

A close-up photograph of a red mushroom with white spots, likely a fly agaric, growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The background is a dense field of dry, yellowish-brown grass.

Analgesics

Less Important Drugs

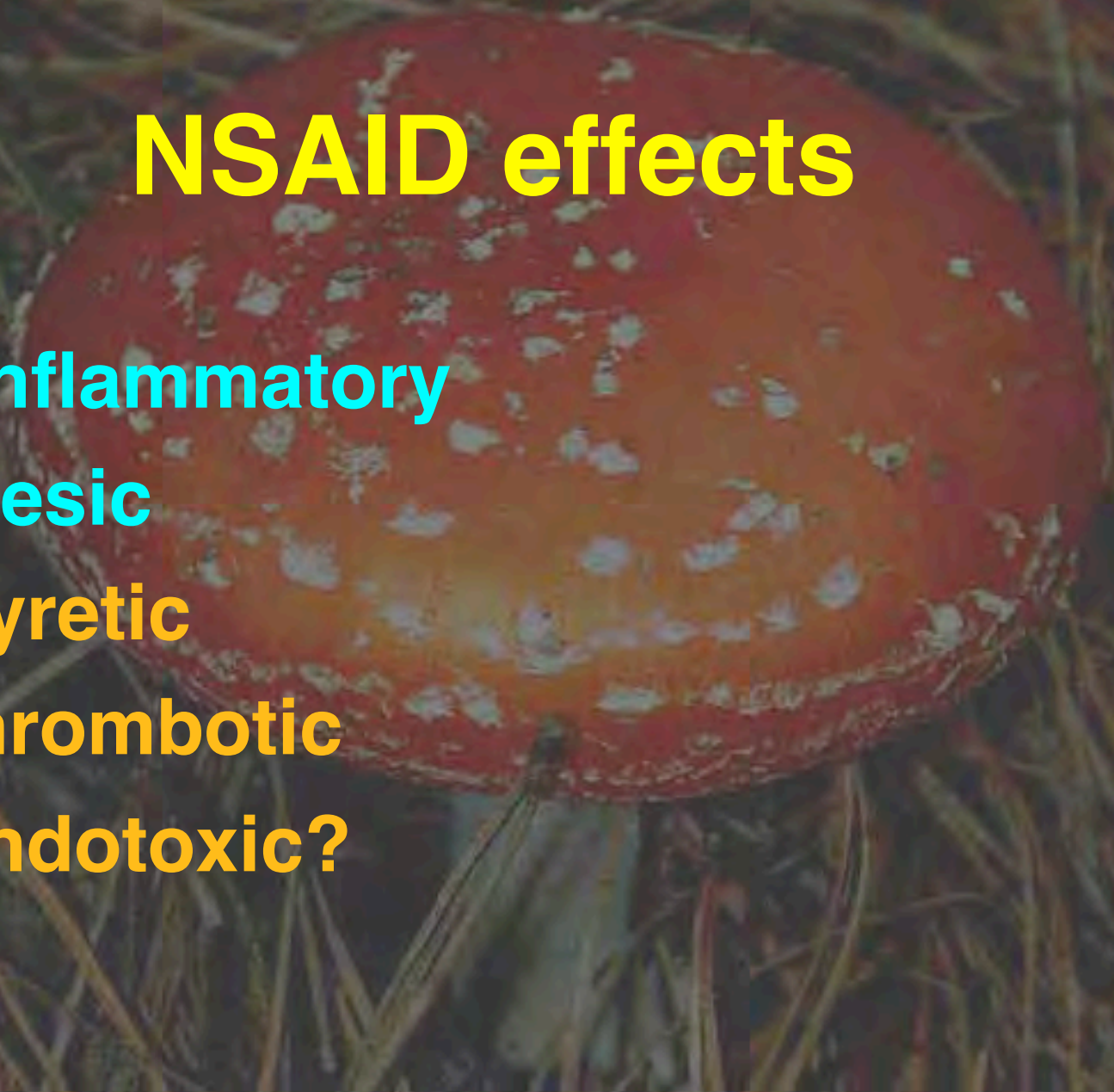
A red mushroom with white spots, likely a fly agaric, is growing in a field of dry grass. The mushroom is the central focus of the image, with its bright red cap and white spots contrasting sharply with the dry, brownish grass. The background is slightly blurred, emphasizing the mushroom.

analgesics

- opioids
- local analgesics
- NSAIDs
- $\alpha 2$ adrenergic agonists
- psychotropics
- odds & sods

