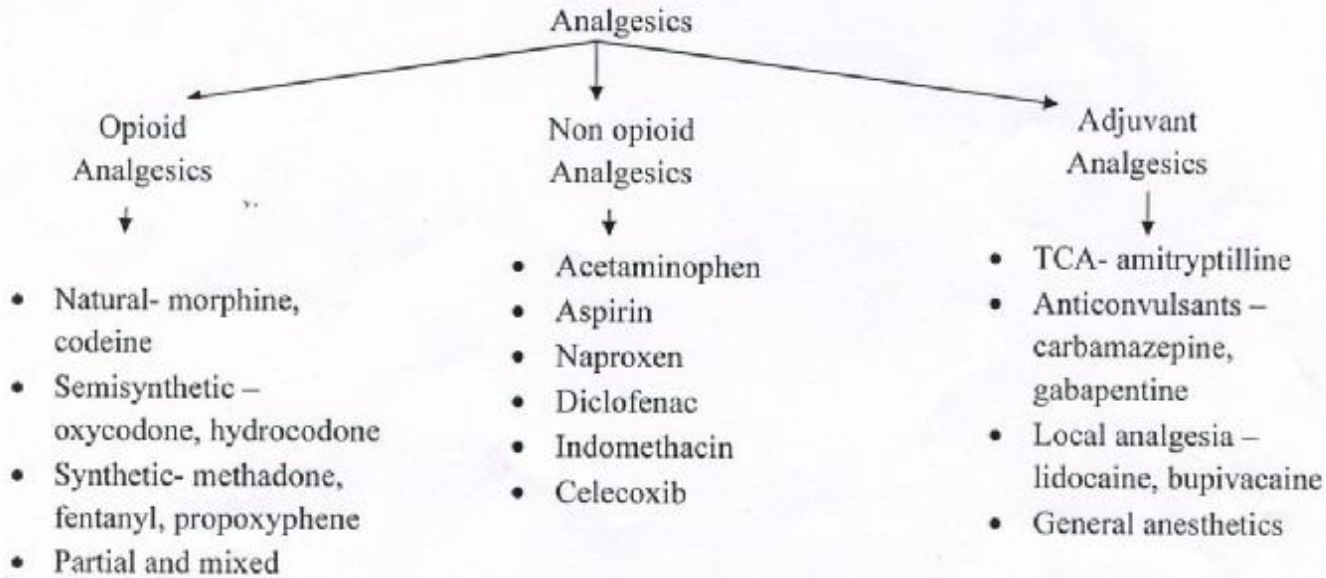
2. Central sensitization – it occurs when repetitive high intensity, snaptic transmission activates intracellular signal transduction cascades in dorsal horn neurons that enhance the response to subsequent stimuli
3. Neuronal plasticity – changes that occur in the established nervous system. Plasticity can result in short term changes that last minutes to hours, or long term changes which may be permanent

Types of pain:

