

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

**Autacoids**



**neurotransmitters**

**neuromodulators**

**inflammatory mediators**





# autacoids

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 have a white or light-colored base. The background is a dense field of dry, yellowish-brown grass.

- 5 hydroxytryptamine
- adenosine
- peptides
- histamine
- eicosanoids
- plus many others



# 5HT

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 white and appears to have a slight constriction at the base. The background is a dense field of dry, yellowish-brown grass.

- gut lining
- platelets
- CNS



A red mushroom with white spots, likely an Amanita muscaria, is centered in the background. The text is overlaid on the image.

# 5HT

- **synthesis, storage, release & uptake very similar to NA**
- **affected by same drugs**
- **co-transmission**
  - **somatostatin**
  - **substance P**
  - **vasoactive intestinal peptide**



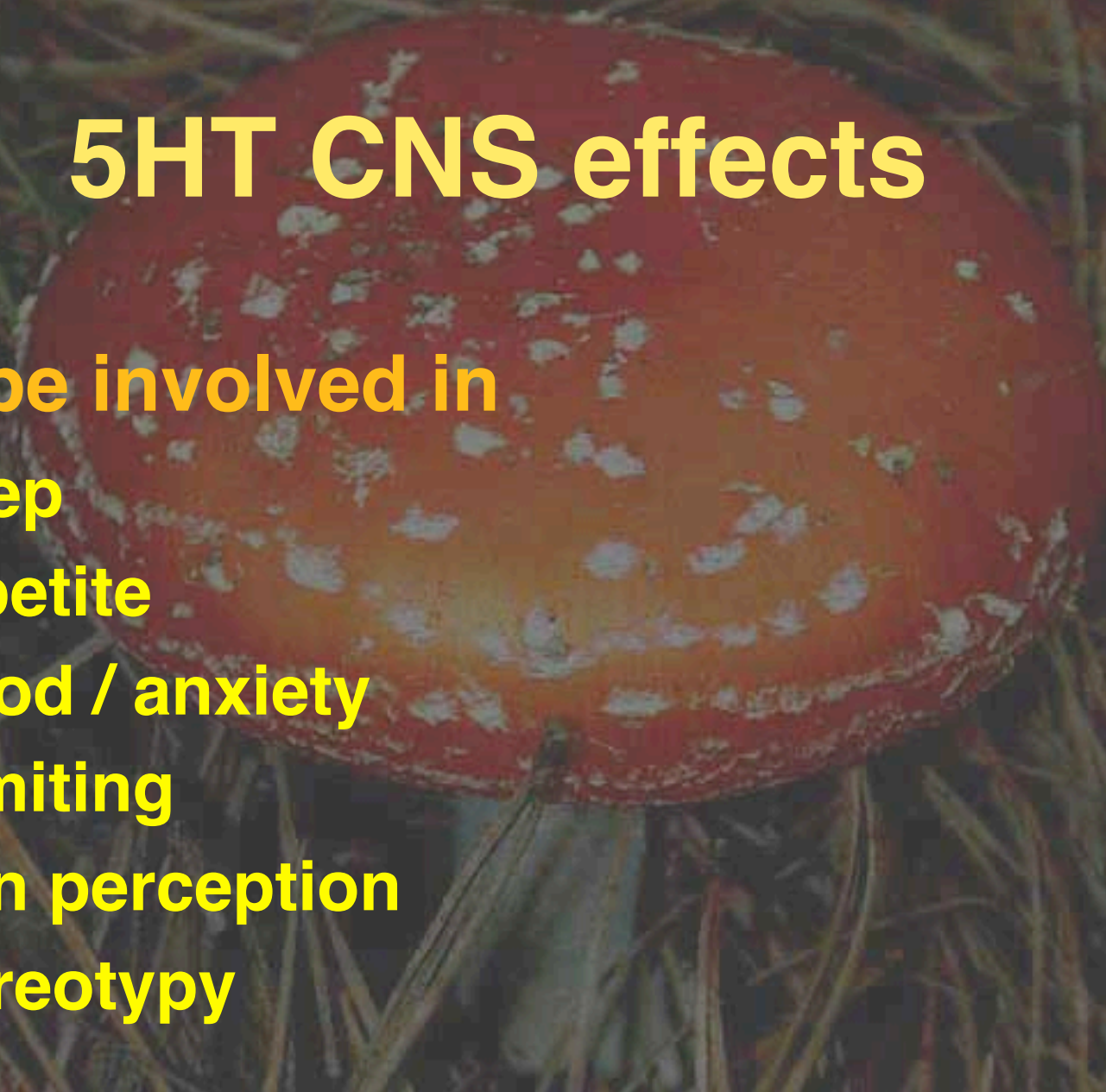
# 5HT effects

- increased gut motility
- vasoconstriction / dilatation
- smooth muscle contraction
- platelet aggregation
- excitation of nociceptors



# 5HT CNS effects

- may be involved in
  - sleep
  - appetite
  - mood / anxiety
  - vomiting
  - pain perception
  - stereotypy





# 5HT receptors

- 15 subtypes at present
  - 5HT<sub>3</sub> ligand gated ion channel
  - rest G protein coupled
- all over the body
- mediate a huge range of effects



# 5HT receptors

- **1A** - CNS - (autoreceptor) sleep, appetite, anxiety
- **1B** - CNS - (autoreceptor) behavioural effects
- **1D** - CNS, blood vessels - vasoconstriction
- **2A** - platelets - aggregation, smooth muscle - contraction
- **2B** - stomach - contraction
- **2C** - choroid plexus - CSF secretion
- **3** - P/CNS - vomiting, anxiety
- **4** - gut - motility
- **5A&B** - CNS - unknown function
- **6** - CNS - unknown function
- **7** - hypothalamus, intestine - unknown function
- other receptors in slimy things



