

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

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.

autacoids

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

5HT

- gut lining
- platelets
- CNS



5HT

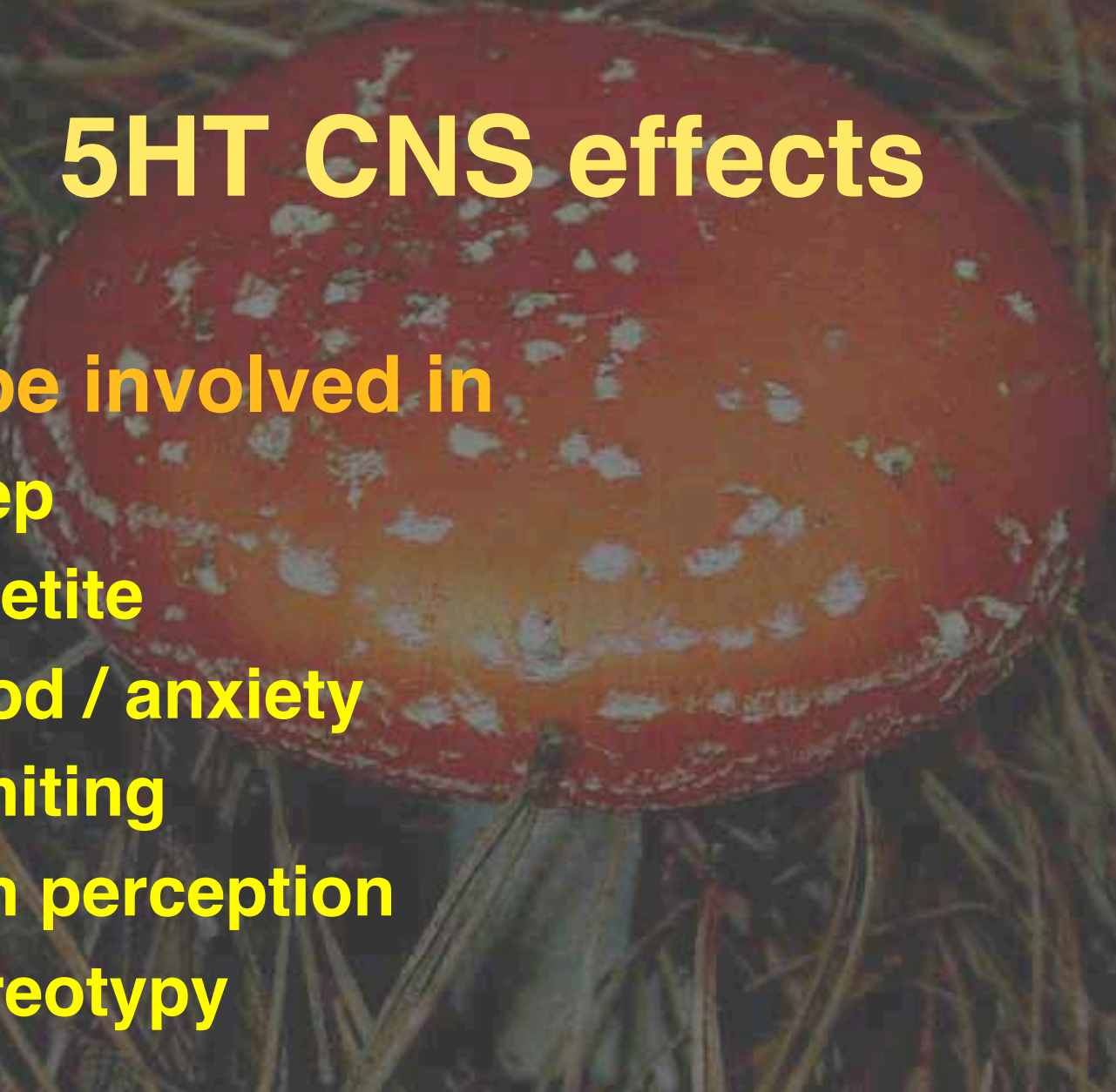
- **synthesis, storage, release & uptake very similar to NA**
- **affected by same drugs**
- **co-transmission**
 - **somatostatin**
 - **substance P**
 - **vasoactive intestinal peptide**

