

A photograph of a red mushroom with white spots, likely a fly agaric, growing in a field of dry grass. The mushroom is the central focus, with its bright red cap and white spots standing out against the muted, brownish-green background of the grass. The text is overlaid on the mushroom's cap.

Analgesic Drugs

Opioids

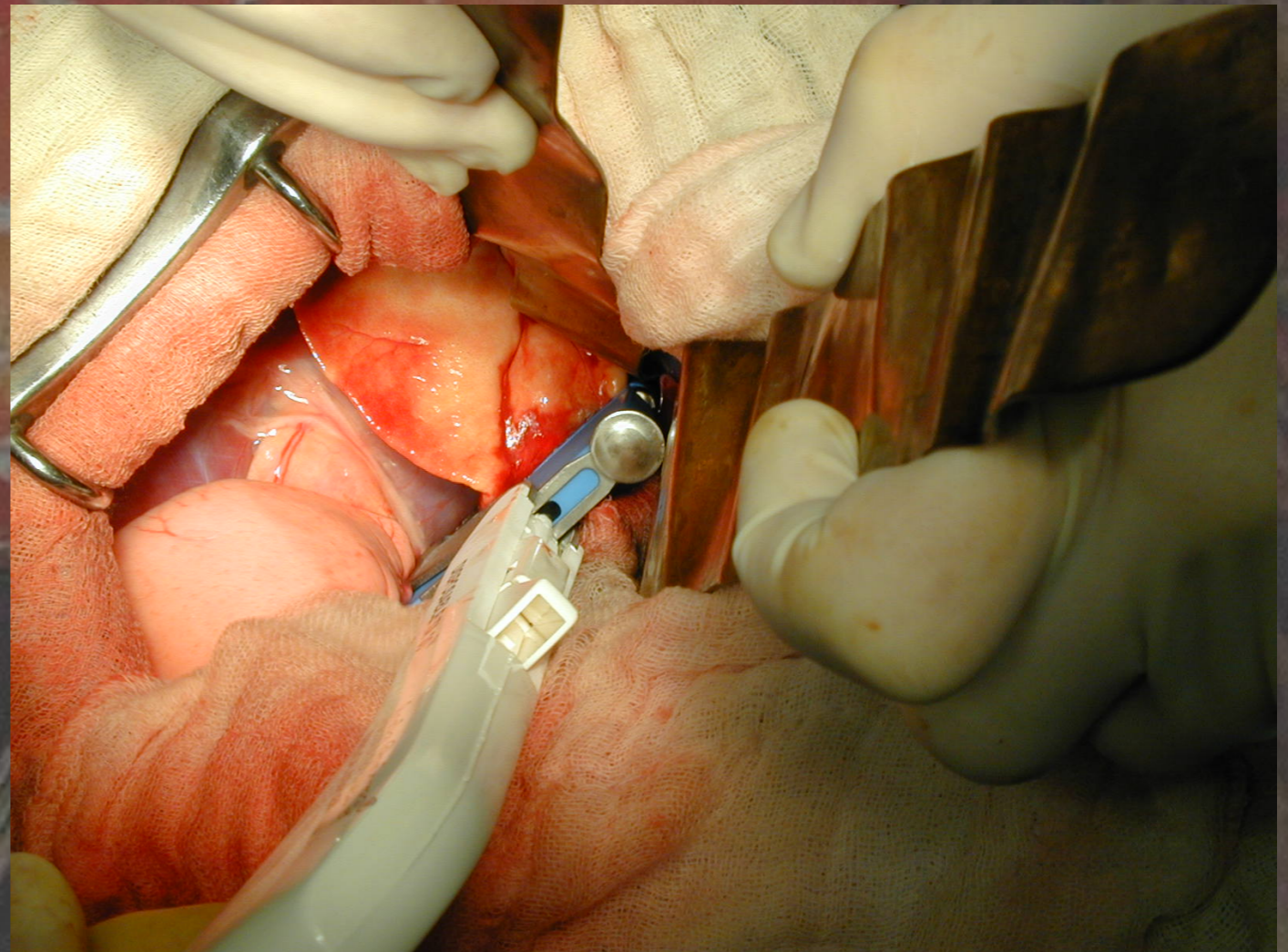
A red mushroom with white spots is the central focus of the image, resting on a bed of dry pine needles. The background is a dense layer of these needles, creating a textured, natural setting. The lighting is soft, highlighting the texture of the mushroom's cap and the surrounding needles.

**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**
- **$\alpha 2$ 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

endogenous ligands

μ β endorphin, endomorphins

δ enkephalins

κ dynorphins

(σ ?)