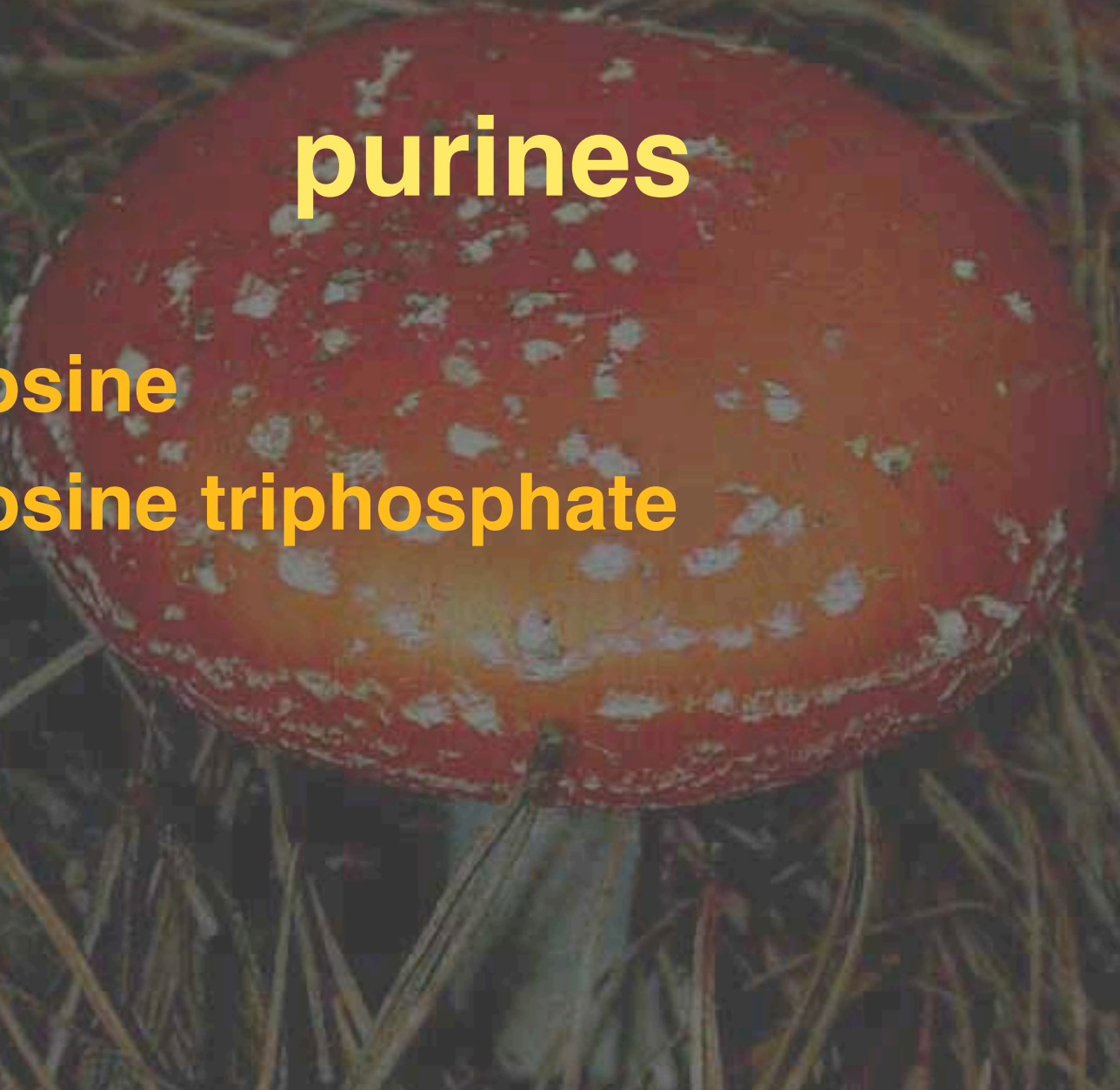
# 5HT drugs

- 5HT1 - ergot (antagonist)
- 5HT1A - buspirone (partial agonist)
- 5HT1D - sumatriptan (agonist)
- 5HT2 - LSD (agonist)
- 5HT3 - ondansetron (antagonist)
- 5HT4 - metaclopramide, cisapride (agonist)
- uptake 1 - fluoxetine (blocker)



# purines

- adenosine
- adenosine triphosphate





# adenosine receptors

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 and a thick, white, ringed stem. The background is a dense field of dry, yellowish-brown grass.

- **A1 - inhibits adenylyl cyclase**
- **A2 - stimulates adenylyl cyclase**



A red mushroom with white spots, likely an Amanita muscaria, is centered in the background. The mushroom has a bright red cap with numerous white, irregular spots. It is growing on a bed of dry, brown grass. The text 'drugs' is overlaid on the upper part of the mushroom cap in a bold, yellow font.

# drugs

- **A1 agonists**
  - adenosine
- **A1 antagonists**
  - caffeine
  - theophylline



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 against the dry, brownish-yellow grass. The text 'peptides' is overlaid on the mushroom's cap in a bold, yellow font.

# peptides

- **very widely distributed**
- **most come from nervous system / endocrine glands**
- **most act as co-transmitters / neuromodulators**



A red mushroom with white spots is centered in the background of the slide. The mushroom is a vibrant red color with numerous small, white, irregular spots scattered across its cap. It is growing on a bed of dry, brown grass. The overall image has a dark, slightly desaturated background, making the mushroom stand out.

# peptides

- 3 - 200 amino acids
- small peptides
  - G protein coupled receptors
- large peptides
  - tyrosine kinase linked receptors
- active peptides cleaved from proteins



# peptides as drugs

- **not often used**
  - **poorly absorbed**
  - **rapidly broken down**
  - **do not cross blood brain barrier**
  - **expensive**
- **metabolic enzyme inhibitors**



A red mushroom with white spots, likely an Amanita muscaria, is the central focus of the image. It is surrounded by dry, brown grass. The word "peptides" is written in yellow text over the mushroom's cap.