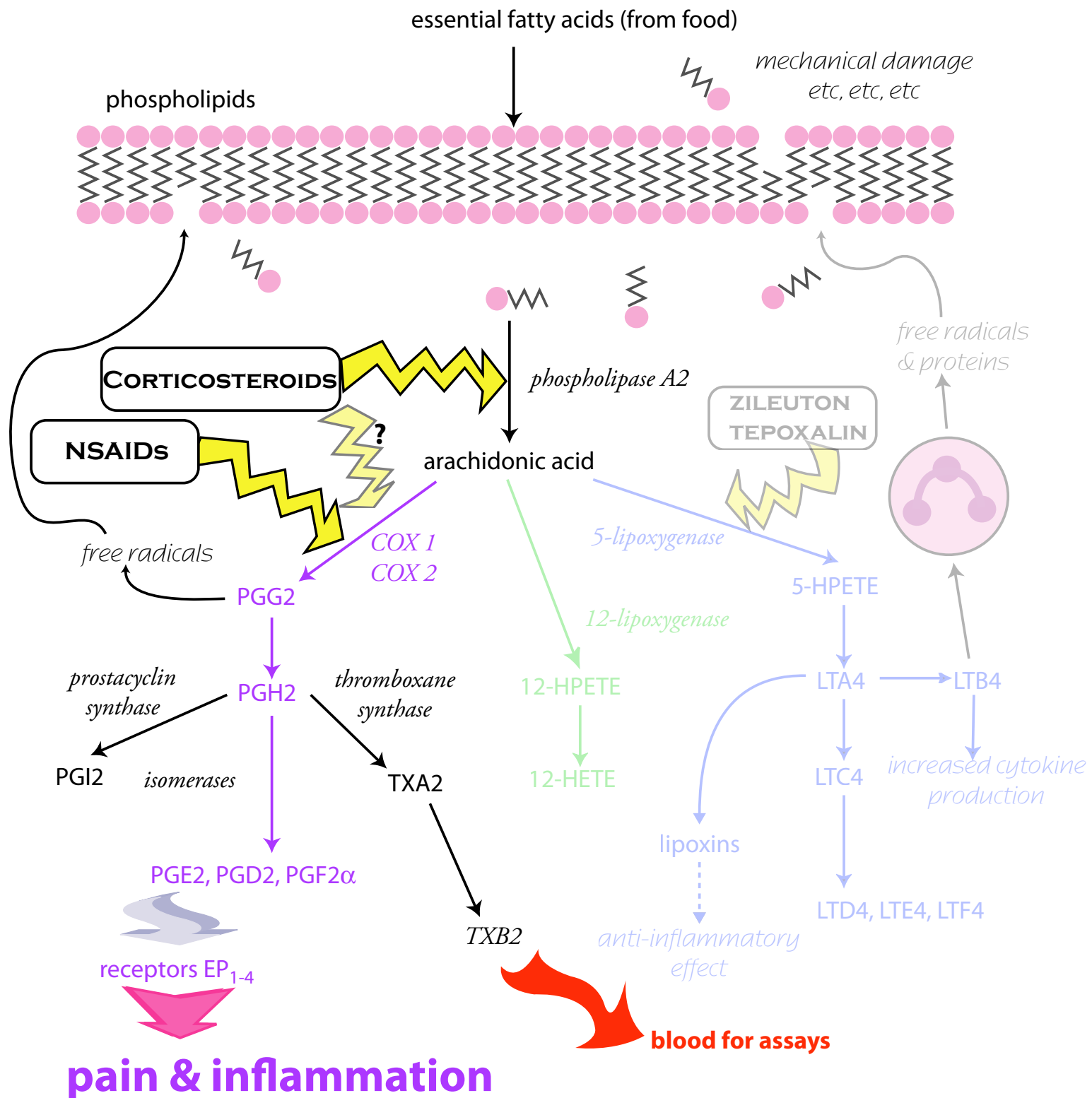
NSAID effects

- anti-inflammatory
- analgesic
- antipyretic
- antithrombotic
- antiendotoxic?



NSAID mechanism

- COX inhibition
- free radical scavenging
- receptor antagonism
- lipoxxygenase inhibition
- etc



