

Second 2008  
VIVA 4

This station will explore the pharmacology related to analgesic medications.

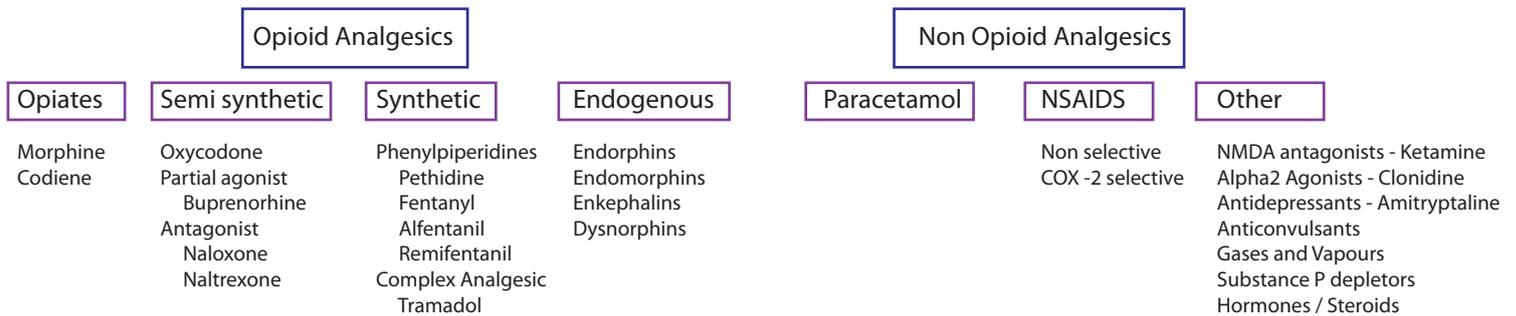
How will you classify non opioid analgesic agents?

This viva explored the candidates' knowledge in relation to the following points

Classification of non opioids, mechanism of actions of non opioids

Classification of opioids, mechanism of action, some aspects of their general pharmacology, contrasting fentanyl and morphine, tolerance to opioids

**"Please provide a classification scheme for analgesics"**



**"What are Opioids?"**

are drugs which act of opioid receptors to produce opiate like responses

they are both naturally occurring and synthetic

most have the general phenanthrene structure - three ringed nucleus, piperidine ring & tertiary amine

**"Please describe Opioid receptors"**

are a family of GPCR ( $G_{i_a}$  and  $G_{o_d}$ )

there are three major classes, delta ( $\delta$ ), kappa ( $\kappa$ ), and mu ( $\mu$ )

in general they are inhibitory via adenylyl cyclase reduction, also K channels ( $\delta$  and  $\mu$ ) Ca Channels ( $\kappa$ )

most clinically used opioids are selective for mu receptors which have three sub types

delta receptors have two subtypes with similar actions to mu, but there are no selective drugs currently

kappa receptors have three subtypes, significant side effects; dysphoria, psychotomimetic, diuretic

**"Describe the comparative pharmacology of the opioids"**

duration of effect is dependent on; delivery route, rate of clearance, active metabolites and lipid solubility

high lipid solubility rapidly cross the BBB, but due to redistribution have a rapid offset as well

pKa determines the % ionised, unionised drugs cross the BBB quicker

**"Please give a brief overview of the main differences between morphine, fentanyl, and remifentanil"**

Fentanyl

is a weak base, pKa 8.4 therefore at physiological pH is mostly ionised

it is extremely lipid soluble however (up to 600 times more soluble relative to morphine)

when bolus dosed has a rapid onset and offset due to redistribution

it has clearance of similar to morphine but a large Vd therefore increase context sensitive half time

is 50-100 times more potent than morphine

Morphine

is a weak base pKa 8.0 therefore at physiological pH is mostly ionised

has rapid clearance of 30mg/kg/min

volume of distribution is similar to fentanyl at 3 L/kg (steady state)

Remifentanil

is a weak base, pKa 7.1 therefore is less than 50% ionised at physiological pH (quicker onset)

equal potency to fentanyl 50-100 times morphine, but only 50 times lipid solubility c/w morphine

metabolised very rapidly by plasma esterases, independent of renal/hepat clearance 40mg/kg/min

**"Please discuss the classification of NSAIDS"**

classification based on cyclooxygenase selectivity, reversibility and chemical structure

salicylates (aspirin), arylpropionic acid (ibuprofen), arylacetic acid (diclofenac), oxicams (meloxicam)

IV options tenoxicam, ketorolac, parecoxib, rapid absorption, small Vds, highly protein bound

COX1 production of prostaglandins, and thromboxane synthesis. COX2 inflammation, COX3 central temp