

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

# **Autonomic Nervous System**

## **Cholinergic Transmission**



# parasympathetic system

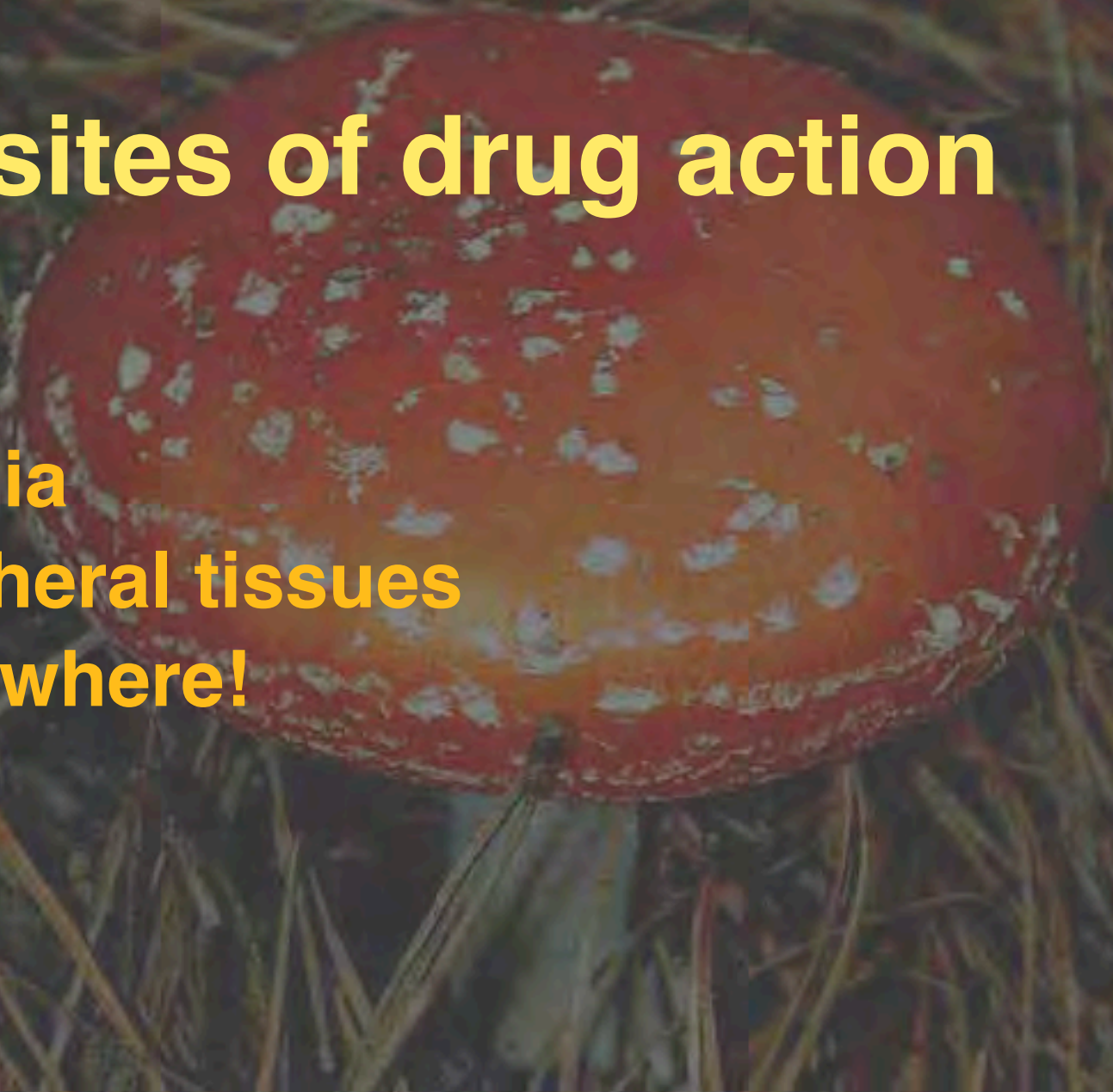
A red mushroom with white spots, likely an Amanita muscaria, is the central visual element. It is positioned in the upper right quadrant of the slide. The background is a dark, textured field of dry grass or straw, which is slightly blurred to emphasize the mushroom. The overall color palette is dark and earthy, with the bright red of the mushroom providing a strong contrast.