(**ORL1** nociceptin)

main effects

analgesia, respiratory depression, euphoria

analgesia, hormonal effects

analgesia, dysphoria, diuresis

psychotic effects, analgesia?)

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

A large, red, gilled mushroom with white spots on its cap, growing on a bed of dry pine needles. The mushroom is the central focus of the image, with its cap showing a gradient from red to orange. The background is a dense layer of dry, brown pine needles.

- **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**

A large, bright red mushroom with white spots, growing on a bed of dry pine needles. The mushroom is the central focus of the image, with its vibrant red color contrasting sharply with the muted, brownish tones of the surrounding pine needles. The text 'side effects' is overlaid on the upper part of the mushroom's cap.

side effects

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

more side effects

A large, red, mushroom-shaped object with white spots, possibly a mushroom or a piece of wood, resting on a bed of dry grass. The object is the central focus of the image, with its cap showing a gradient from red to orange and yellow, and white spots scattered across its surface. The stem is short and thick. The background is a dense layer of dry, brown grass.

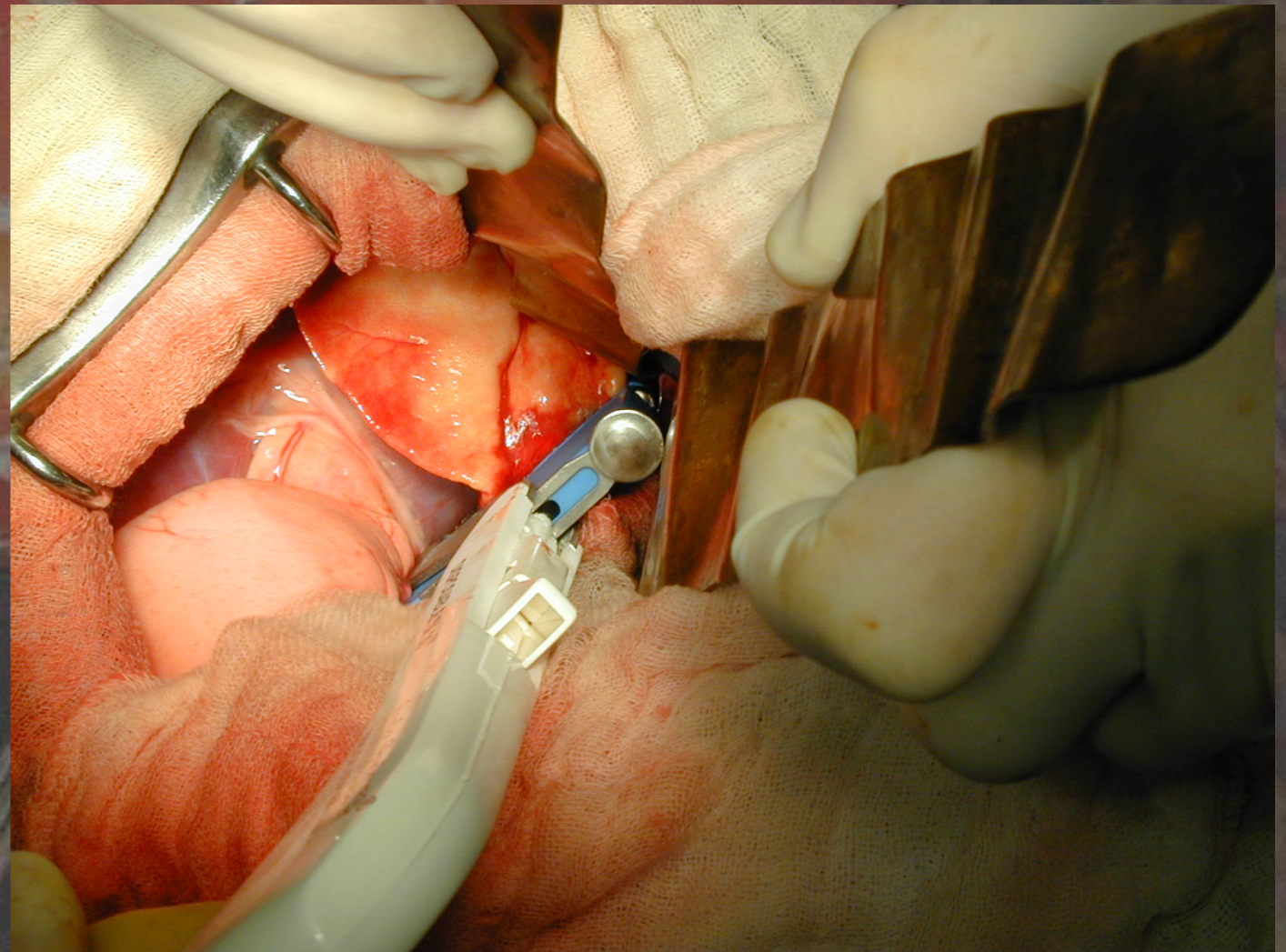
- increased intra-cranial pressure
- histamine release
 - dogs!
- bradycardia
- miosis
 - not cats
- addiction

morphine pharmacokinetics

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

What do you do?