cyclo-oxygenase

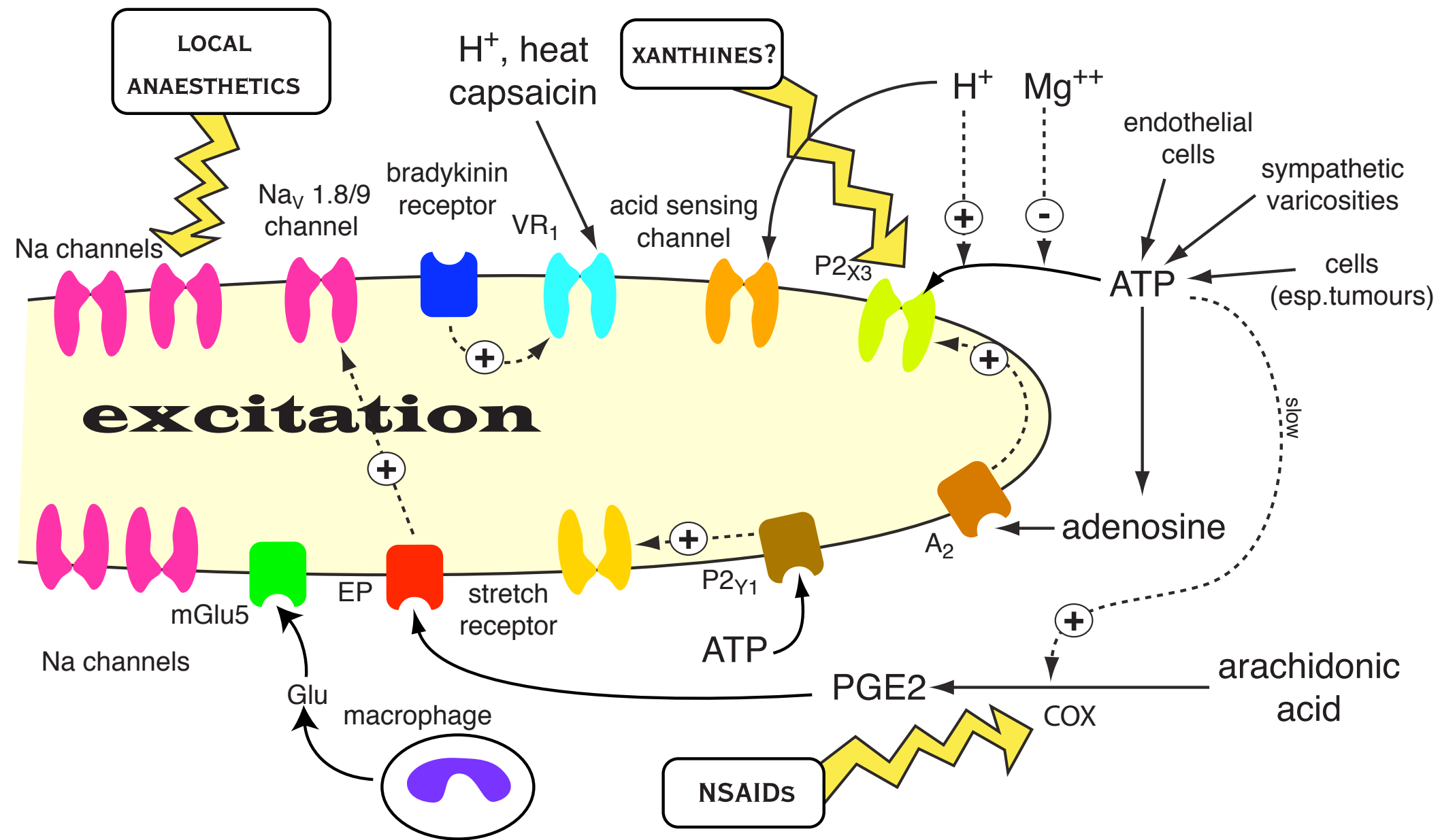
A red mushroom with white spots, likely a fly agaric (Amanita muscaria), is growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The background is a dense field of dry, yellowish-brown grass.

- COX inhibition
- free radical scavenging
- receptor antagonism
- lipxygenase inhibition
- etc

prostaglandins

A red mushroom with white spots, likely an Amanita muscaria, is growing in a field of dry grass. The mushroom is the central focus of the image, with its bright red cap and white spots contrasting sharply with the dry, brownish-yellow grass. The background is slightly blurred, emphasizing the mushroom.

- **peripheral**
 - PGs sensitise nociceptors
- **central**
 - PGs used as neuromodulators?