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
 - 5HT₃ ligand gated ion channel
 - rest G protein coupled
- all over the body
- mediate a huge range of effects

5HT receptors

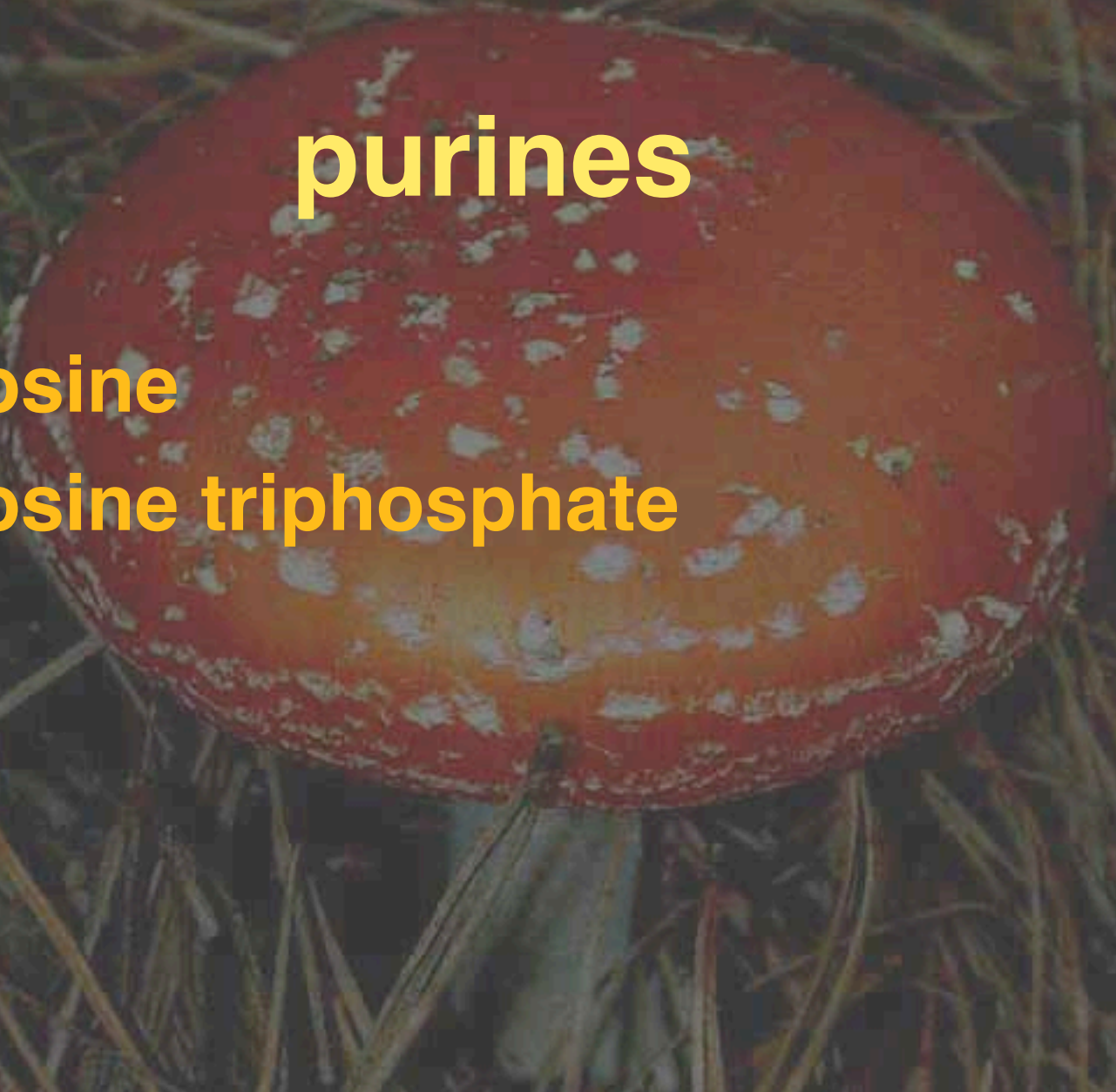
- **1A** - CNS - (autoreceptor) sleep, appetite, anxiety
- **1B** - CNS - (autoreceptor) behavioural effects
- **1D** - CNS, blood vessels - vasoconstriction
- **2A** - platelets - aggregation, smooth muscle - contraction
- **2B** - stomach - contraction
- **2C** - choroid plexus - CSF secretion
- **3** - 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)