- medullary outflow
  - eye
  - lacrimal glands
  - salivary glands
  - heart
  - lung
  - upper gut
- sacral outflow
  - lower gut
  - bladder
  - genitals



# sites of drug action

- CNS
- ganglia
- peripheral tissues
- everywhere!





# release of ACh

- arrival of action potential
- opening of Ca channels
- increase in  $[Ca^{++}]$
- exocytosis of vesicle
- co-transmission?

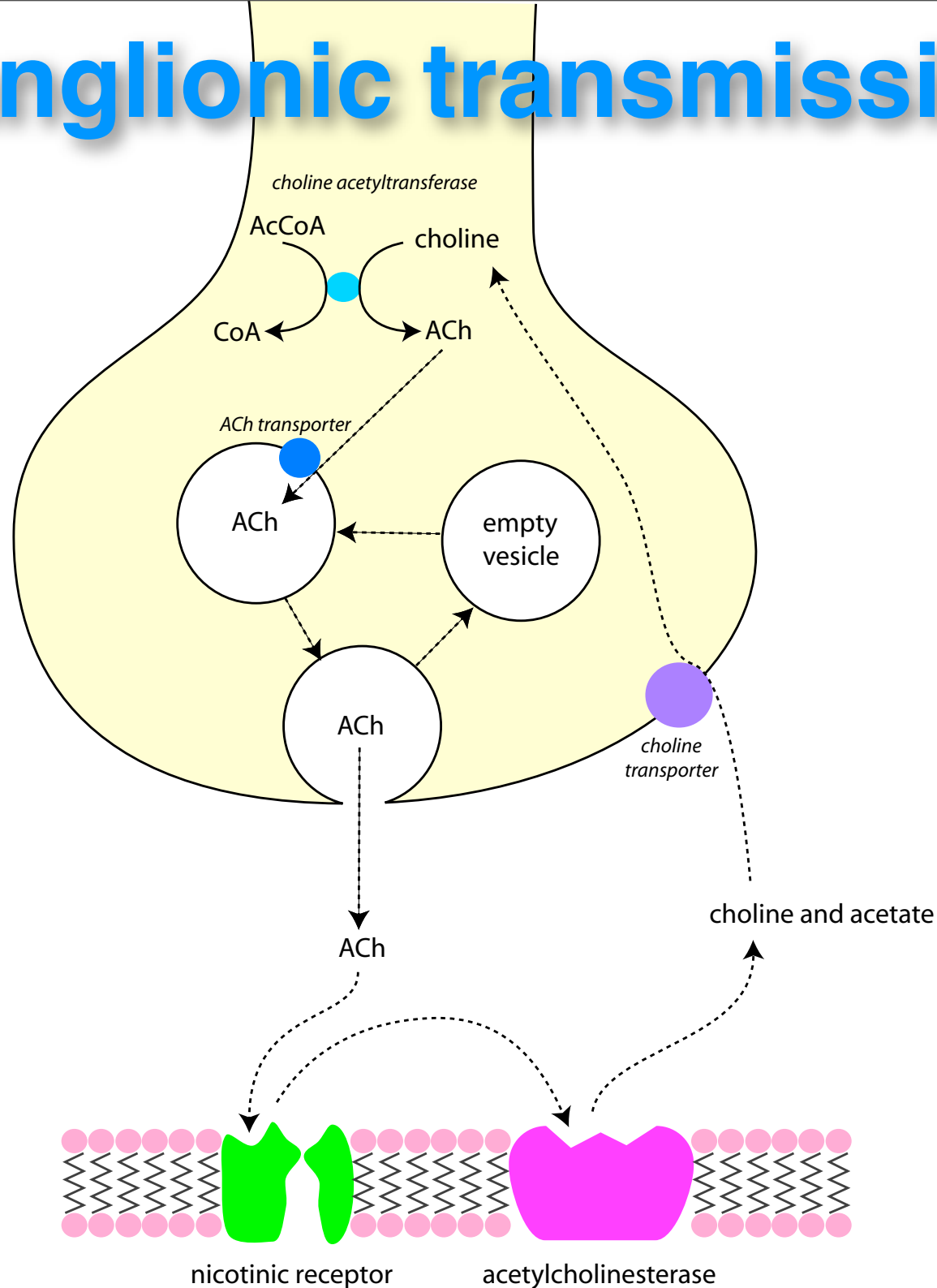


# acetyl choline receptors

- **nicotinic**
  - **ionotropic**
- **muscarinic**
  - **metabotropic**



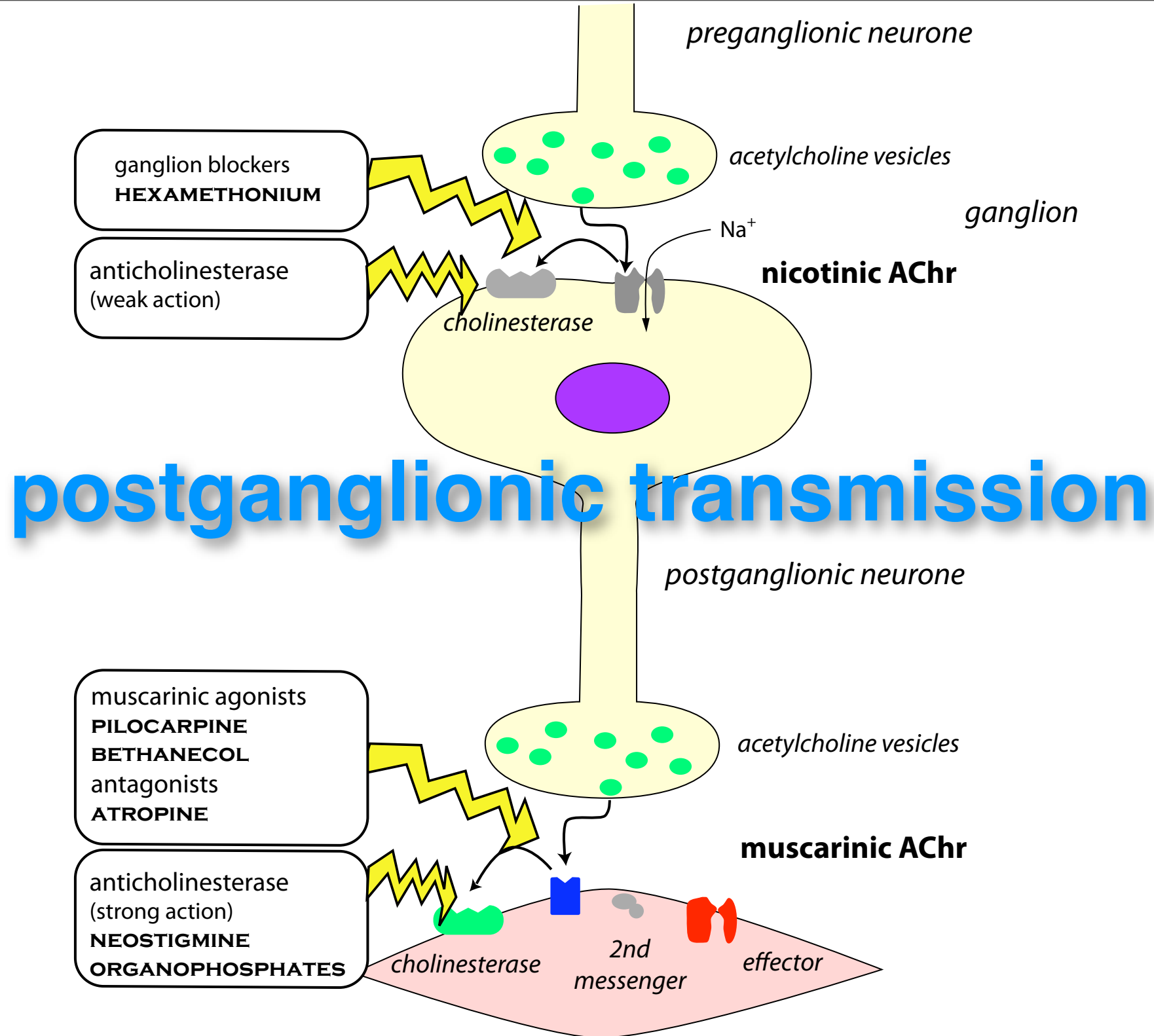