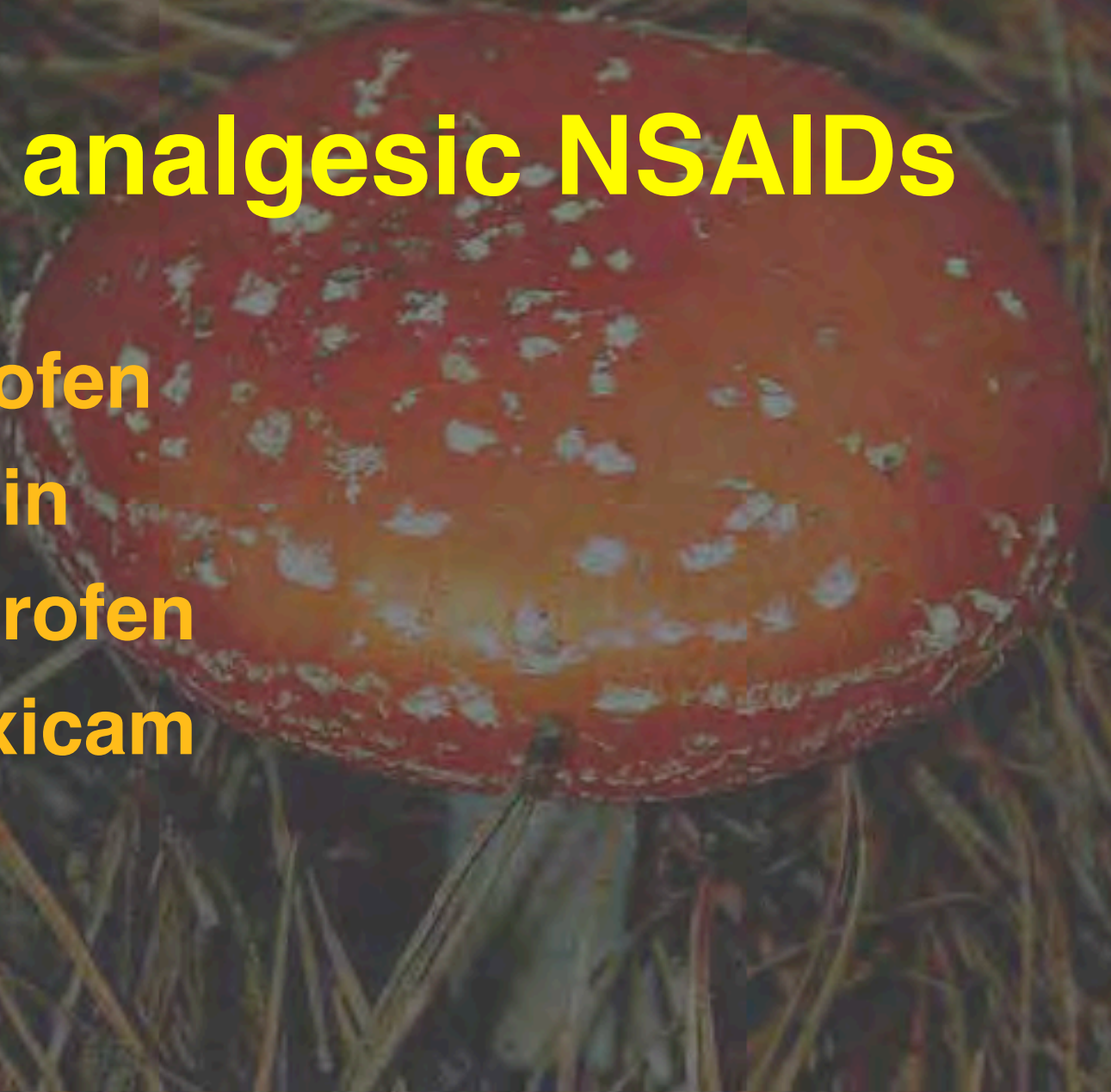


NSAID side effects

- **gastric ulceration**
 - common – not usually serious
 - limits use to about 5 days
- **kidney failure**
 - rare – often fatal
 - occurs when blood pressure drops
- **lots of minor side effects**

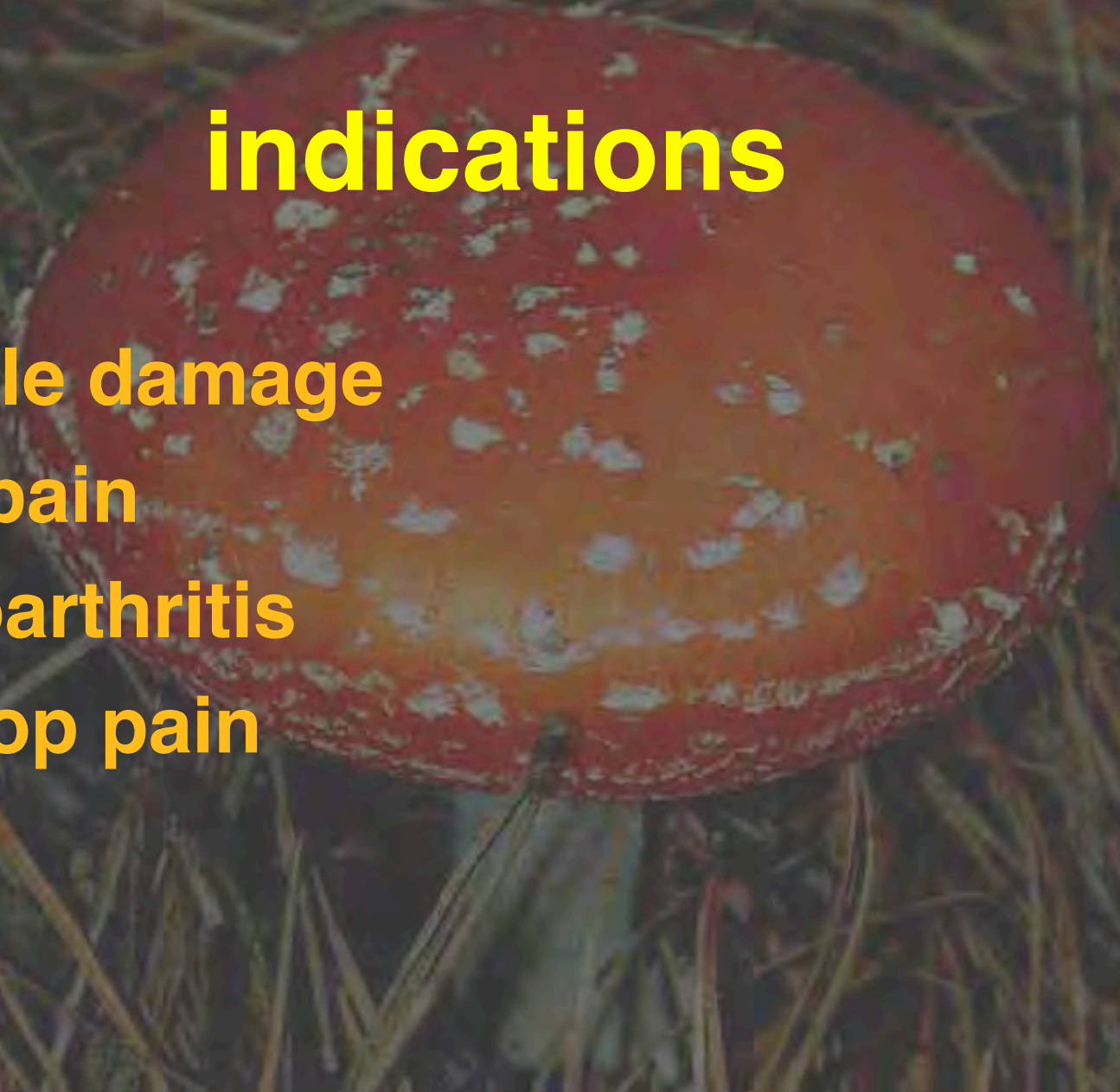
analgesic NSAIDs

- carprofen
- flunixin
- ketoprofen
- meloxicam



indications

- muscle damage
- mild pain
- osteoarthritis
- post op pain
- colic



pharmacokinetics

- **extreme variation between species!!!**
 - **aspirin half life**
 - **cat 22 hours**
 - **cattle 25 minutes**

