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"

Opioid Analgesics

Opiates
- Morphine
- Codiene

Semi synthetic
- Oxycodone
- Partial agonist
  - Buprenorhine
- Antagonist
  - Naloxone
  - Naltrexone

Synthetic
- Phenylpiperidines
  - Pethidine
  - Fentanyl
  - Alfentanil
  - Remifentanil
- Complex Analgesic
  - Tramadol

Endogenous
- Endorphins
- Endomorphins
- Enkephalins
- Dysnorphins

Non Opioid Analgesics

Paracetamol

NSAIDS
- Non selective
- COX -2 selective

Other
- NMDA antagonists - Ketamine
- Alpha2 Agonists - Clonidine
- Antidepressants - Amitryptaline
- Anticonvulsants
- Gases and Vapours
- Substance P depletors
- Hormones / Steroids

"What are Opioids?"

are drugs which act of opioid receptors to produce opiate like responses
they are both naturally occuring and synthetic
most have the general phenanthrene structure - three ringed nucleus, piperidine ring & tertiary amine

"Please describe Opioid receptors"

are a family of GPCR ($G_{i\alpha}$ and $G_{o\alpha}$)
there are three major classes, delta (δ), kappa (κ), and mu (μ)
in general they are inhibitory via andenylyl cyclase reduction, also K channels (δ and μ) Ca Channels (κ)
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 then 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 solubity 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 cycloxygenase selectivity, reversibility and chemical structure
salicylates (aspirin), arylpropionic acid (ibuprofen), arylacetic acid (diclofenac), oxicams (meloxicam)
IV options tenoxicam, ketorolac, parecoxib, rapid absortion, small Vds, highly protien bound
COX1 production of prostaglandins, and thromboxane synthesis. COX2 inflammation, COX3 central temp