Analgesic Drugs

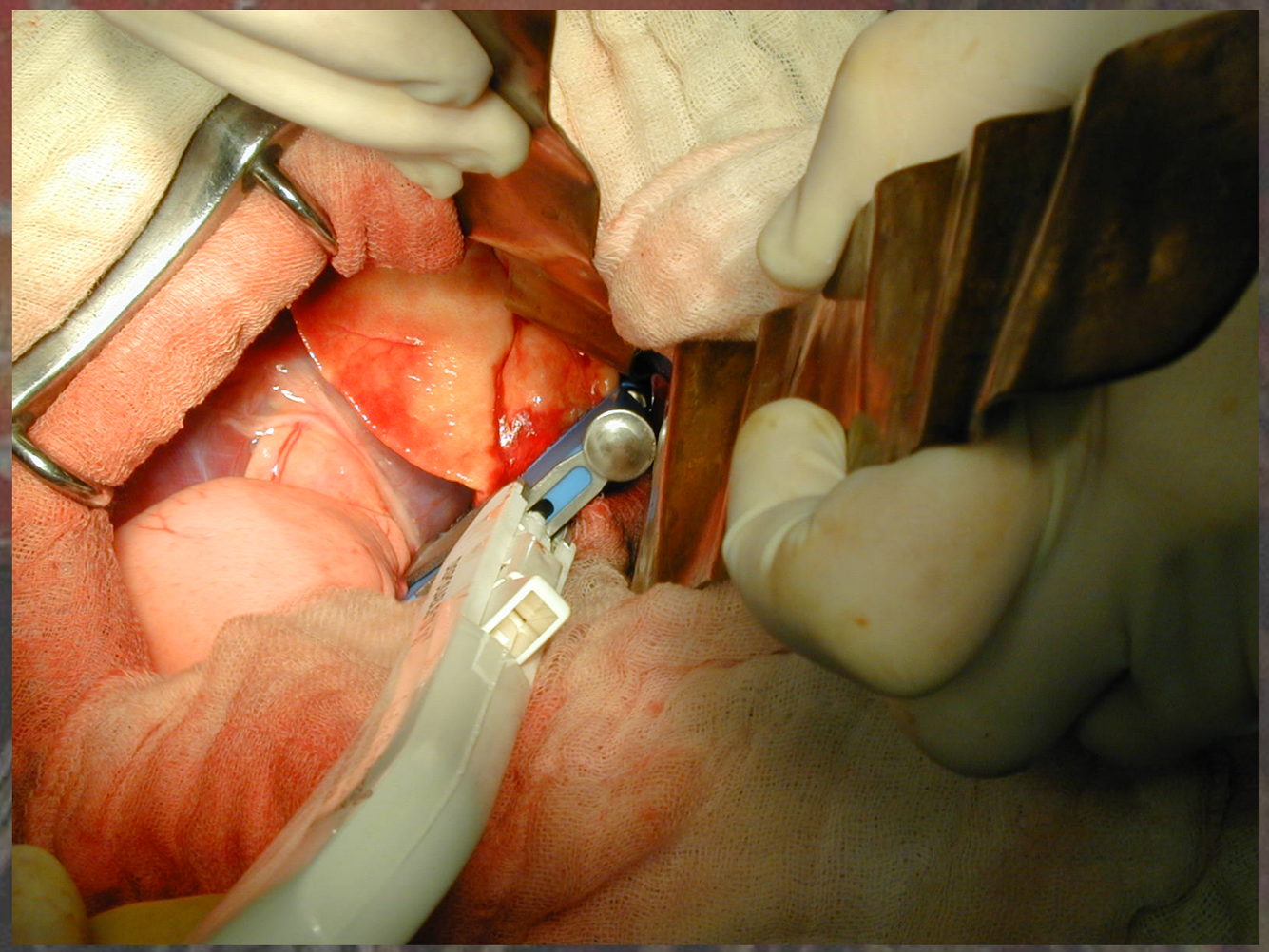
Opioids

by the end of this lecture you should be able to

- formulate an analgesia plan using opioids
- know when the plan needs to be adjusted

What do you do?

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



analgesic drugs

- opioids
- NSAIDs
- α2 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

	endogenous ligands	*main effects*
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
- ORL_1 = NOP

receptor subtypes

?