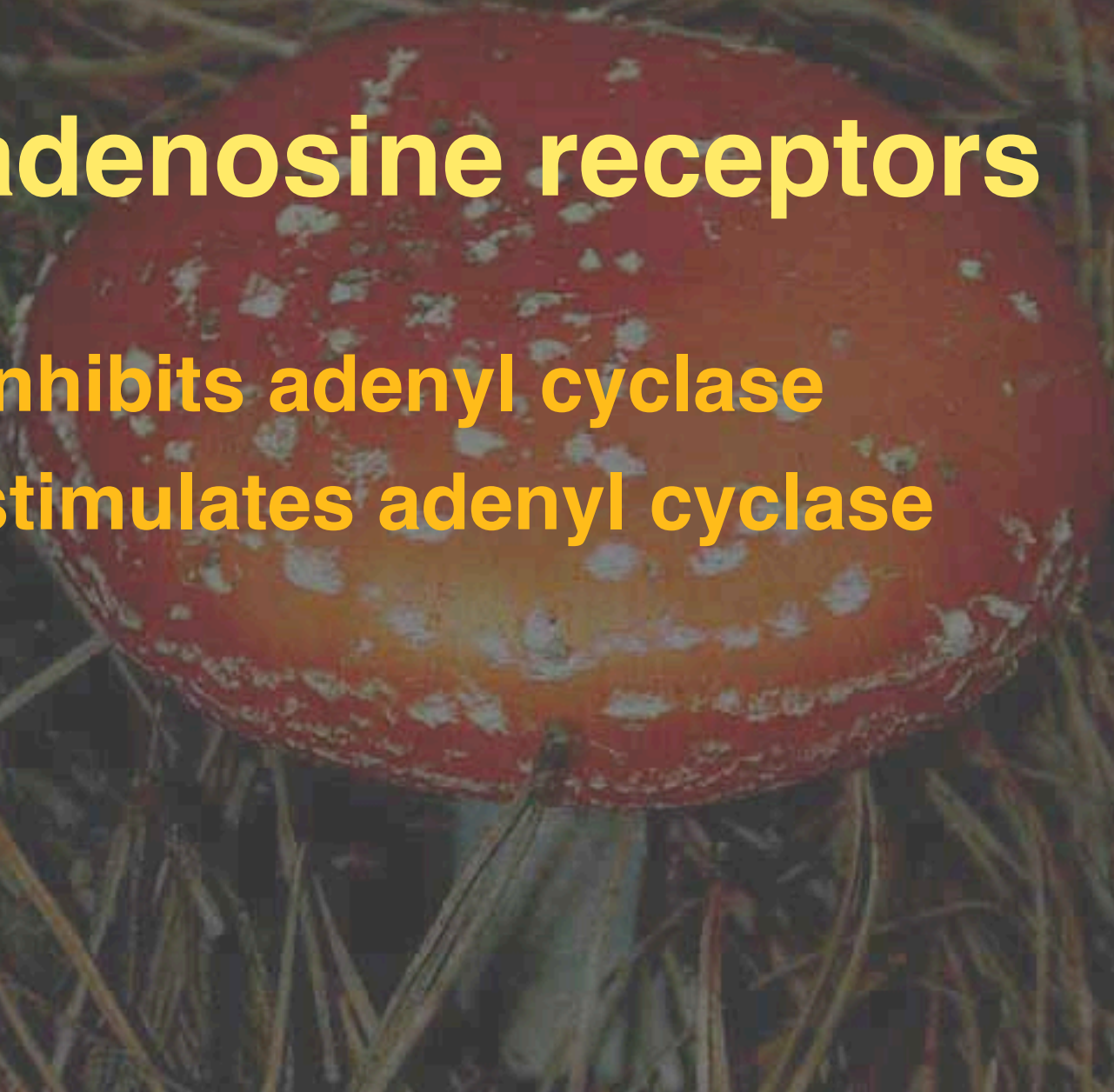
purines

- adenosine
- adenosine triphosphate



adenosine receptors

- **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 right portion of the mushroom's 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 sharply with the dry, brownish-yellow grass. The text 'peptides' is overlaid on the upper part of the mushroom cap.