A large, red mushroom with white spots, resembling a fly agaric, is growing in a field of dry grass. The mushroom has a thick, slightly flattened cap and a thick, white stem. The background is a dense field of dry, yellowish-brown grass.

beware

- cats
 - aspirin & paracetamol
- cattle
 - phenylbutazone
- dogs
 - naproxen

A large, red mushroom with white spots is the central focus of the image. It is growing in a field of dry, yellowish-brown grass. The mushroom has a thick, slightly textured cap and a short, white stem. The background is a soft-focus field of similar grass.

analgesics

- opioids
- local analgesics
- NSAIDs
- $\alpha 2$ adrenergic agonists
- psychotropics
- odds & sods

α_2 effects

- analgesia
- sedation
- bradycardia
- spasm then relaxation of smooth muscle
- skeletal muscle relaxation
- vomiting
- hypothermia

A large, red mushroom with white spots, resembling a fly agaric, is the central focus of the image. It is set against a background of dry, brown grass. The word "drugs" is written in yellow text over the top of the mushroom. To the left of the mushroom, a list of drug names is written in yellow text.

drugs

- **xylazine**
- **detomidine**
- **medetomidine**
 - **dexmedetomidine**
- **romifidine**
- **clonidine**

$\alpha 2$ side effects

- bradycardia
- spasm then relaxation of smooth muscle
 - blood vessels
 - gut
 - uterus
- skeletal muscle relaxation
- vomiting
- hypothermia

$\alpha 2$ side effects

- **ruminants**
 - grunting respiration
 - hypoxia
 - rarely death



mechanism

- **G protein coupled receptors**
- **same effectors as opioids?**
- **increase K^+ conduction**
- **hyperpolarise neurones**
- **also bind to imidazoline Rs**

sites of action

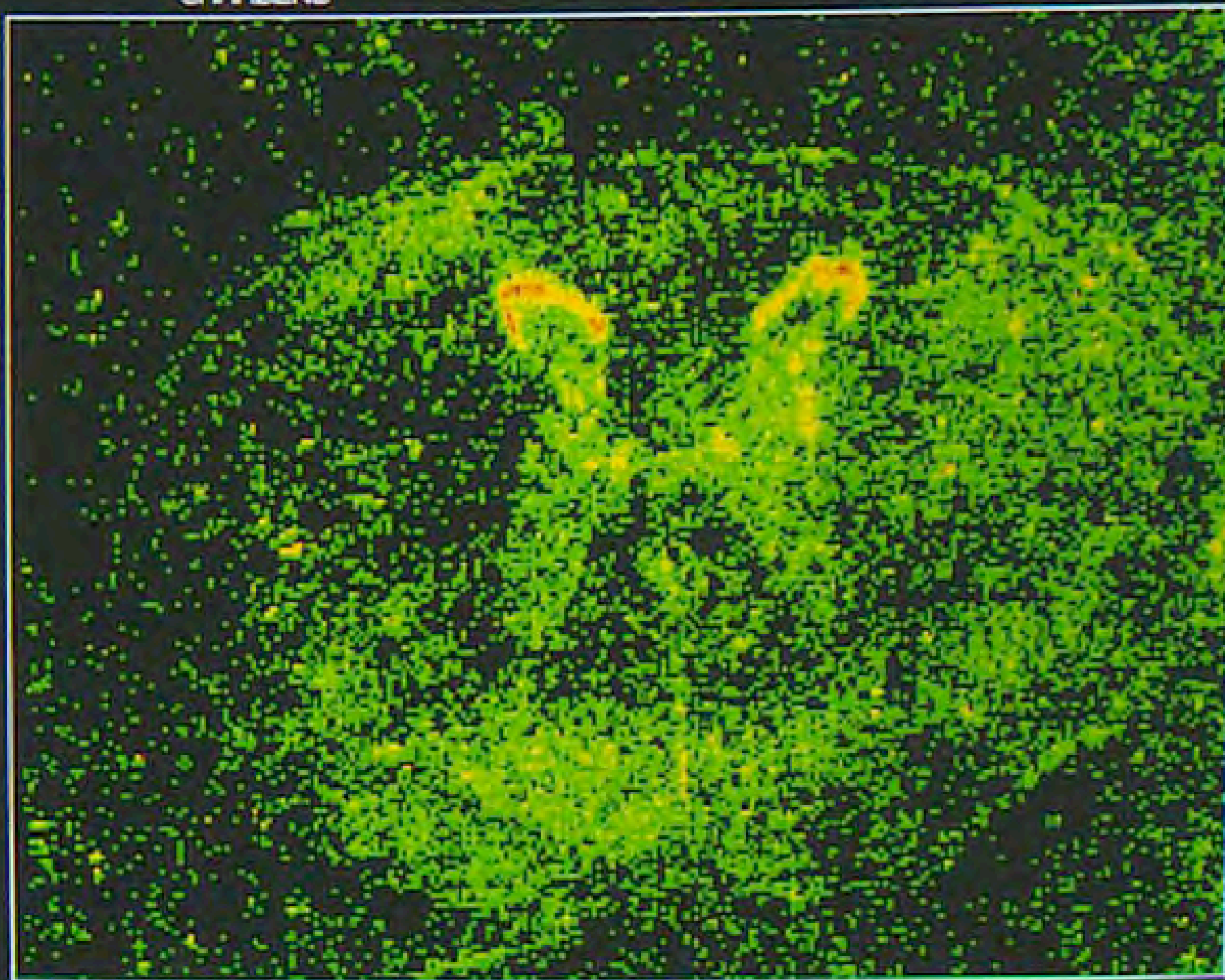
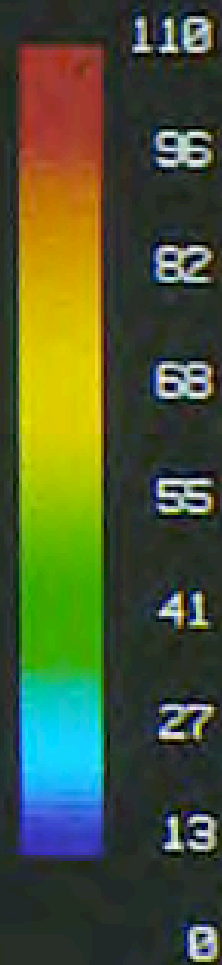
- spinal cord
- locus coeruleus
- cortex?
- medulla
- thoracic cord
- sympathetic varicosities