# peptides

- **opioids**
  - $\beta$  endorphin, endomorphins
  - enkephalin
  - dynorphin
  - nociceptin



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# peptides

- **tachykinins**
  - substance P (NK1 receptor)
  - neurokinin A (NK2 receptor)
  - neurokinin B (NK3 receptor)



# tachykinin effects

- smooth muscle contraction
- increased capillary permeability
- burning pain / hyperalgesia
- pruritus
- exocrine gland secretion



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# drugs

- **capsaicin**
  - depletes substance P
- **many experimental NK1 antagonists**
  - spantide



# inflammatory mediators

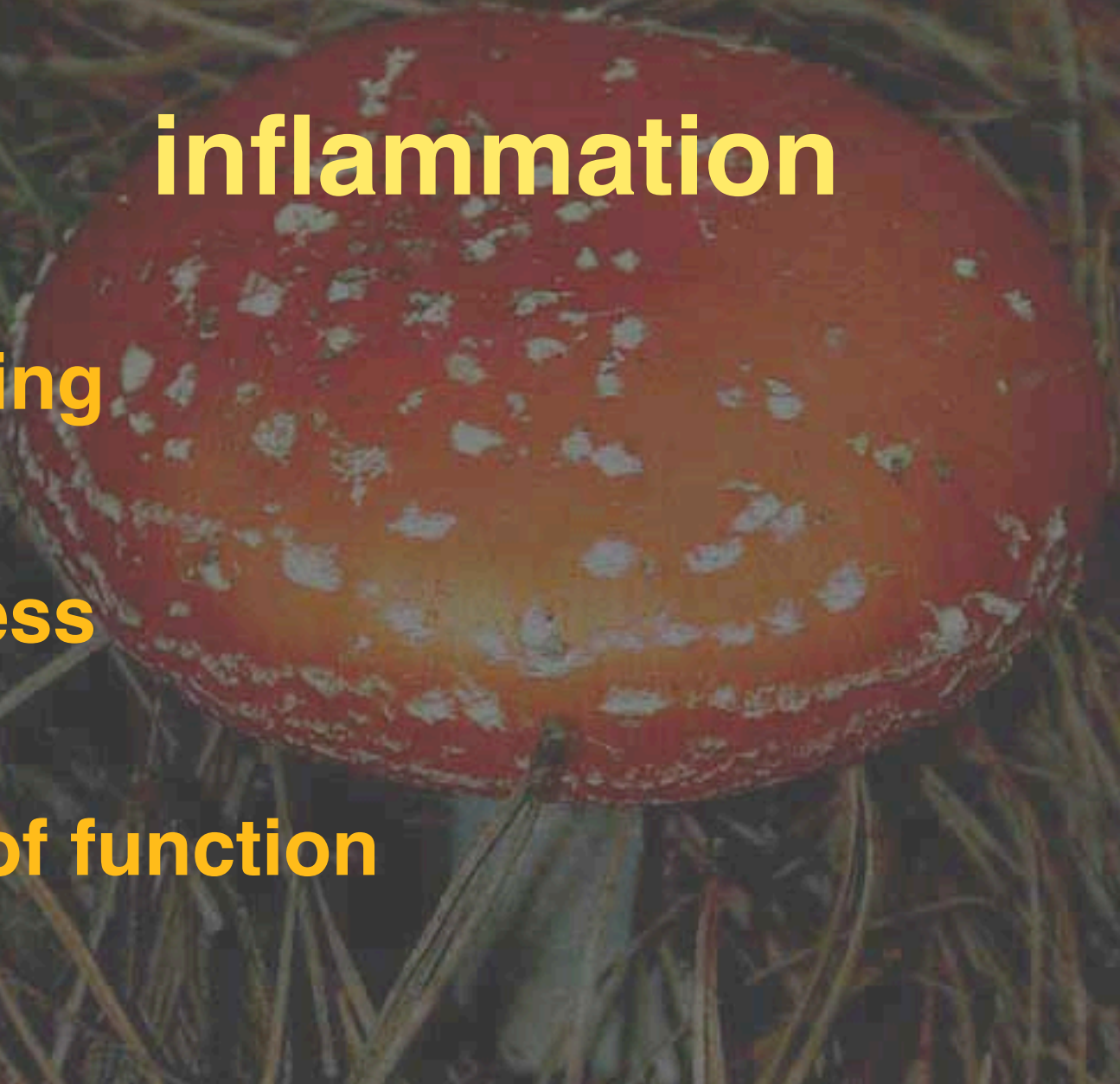
A red mushroom with white spots, likely an Amanita muscaria, is growing in a field of dry grass. The mushroom is the central focus of the image, with its bright red cap and white spots contrasting sharply with the dry, yellowish-brown grass. The background is slightly blurred, emphasizing the mushroom.