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, yellowish-brown grass. The overall image has a slightly dark, muted tone, typical of a presentation background.

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**
 - β 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

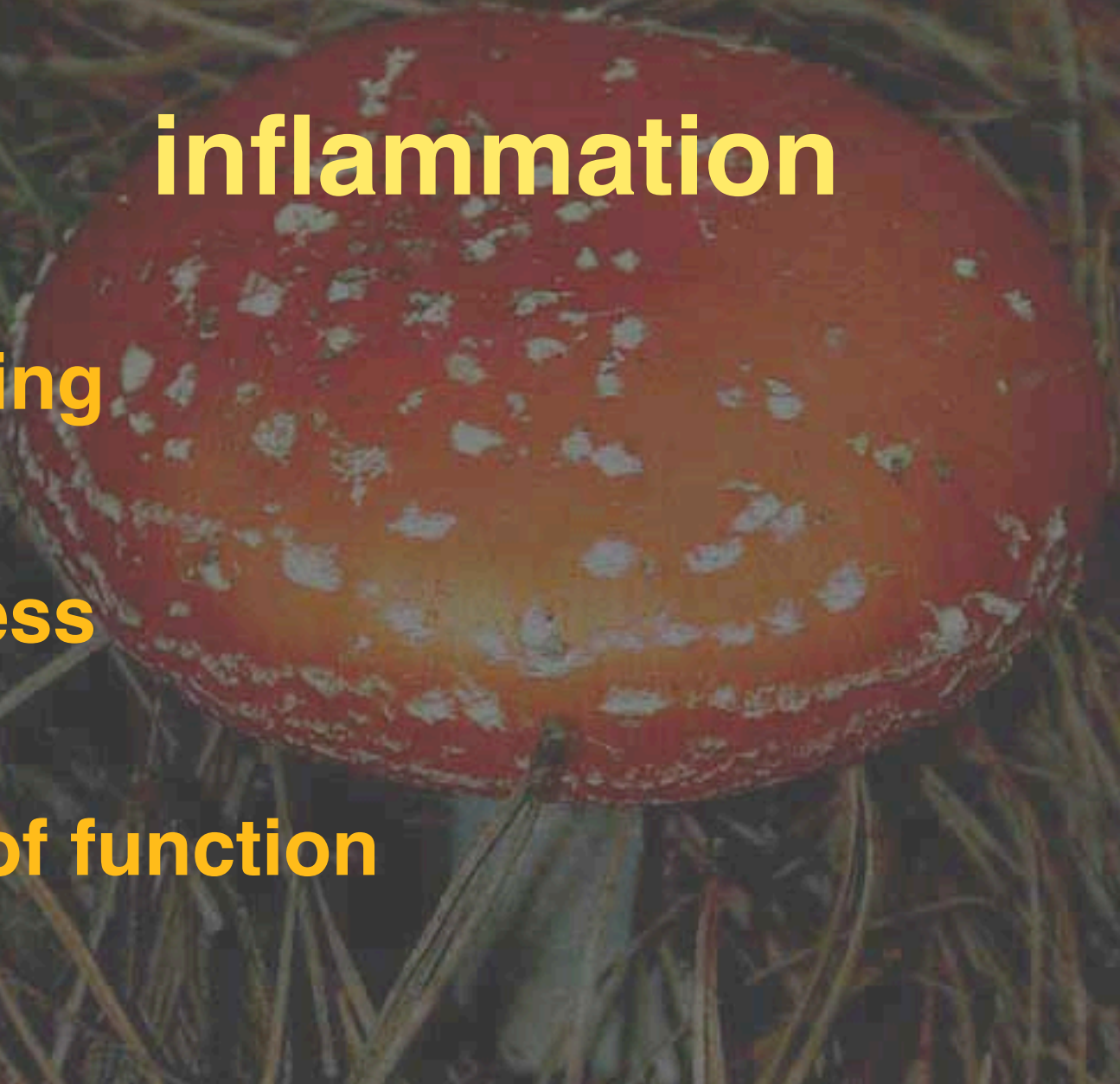
inflammatory mediators

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

A large, red mushroom with white spots, resembling a fly agaric, is the central focus of the image. It is growing in a field of dry, yellowish-brown grass. The mushroom has a thick, white stem and a slightly flattened, convex cap. The background is a dense field of similar dry grass, creating a textured, natural setting.