# ganglionic transmission





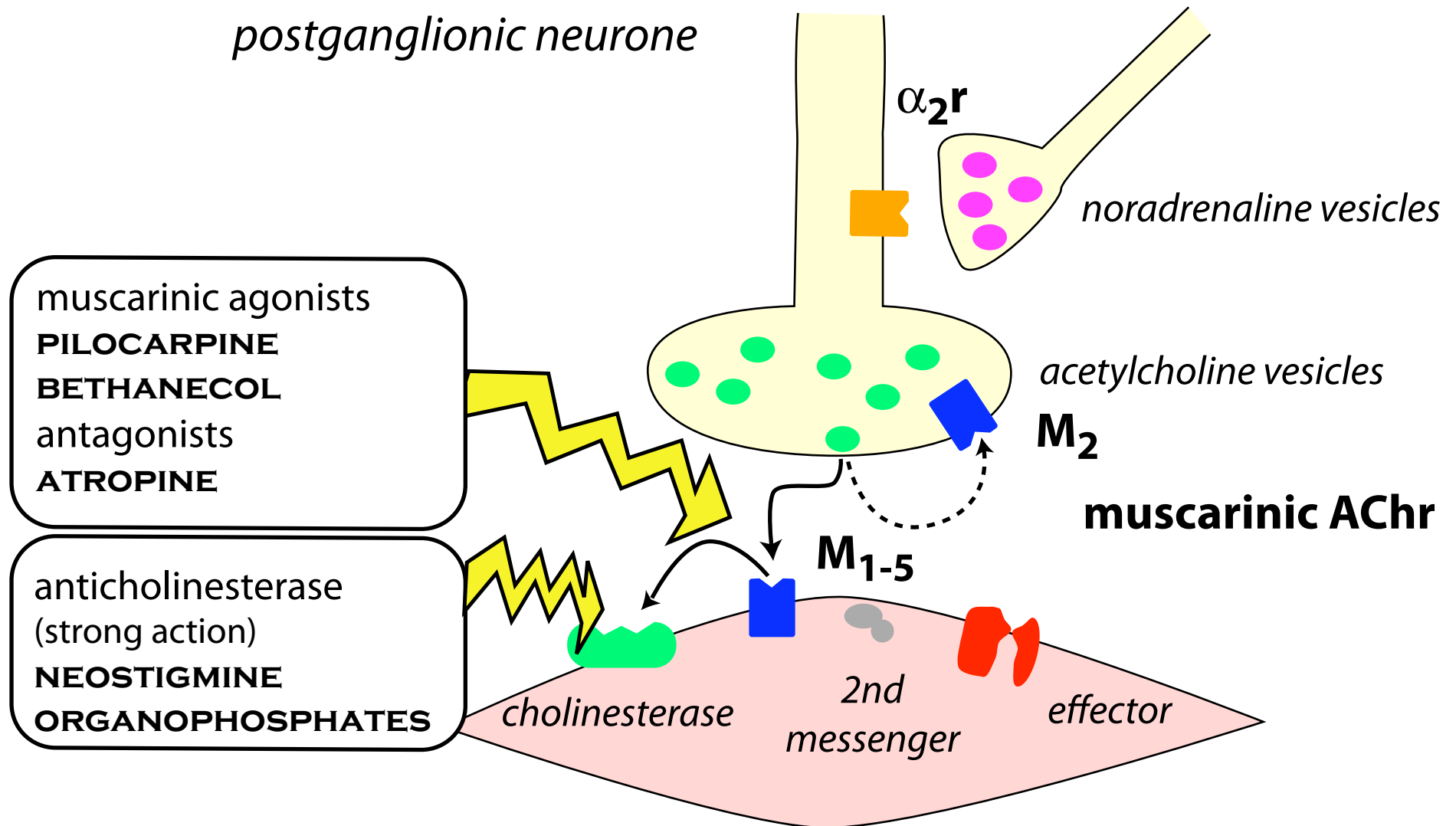
# nicotinic receptor subtypes

- ion channels with 5 subunits
- at least 16 different subunits cloned
  - ganglionic –  $(\alpha 3)_2(\beta 4)_3$
  - CNS –  $(\alpha 3)_2(\beta 4)_3$  &  $(\alpha 7)_5$
  - neuromuscular junction –  $(\alpha 1)_2\beta 1\gamma\epsilon$





# postganglionic transmission



# muscarinic receptors

- **M1 – neural**
  - CNS excitation, gastric acid secretion, gut motility
- **M2 – cardiac**
  - cardiac & neural inhibition
- **M3 – glandular**