- histamine
- eicosanoids
- platelet activating factor
- bradykinin
- cytokines



# inflammation

- swelling
- pain
- redness
- heat
- loss of function





# histamine

- released from mast cells
- lungs, skin, gut, CNS
- species differences in response
  - mice very resistant
  - guinea pigs very susceptible
  - dogs act more like guinea pigs



# histamine receptors

- H1 - skin, smooth muscle
  - antagonists commonly used
- H2 - gastric parietal cells
  - antagonists block acid production
- H3 - presynaptic on neurones (inhibition)
- H4??



# H1 antagonists

- (acepromazine)
- promethazine
- chlorpheniramine
- mepyramine
- newer human drugs
  - terfenadine
  - astemizole
  - cetirizine



# H2 antagonists

- cimetidine
- ranitidine
- etc, etc





**non-specific antagonist**

- **tripelennamine**





# eicosanoids

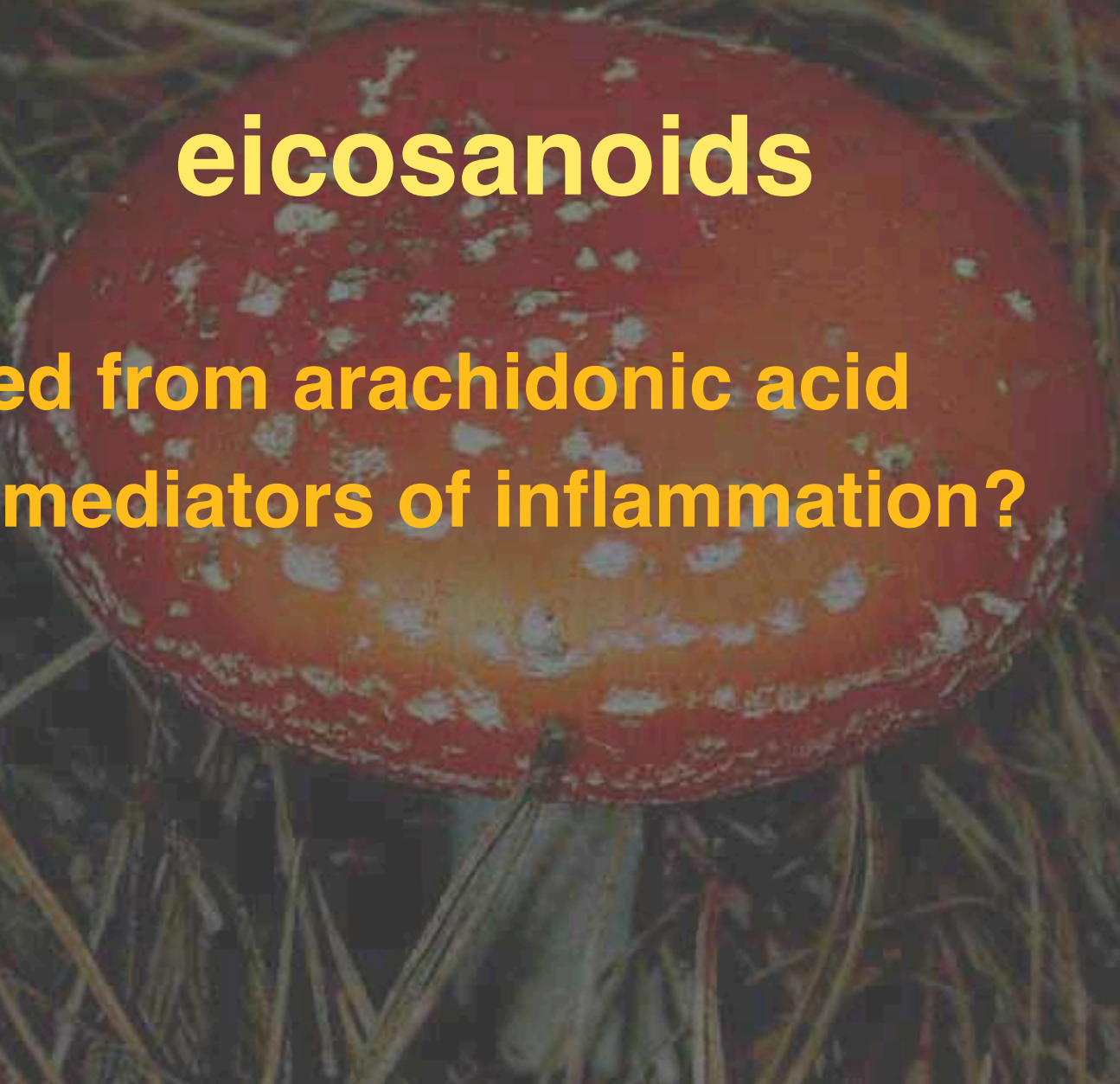
- prostaglandins
- thromboxanes
- leukotrienes
- lipoxins





