

Analgesic Drugs

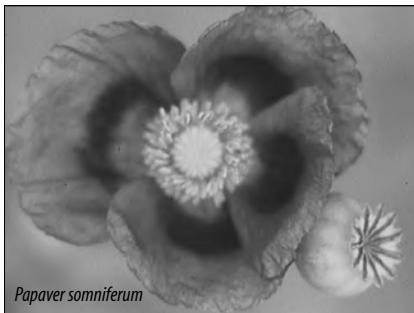
Opioids

analgesic drugs

- opioids
- NSAIDs
- $\alpha 2$ agonists
- local anaesthetics
- others

opioids

- opiates
 - from opium
 - morphine, codeine
- opioids
 - anything which binds to opioid receptors and can be displaced by naloxone



Papaver somniferum



opioid receptors

	<i>endogenous ligands</i>	<i>main effects</i>
μ	β endorphin, endomorphins	analgesia, respiratory depression, euphoria
δ	enkephalins	analgesia, hormonal effects
κ	dynorphins	analgesia, dysphoria, diuresis
(σ ?)		psychotic effects, analgesia?)
(ORL1	nociceptin	increases pain??)

new names

- μ = MOP (μ opioid peptide)
- δ = DOP
- κ = KOP
- ORL₁ = NOP

receptor subtypes

?

μ agonists

- morphine
- (heroin)
- pethidine (=meperidine USAN)
 - pethidine derivatives
- methadone

phenylpiperidines

- fentanyl
- alfentanil
- carfentanil
- sufentanil
- lofentanil
- remifentanil, etc

morphine effects

- analgesia
- euphoria

μ receptor effects

- open K⁺ channels
- close Ca⁺⁺ channels
- direct inhibition of neurotransmitter release?

morphine's sites of action

- spinal cord
- thalamus
- periaqueductal grey matter
- nucleus raphe magnus
- ventral tegmental area
- cortex?
- peripheral nerves?
- macrophages?

side effects

- vomiting
- sedation / excitation
- euphoria
- gut effects
- muscle rigidity
- respiratory depression
- urinary retention
- cough suppression

more side effects

- increased intra-cranial pressure
- histamine release
- bradycardia
- miosis
- addiction

morphine pharmacokinetics

- **poor systemic availability po**
 - bioavailability 20%
- **fat soluble**
- **metabolised by glucuronidation**
 - cats!
- **eliminated by kidney and in bile**
 - enterohepatic recirculation!
- **elimination variable**

indications

- **strong analgesia**
- **anaesthesia premed**
 - give before pain starts if possible!
- **diarrhoea**
- **coughing**

contra-indications

- **severe head injury**
- **upper respiratory tract injury**
- **unconsciousness?**

morphine dose

- **all species 0.1 – 1mg/kg sc/im**
- **only one dose in cats**
- **use low dose in horses**

tolerance

- increased metabolism
- decreased receptor affinity
- receptor down regulation
- receptor – effector uncoupling
- effector system adaptation
- neuronal plasticity

dependence

- physical
 - withdrawal syndrome
- psychological
 - operant conditioning

red tape

- most useful drugs are controlled under the Misuse of Drugs Act
 - must be locked away
 - use recorded
 - given by a vet
 - (much) more later in the course

other drugs

- methadone
- pethidine
- fentanyl & analogues

phenylpiperidines

- fentanyl
- alfentanil
- carfentanil
- sufentanil
- lofentanil
- remifentanil, etc

mixed agonists

	μ	δ	κ	σ
butorphanol	~(++)		(++)	+
buprenorphine	(+++)	0	(+)?	0
nalbuphine	-	-	(++)	+?
pentazocine	-	+	++	+
etorphine	+++	+++	+++	0
tramadol				

severe pain

- morphine
- methadone
- fentanyl

moderate pain

- morphine
- methadone
- buprenorphine
- (butorphanol)

anaesthetic premed

- morphine
- (pethidine)
- (butorphanol)

intra-op analgesia

- fentanyl
- alfentanil

chemical immobilisation

- carfentanil
- etorphine

routes

- iv (care with morphine in dogs)
- im / sc
- intra-articular
- epidural / intrathecal
- po

antagonists

- **naloxone**
 - have some handy when using carfentanil or etorphine
- **naltrexone**
- **partial agonists**
 - diprenorphine
 - levorphanol

other uses

- **diarrhoea**
 - loperamide
 - diphenoxylate
 - codeine
- **coughing**
 - codeine
 - butorphanol

What do you do?

- 9yr old labrador
- lung lobectomy
- premed morphine & sedative
- anaesthesia – thio & halothane
- still responds to surgery



opioids

- the main group of strong analgesics
- main effects – analgesia & euphoria, interact with anaesthetics to increase depth
- side effects vomiting and possible respiratory depression, but not usually in animals in pain
- overdose causes excitement in cats and horses
- metabolised slowly in cats
- if in doubt about an animal's pain – give morphine