μ agonists

- morphine
- (heroin)
- pethidine (=meperidine USAN)
  - – pethidine derivatives
    - phenylpiperidines
- 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
  - dogs!
- bradycardia
- miosis
  - not cats
- addiction

morphine pharmacokinetics

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

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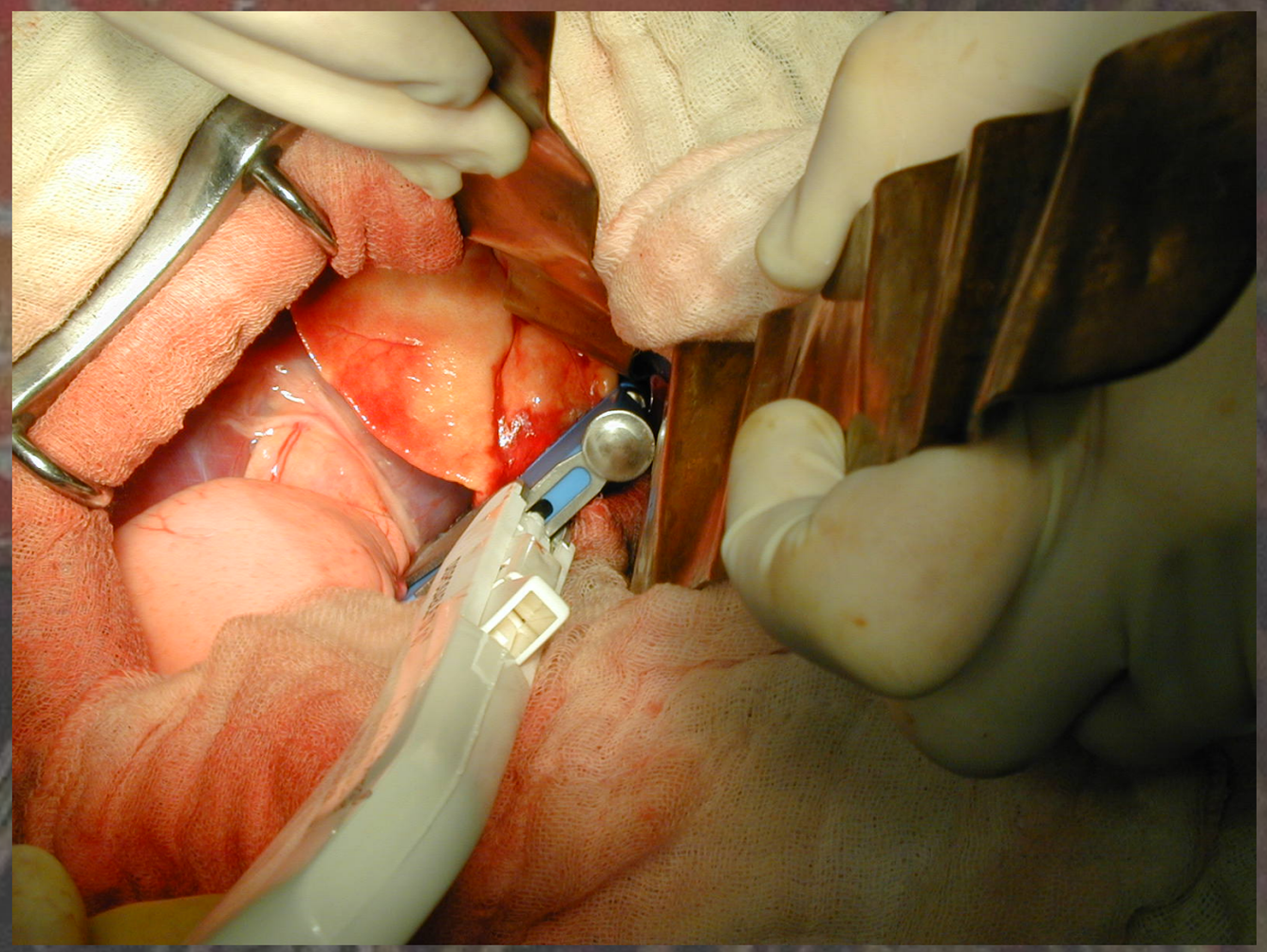

indications

- 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
- care with more than one dose in cats
- use low dose in horses

tolerance

- increased metabolism
- decreased receptor affinity
- receptor down regulation
- receptor - effector uncouplinng
- 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				

tramadol

- one of its stereoisomers is a μ agonist
  - M1 metabolite more potent
  - dogs do not produce M1
- other isomer is a monoamine reuptake inhibitor
- dysphoria in some people & cats

severe pain

- morphine
  - 90c
- methadone
  - $9.50
- fentanyl
  - 30c

moderate pain

- morphine
- methadone
- buprenorphine
- (butorphanol)