autoradiography



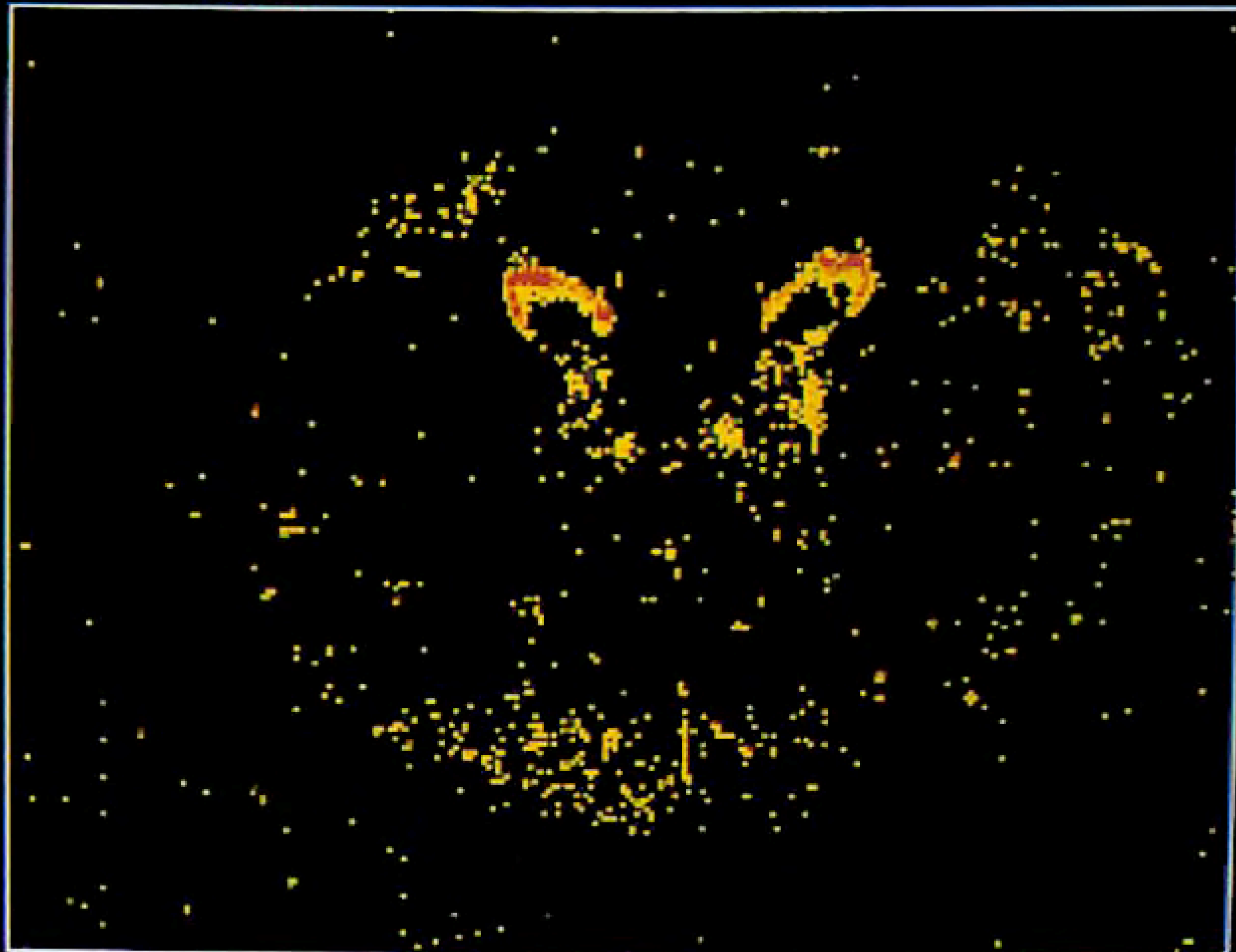
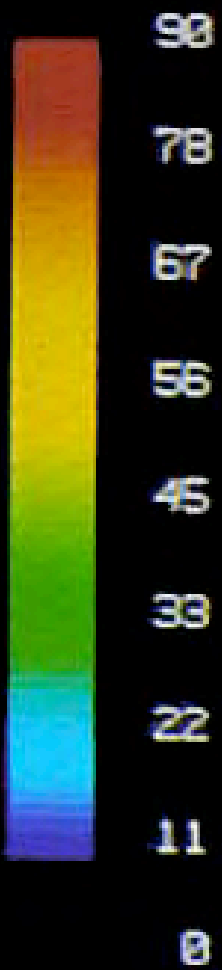
QUANTITATIVE AUTORADIOGRAPHY
ALAN
CHAMBERS

