## Introduction to pain

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| **Definition of pain** | An unpleasant sensory & emotional experience associated with actual/potential tissue damage |
| **Purpose of pain** | 1. As a protective mechanism |
| | 2. Cause individual to react to remove pain stimulus |

## Nociceptive pain mechanism

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| | Wide spread in superficial layers of skin & certain internal tissues |
| | Excited by 3 different stimuli : mechanial, thermal, chemical |
| | Pain is related to degree of receptor stimulation by processes causing tissue injury (more receptor stimulated=more pain) |
| **2 nociceptor systems** | 1. A delta fibres (faster) |
| | 2. C fibres (slower) |
| **Chemicals that stimulate nociceptors** | Histamine |
| | Bradykinins |
| | 5-HT (serotonin) |

## Nociceptive pain mechanism (cont)

| | | |
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| | some metabolic substances released from damaged cells (lactic acid,ATP) | |
| **Sources of nociceptive pain** | Somatic pain | |
| | Visceral pain | Pain from internal structures, poorly localised, often radiates or referred to other areas |

## Neuropathic pain

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| Pain resulting from pathophysiologic changes in peripheral or CNS |
| A state of chronic pain is sustained |

## Idiopathic pain

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| Patient's psychological state contribute to pain | May be due to anxiety,depression, other psychological disorders |

## Pharmacotherapy in management of pain

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| 1. Opioid analegesics |
| 2. NSAIDs |
| 3. Local anaesthetics |
| 4. Alpha 2 agonists |

## Opioids

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| **MOA** | Binds to opioid receptors and inhibit action on neurons |

## Opioids (cont)

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| **Type of opioid receptors** | 1. Mu receptors | effects: analgesia,respiratory&physical depression,miosis,reduced GI motility |
| | 2. Kappa receptors | effects: sedation,-miosis |
| | 3. Delta receptors | effects: dysphoria,hallucinations |

## Classification of opioids

| | |
|---|---|
| **Strong agonists** | Morphine |
| | Pethidine |
| | Methadone |
| | Fentanyl |
| | Sufentanil/Alfentanil |
| **Mild to moderate agonists** | Codeine |
| **Mixed agonist-anatagonists** | Pentazocine |
| | Buprenorphine |

## Strong agonist opioid's desirable effects

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| **Analgesia** | Centrally mediated |
| | Alters emotional perception of pain |
| **Sedation** | |
| **Sense of well being** | |
| **Cough supression** | |
| **Reduce GI motility** | Can help with diarrhoea |

## Strong agonist opioid's adverse effects

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|---|---|
| **Respiratory depression** | Dose related |
| | Most important side effect which limits clinical use |
| **Miosis** | Constriction of pupil |
| | Decreases ability to see in dim light |

## Strong agonist opioid's adverse effects (cont)

| | |
|---|---|
| **Orthostatic hypotension** | |
| **Nausea & vomiting** | |
| **Constipation** | |
| **Anorexia** | |
| **Sedation** | |
| **Development of dependence** | Cause addiction |

Caution:
*Eldery are more prone to adverse effects of narcotic analgescis, thus lower dose is required

## Tolerance of strong agonist opioids

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|---|---|
| **Due to regular/intermittent use** | Regular administration of fixed dose of drug give rise to progressively decreasing effect |
| | Progressively higher dose has to be administered to achieve the same effect |
| **Develops gradually** | |
| **Cross tolerance between opioids** | Will develop tolerance to drugs of similar pharmacological action |

## Clinical uses of strong agonists opioids

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| **Severe pain** | |
| **Pre-medication for anaesthesia** | |
| **Methadone** | Substitution therapy in drug dependence clinics |
| | Chronic use: long term treatment in terminal cancer patients |

## Mild-moderate agonists (CODEINE)

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| **Indications** | Mild-moderate pain | Usually in combination with non-opioid analgesics |
| | Cough supression | At lower dose than that for analgesia |

## Mixed agonist-antagonist opioids

Opioids with full agonist activity at one receptor subtype but behaves like an antagonist or partial agonist at another receptor subtype

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|---|---|
| Examples: | Pentazocine |
| | Buprenorphine |
| **Clinical uses** | Chronic severe pain |
| | Drug abusers |

## Advantages of mixed agonist-antagonist

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| **Less adverse effects mediated by specific receptors** |
| **Less prone to cause dependence and abuse** |

Caution:
*Should not be given to patients that are already on treatment with pure strong agonist as it may precipate severe withdrawal syndrome

## Tramadol

Chemically unrelated to other opioid drugs

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| **MOA** | Partial mu agonist | Less affinity than morphine |
| | Inhibition of serotonin and noradrenaline reuptake | Levels of serotonin&noradrenaline increase |
| | Block nociceptor impulse at spinal level | |
| **Clinical use** | Mild to moderate pain | |
| **Adverse effects** | Less constipation,less respiratory depression,less dependence than opioids | |
| | Dizziness,sedation,nausea,vomiting | |
| | Constipation,headache | |

## Counselling points for opioids

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| **Drug may cause drowsiness,dizziness,blurring of vision** | Do not drive or operate heavy machinery |
| **Avoid alcohol** | |
| **If patient experience GI effects** | Drug can be taken with food |
| **Seek medical attention if** | Experience severe nausea,vomiting,constipation |