anaesthetic premed

- morphine
- (pethidine)
- (butorphanol)

intra-op analgesia

- fentanyl
- alfentanil
- remifentanil

chemical immobilisation

- carfentanil
- etorphine

routes

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

antagonists

- naloxone
  - have some handy when using carfentanil or etorphine
  - someone you trust to give you an iv injection!!
- naltrexone
- partial agonists
  - diprenorphine
  - levorphanol

other uses

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

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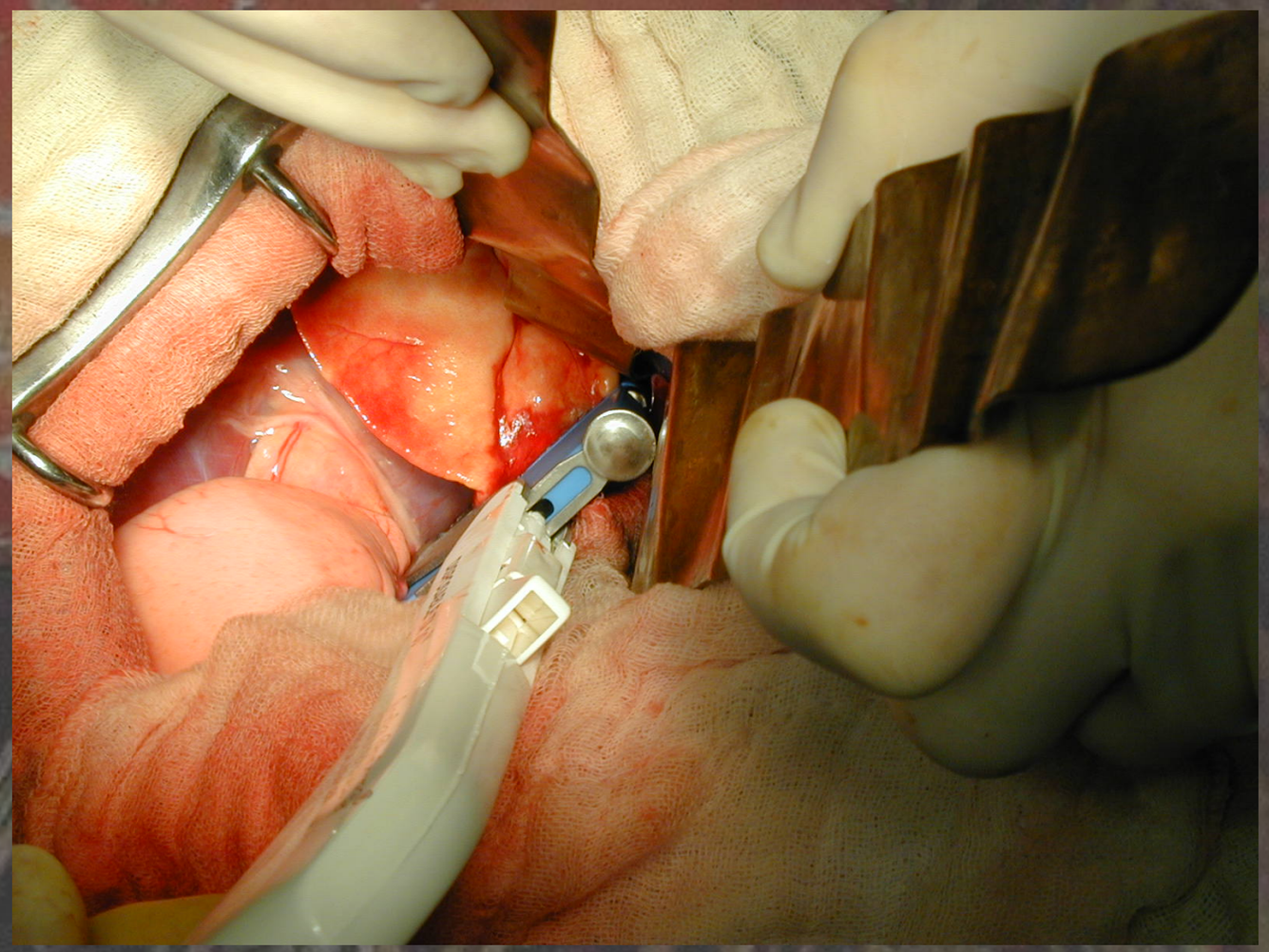

opioids

- 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 excitment in cats and horses
- metabolised slowly in cats
- if in doubt about an animal's pain - give morphine