TOTAL
BINDING
fmol/mg



ALAN
CHAMBERS

TOTAL
BINDING
fmol/mg



A red mushroom with white spots, likely a fly agaric, is shown in the background. The mushroom has a bright red cap with numerous white, irregular spots. It is growing in a field of dry, brown grass. The text 'indications' is overlaid on the mushroom's cap in a bold, yellow font.

indications

- minor operations
- deep sedation
- anaesthetic premed
- (induce vomiting)

A red mushroom with white spots on a grassy background. The mushroom is the central focus, with its cap showing a pattern of white spots. The background is a dense field of dry, brown grass.

minor ops

- mainly large animals
- \pm local anaesthetic
- better analgesia at front end??
- ruminants sensitive to xylazine
- hypersensitivity in some deer to xylazine
 - respiratory problems
 - death in extreme cases

sedation / premed

- depth
- duration
- cardiovascular side effects
- interaction with anaesthetics



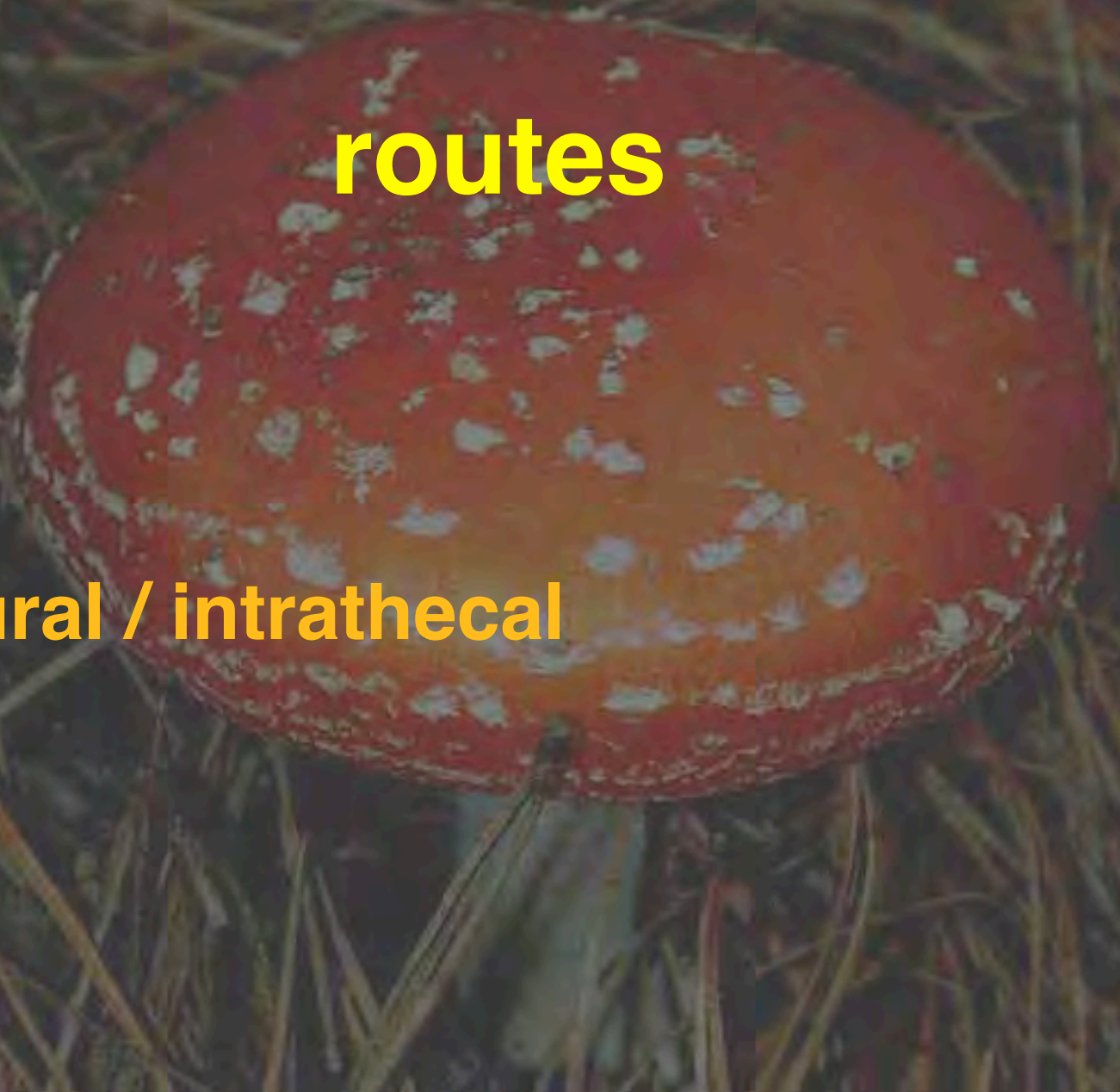
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vomiting

- 30% of dogs
- 40% of cats
 - higher doses – up to 100%

routes

- iv
- im
- epidural / intrathecal



A large, red mushroom with white spots, resembling a fly agaric, is the central focus of the image. It is set against a background of dry, brown grass. The word 'analgesics' is written in yellow text across the top of the mushroom's cap.

analgesics

- opioids
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- NSAIDs
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psychotropics

A red mushroom with white spots, resembling a fly agaric, is growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The background is a dense field of dry, yellowish-brown grass.