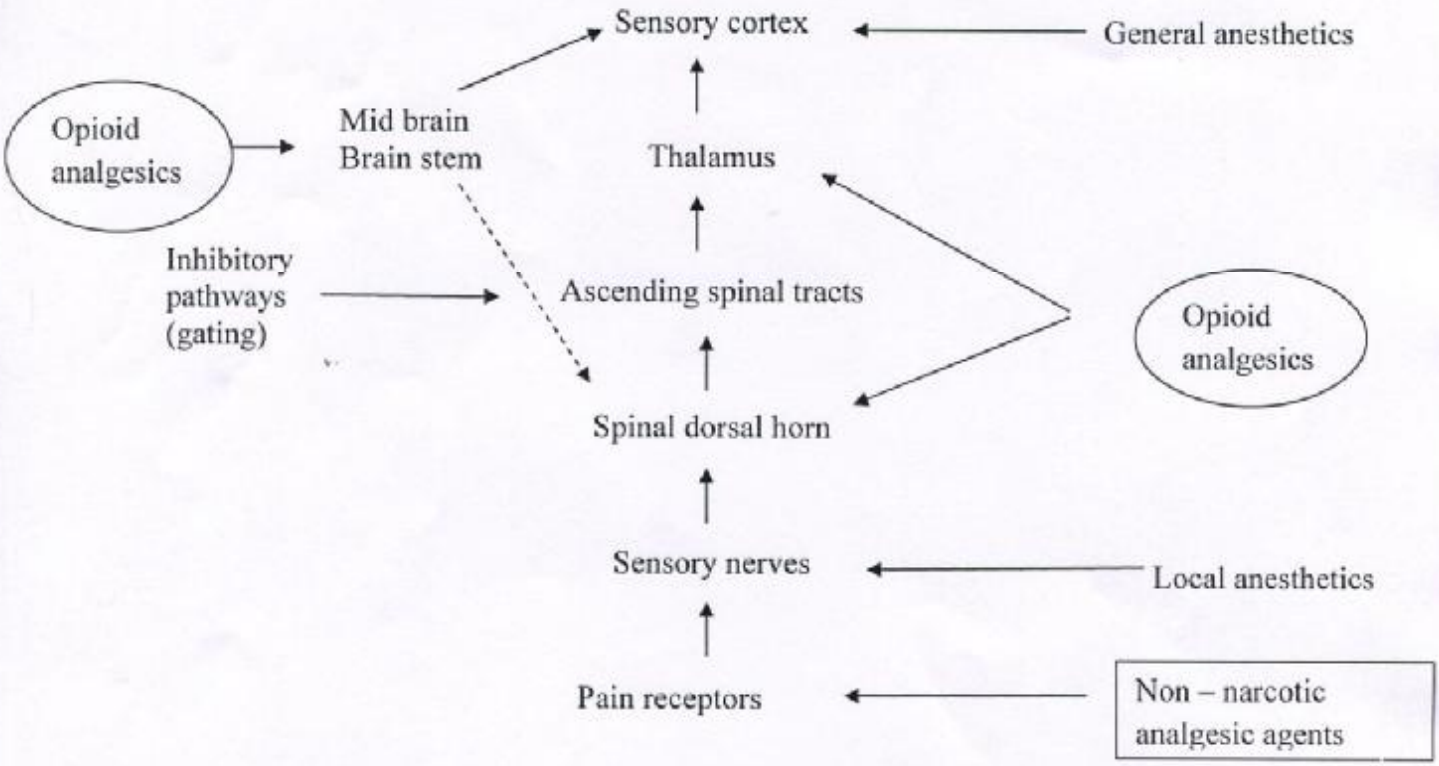
1. Superficial or cutaneous pain arising from skin and superficial mucous membranes or nerves, pricking, stinging, or burning
2. Deep non-visceral pain – dull character, accompanied b sickening sensation due to an autonomic response
3. Visceral pain – dull aching, or colicky in nature with sweating, nausea, fall in BP and even shock
4. Referred pain – deep pain may be misinterpreted as arising from some part of body other than the actual site of stimulation
5. Deafferentiation pain – caused by partial damage to axons and nerve membranes which become very sensitive to mechanical and chemical stimuli.
6. Psychogenic or functional pain – vague pain which follows no definite anatomical pattern of distribution

Classification of analgesics

Analgesics are the drugs that selectively relieve pain by acting in the CNS or on peripheral pain mechanisms without significantly altering consciousness.



Neural pathways of pain and sites of action of analgesics and other agents



Opioid analgesics

The principal active ingredient in crude opium was isolated in 1806 by Friedrich Serturner. The analgesic effects of opioids are due to decreased perception to pain, decreased reaction to pain, as well as increased pain tolerance. An opioid is a chemical that works by binding to opioid receptors which are principally found in CNS and GIT. The principal classes of opioid receptors are μ, κ, δ and orphanin FQ which are GPCRs acting on GABAergic neurotransmission. The pharmacodynamic response to an opioid depends on which receptor it binds, its affinity for that receptor and whether the opioid is an agonist or an antagonist.

The side effects include sedation, respiratory depression and constipation. Physical dependence can develop with ongoing administration of opioids, leading to withdrawal syndrome with abrupt discontinuation. Opioids can produce a feeling of euphoria and this effect coupled with physical dependence can lead to recreational use of opioids by some individuals. The withdrawal symptoms include severe dysphoria sweating, nausea, rhinorrhoea, depression, severe fatigue, vomiting and pain.

They are used in acute pain, on malignant chronic pain, induction and maintenance of anesthesia, cough (codeine), diarrhea (loperamide), and anxiety due to shortness of breath (oxymorphine), pulmonary edema (morphine).

Non opioid analgesics

NSAIDs are used to treat mild to moderate pain and may by combined with opioids to treat moderate to severe pain. They also reduce inflammation that often accompanies and worsens the pain. They provide symptomatic relief from pain and swelling in chronic joint disease such as rheumatoid arthritis and in more acute inflammatory conditions. They also provide relief from post operative pain, dental and menstrual pain and from pain of headaches and migraine. As several NSAIDs are available over the counter they are often taken without prescription for minor aches and pain.

The three main therapeutic effects are anti inflammatory, analgesic and antipyretic effect. The main side effects include gastric irritation; prolong bleeding time, skin reactions, analgesic associated nephropathy, bronchospasm, liver disorders, bone marrow depression.

Uses: for analgesia, anti inflammatory effect, to lower temperature, cardiovascular disorders, radiation induced diarrhea, colonic and rectal cancer, pregnancy induced hypertension, cerebral infarction, transient cerebral ischemia.