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

H2 antagonists

- cimetidine
- ranitidine
- etc, etc



non-specific antagonist

- **tripelennamine**



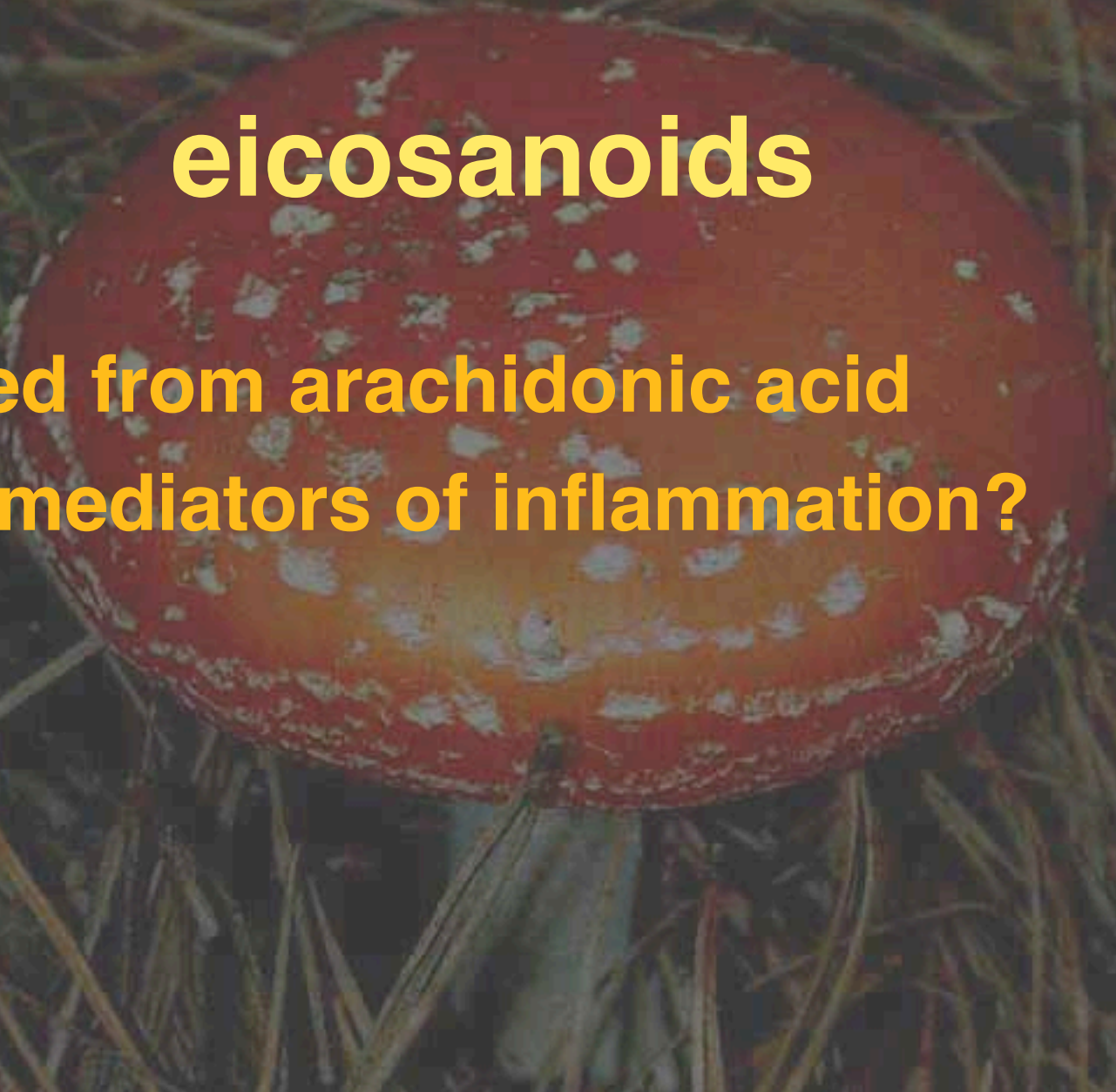
eicosanoids

- prostaglandins
- thromboxanes
- leukotrienes
- lipoxins



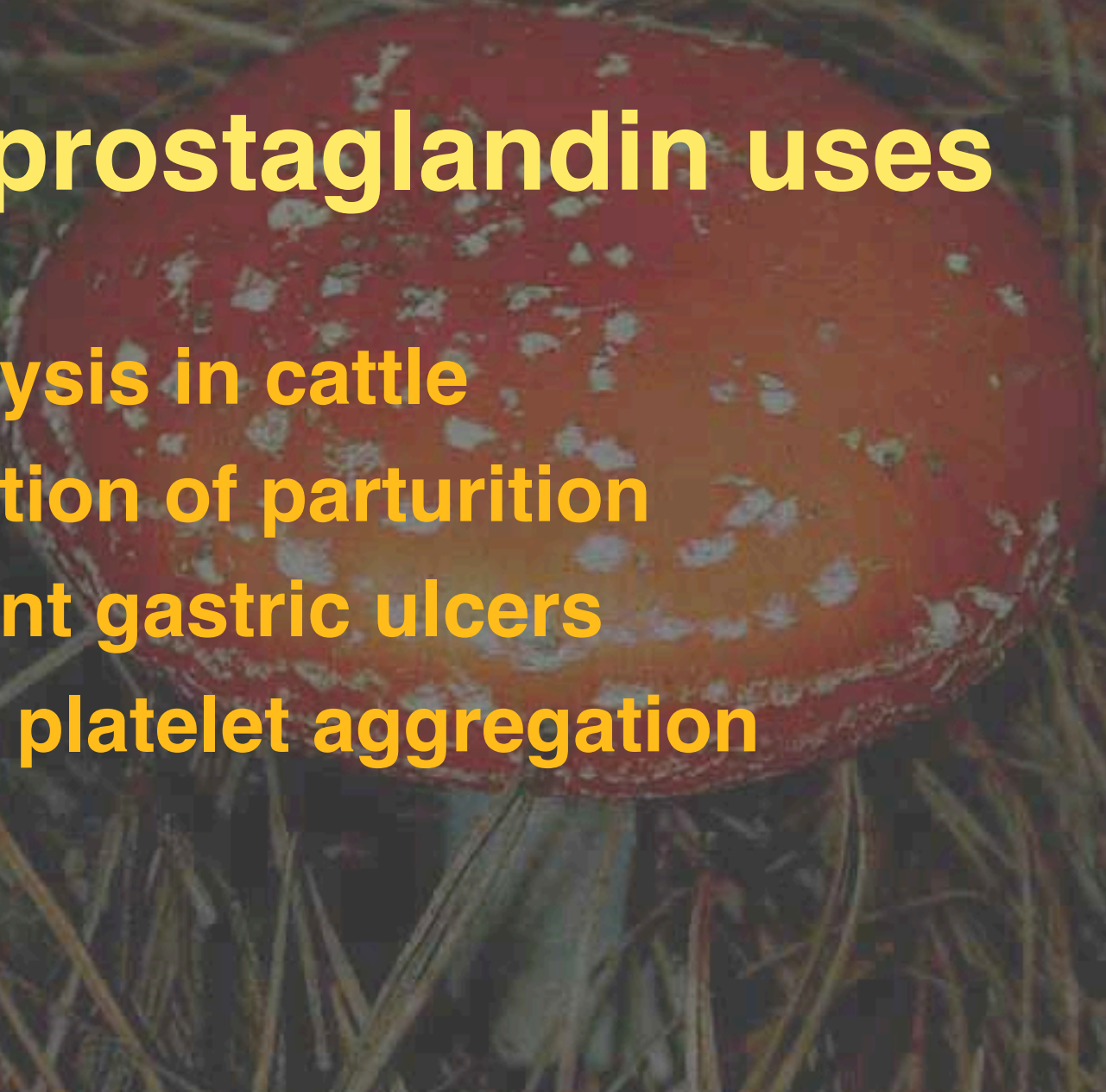
eicosanoids

- 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

bradykinin

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

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

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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