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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 uncoupling**
- **effector system adaptation**
- **neuronal plasticity**

dependence

A large, red, spotted mushroom with a white stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots. The stem is thick and white. The background is a dense field of dry, brown grass.

- **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

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- **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**

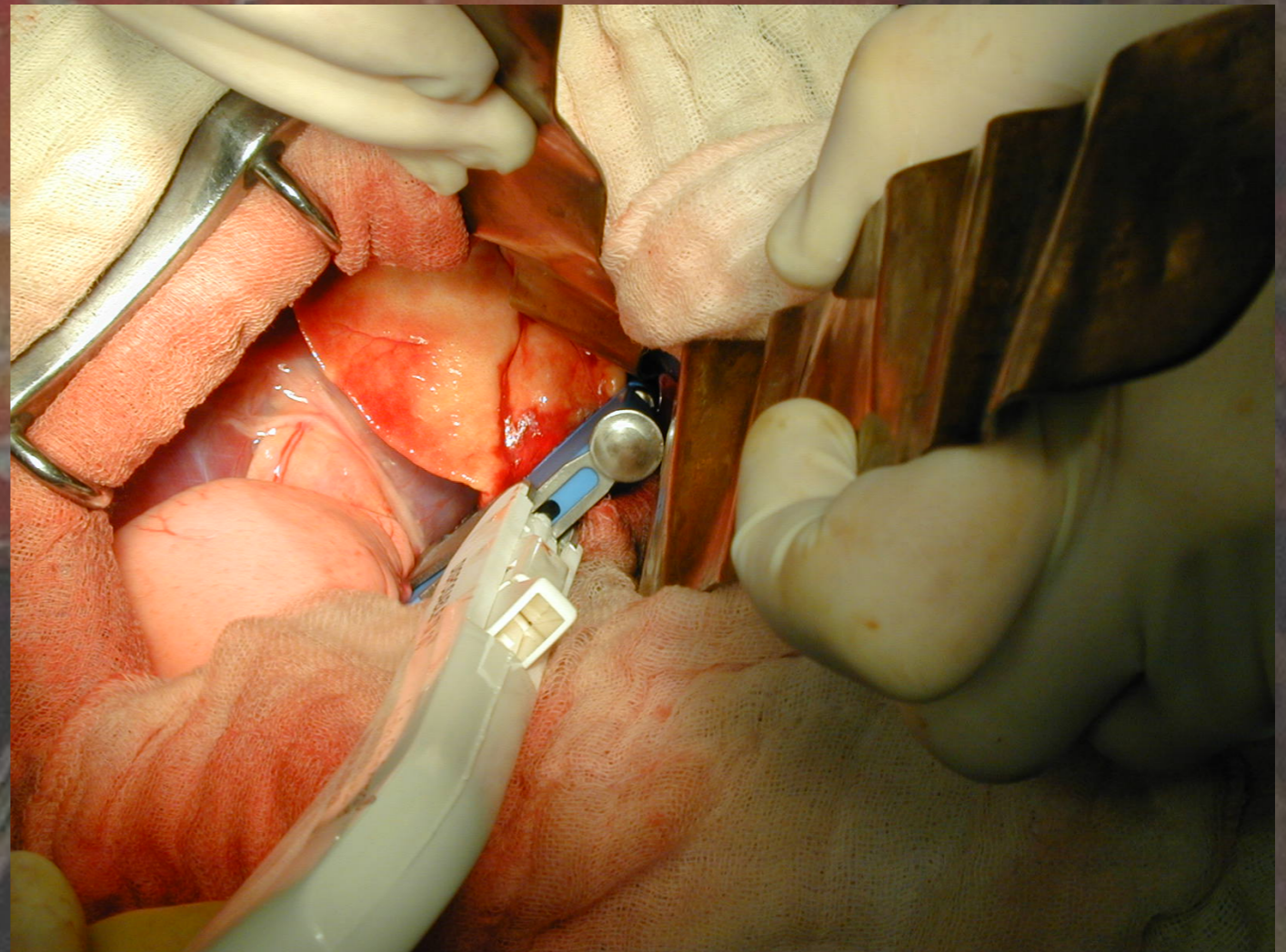


other uses

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

What do you do?

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- anaesthesia - thio & halothane
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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 excitement in cats and horses**
- **metabolised slowly in cats**
- **if in doubt about an animal's pain - give morphine**