  - secretion, smooth muscle contraction, vasodilatation (NO)
- **M4 – CNS / smooth muscle**
- **M5 – substantia nigra, salivary gland, iris**



# muscarinic agonists

A red mushroom with white spots, likely Amanita muscaria, 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.

- **acetylcholine**
- **bethanecol – po**
- **pilocarpine – eye**
- **carbachol**
- **muscarine**



# muscarinic antagonists

- atropine
- hyoscine
- glycopyrrolate
- pirenzepine (M1 – gut only)





# muscarinic antagonists

**log Ki**

**M1 M2 M3 M4 M5**

**atropine 9 8.8 9.3 8.9 9.2**

**oxybutynin 8.2 7.5 8.3 8.1 7.7**

**pirenzepine 8.2 6.5 6.9 7.4 7.2**

**tolterodine 8.4 8.1 8.2 7.9 8.4**



deadly nightshade  
*Atropa belladonna*



# atropine effects

- dries secretions
- reduces salivation
- slows gut
- tachycardia
- dilates pupil
- blurred vision
- difficulty with urination





# atropine indications

- anaesthetic premedication
  - in cats (and pigs?)
  - in conjunction with irritant anaesthetics like ether
- treating gut spasm
  - not very effective
- treating bradycardia
  - depends on cause
- organophosphate poisoning