- ketamine
- tricyclic antidepressants
 - NMDA antagonists
 - prevent / stop hyperalgesia
- (amantadine)

psychotropics

A large, red mushroom with white spots, resembling a fly agaric, is the central focus of the image. It is set against a background of dry, brown grass. The mushroom's cap is broad and slightly flattened, with numerous white, irregular spots scattered across its red surface. The stem is thick and white, with some darker spots near the base. The overall lighting is soft, highlighting the texture of the mushroom and the surrounding grass.

- **anticonvulsants**
 - carbamazepine
 - phenytoin
- **inhalation anaesthetics**
 - nitrous oxide
 - (trichloroethylene)
 - (methoxyflurane)

A red mushroom with white spots, likely an Amanita muscaria, is growing in a field of dry grass. The mushroom has a bright red cap with numerous white, irregular spots. The stem is thick and appears to be covered in a fine, white, hair-like texture. The background is a dense field of dry, yellowish-brown grass.

others

- **capsaicin**
- **NOS inhibitors?**
- **cannabinoids?**

balanced analgesia

A large, red mushroom with white spots, resembling a fly agaric, is the central focus of the image. It is set against a background of dry, brown grass. The text 'balanced analgesia' is overlaid in yellow at the top, and a list of analgesic categories is overlaid in yellow on the left side.

- opioids
- local analgesics
- NSAIDs
- $\alpha 2$ adrenergic agonists
- psychotropics
- odds & sods

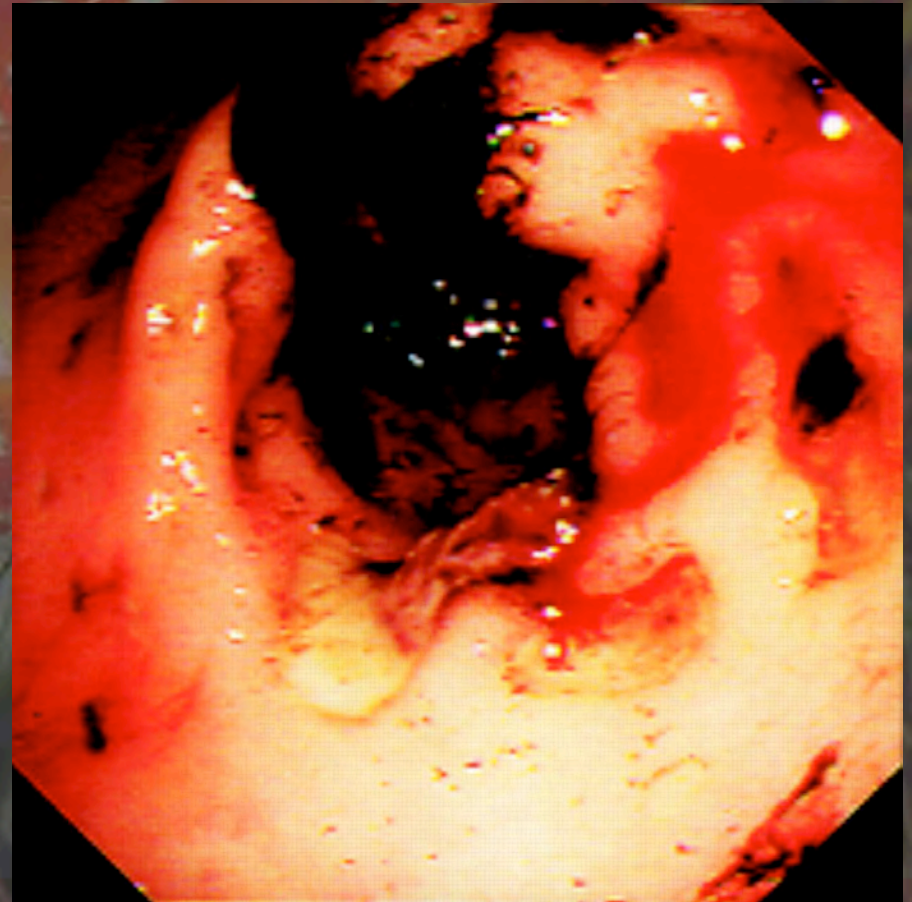
What would you do?

- 7 year old mare
- went lame after heavy work
- now reluctant to use right fore



What would you do?

- 9 year old Lab with arthritis
- off food
- “looking miserable”
- initially improved on ketoprofen



other analgesics

- NSAIDs and $\alpha 2$ agonists most commonly used
- NSAID side effects
 - gastric ulceration
 - kidney failure
- $\alpha 2$ side effects
 - cardiovascular depression
 - vomiting
- combinations, usually with opioids, produce best analgesia with fewest side effects
- remember local anaesthesia!