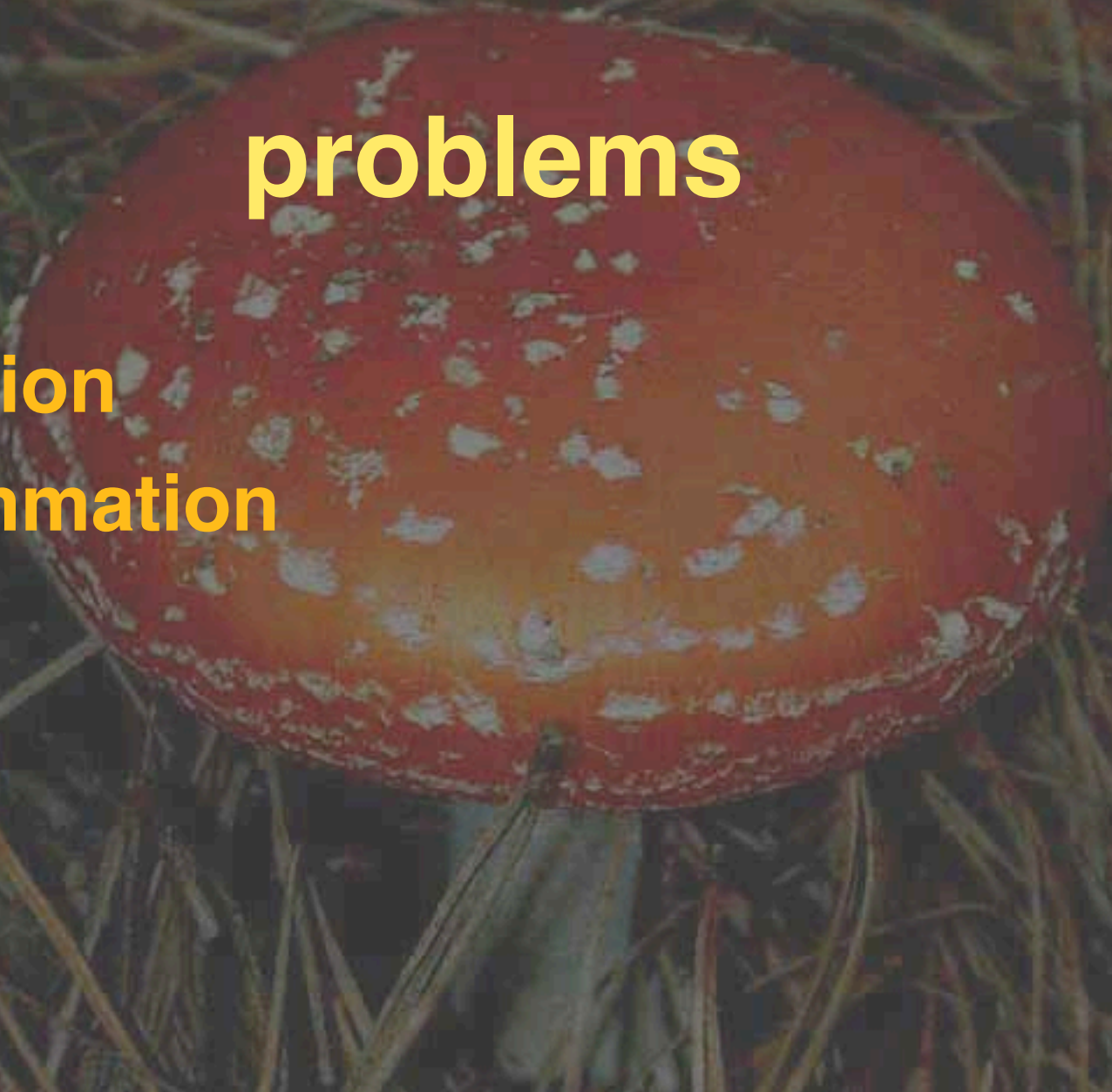


What would you do?



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