# eicosanoids

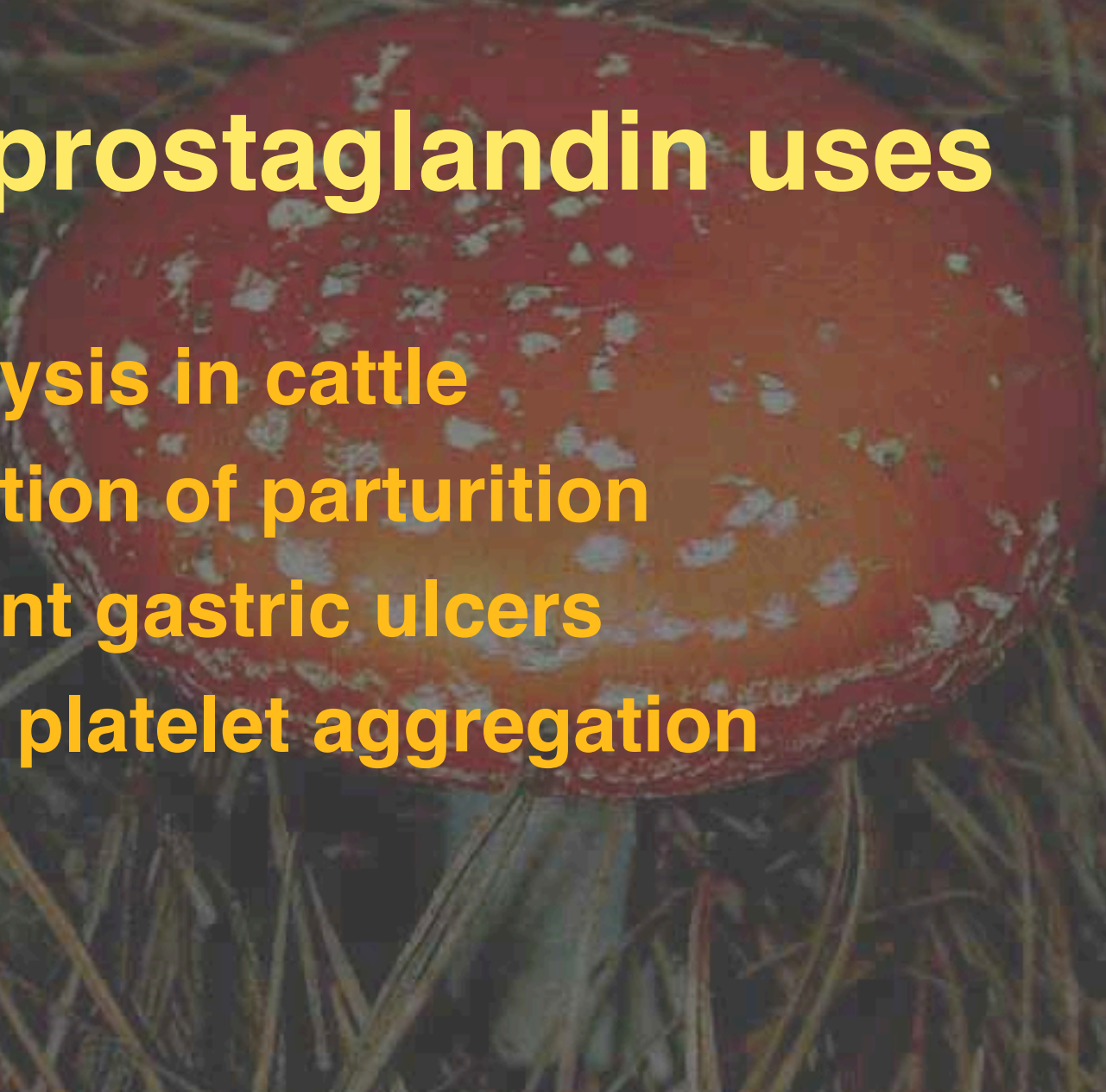
- derived from arachidonic acid
- main mediators of inflammation?





# prostaglandin uses

- luteolysis in cattle
- induction of parturition
- prevent gastric ulcers
- block platelet aggregation





# eicosanoid blockers

- **steroids**
- **nonsteroidal anti-inflammatory drugs**
- **experimental drugs**
  - **prostaglandin receptor antagonists**
  - **5 lipoxygenase inhibitors**



# platelet activating factor

- important inflammatory mediator
- synthesis blocked by steroids
- experimental receptor antagonists
- PAF antagonists in many plants



A red mushroom with white spots, likely an Amanita muscaria, is the central focus of the image. It is surrounded by dry, brown grass. The text 'bradykinin' is overlaid on the mushroom's cap in a bold, yellow font.

# **bradykinin**

- **vasodilatation**
- **slow contraction of smooth muscle**
- **pain**
- **increased fluid secretion**
  - **airways and gut**



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# **bradykinin**

- **broken down by angiotensin converting enzyme**
- **involved in diarrhoea???**
- **experimental receptor antagonists**



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# cytokines

- large (c200 amino acid) peptides
- regulate inflammatory / immune reactions



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, yellowish-brown grass. The mushroom's cap is bright red with numerous white, irregular spots. The stem is thick and appears to have a similar pattern. The overall lighting is somewhat dim, giving the image a slightly moody or naturalistic feel.

# cytokines

- interleukin 1 (IL1)
- IL2 - 10
- tumour necrosis factor a & b
- interferons
- growth factors
- etc, etc, etc



# anti-cytokine drugs

- all have lots of other effects!!
  - steroids
  - cyclosporin
  - tacrolimus





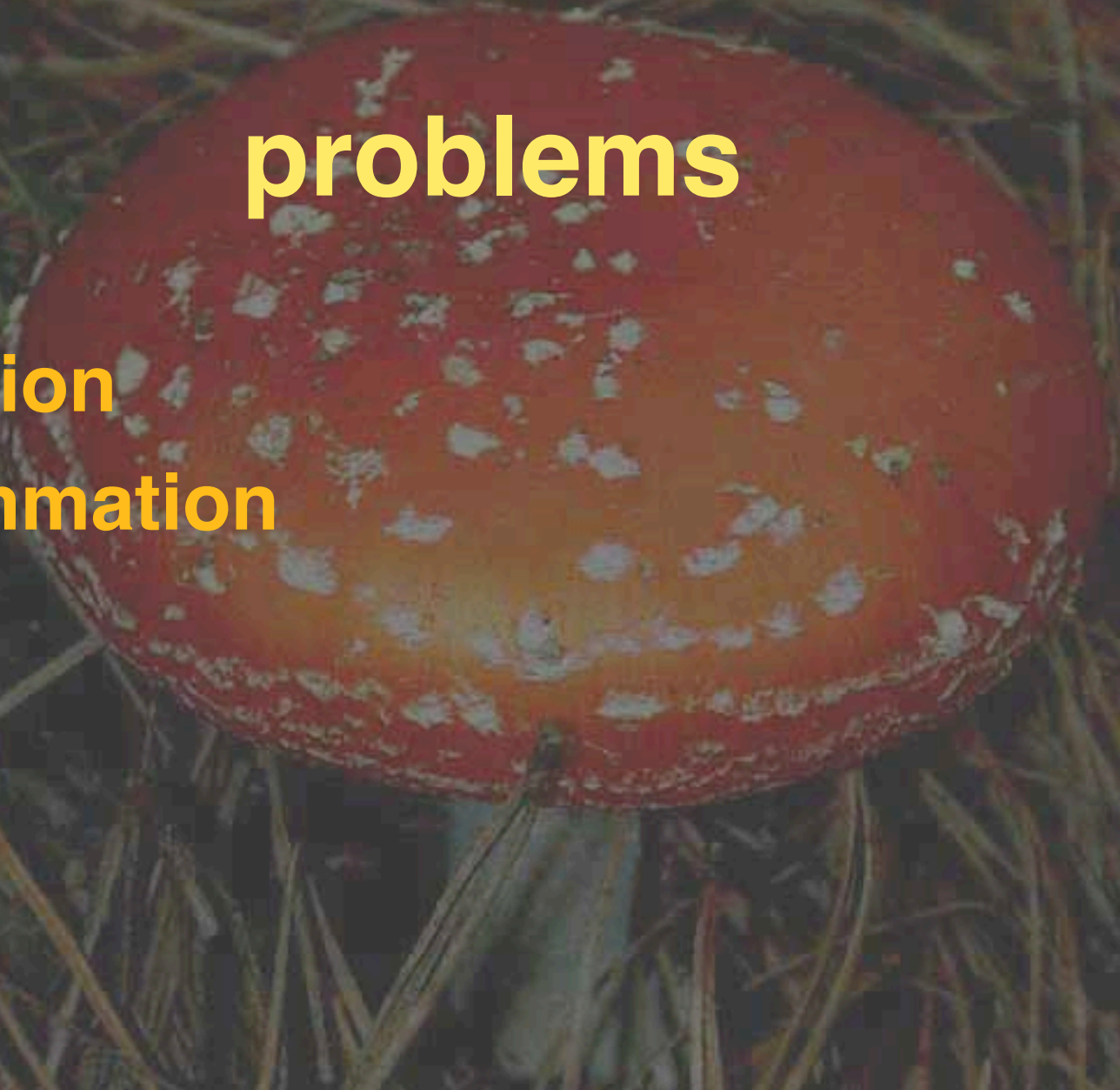
**What would you do?**





# problems

- infection
- inflammation
- pain





# autacoids

- autacoids are a large and important group of neuromodulators / inflammatory mediators
- rarely act alone - potentiate or inhibit other transmitters
- most drugs which alter smooth muscle function or inflammation interact with autacoids
- important as CNS neuromodulators