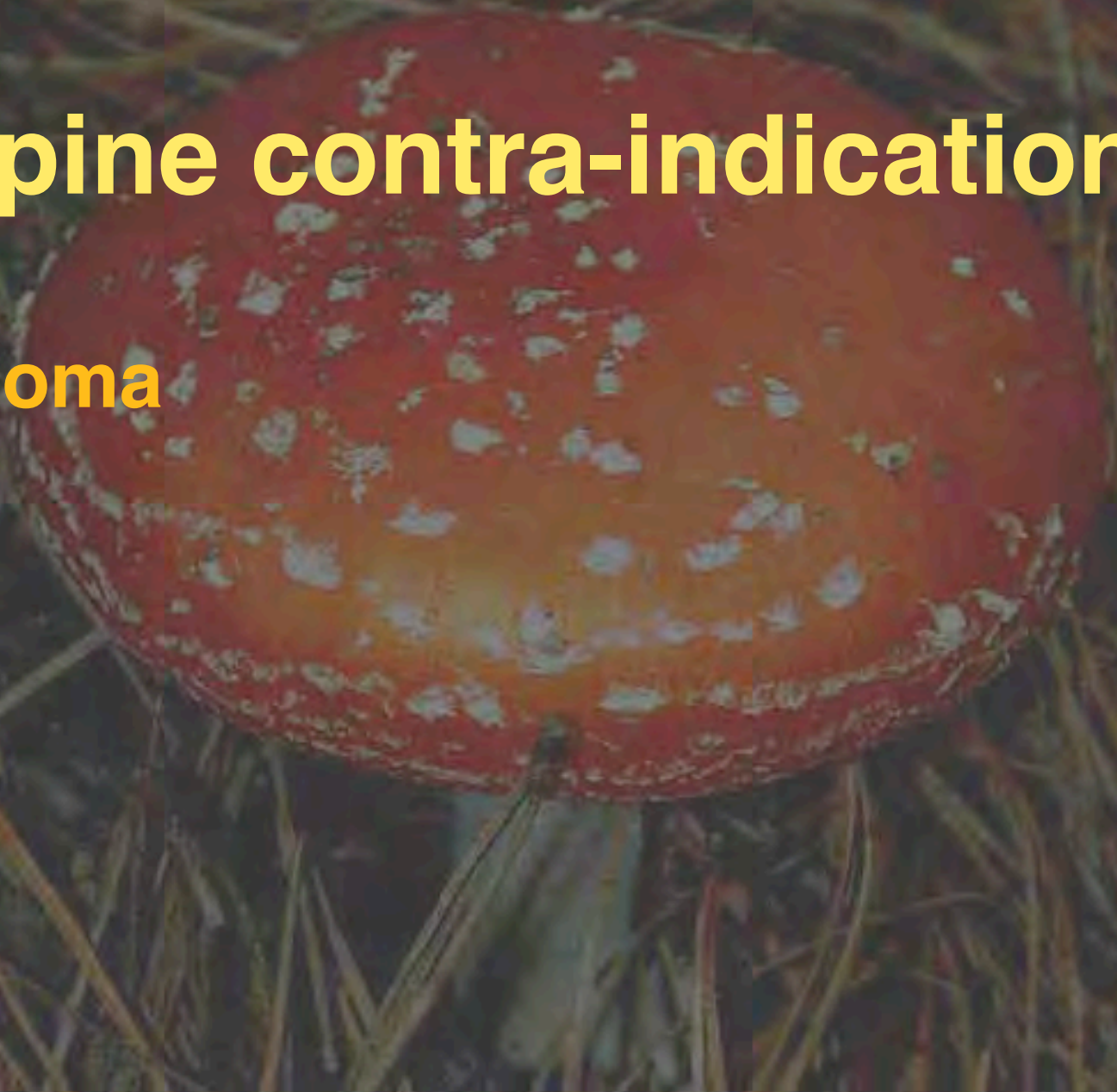
**atropine contra-indications**





# atropine contra-indications

- glaucoma





# atropine contra-indications

- glaucoma
- tachycardia





# atropine precautions

- **care in cardiac disease**
- **horses**
  - **cycloplegia often causes panic**
- **ruminants**
  - **blocks parotid secretions but not submandibular – very sticky saliva**
- **rabbits**
  - **break atropine down rapidly**



A red mushroom with white spots growing in grass. The mushroom is the central focus, with its bright red cap and white speckles standing out against the dry, brownish grass. The text is overlaid on the image.

# hyoscine

- very similar to atropine
- may have more CNS effects
- used for motion sickness in man
- not very effective in dogs



# glycopyrrolate

- **quaternary ammonium compound**
  - **does not cross blood brain barrier**
- **more specific for heart**
- **longer action than atropine**
- **expensive!**



# cholinesterases

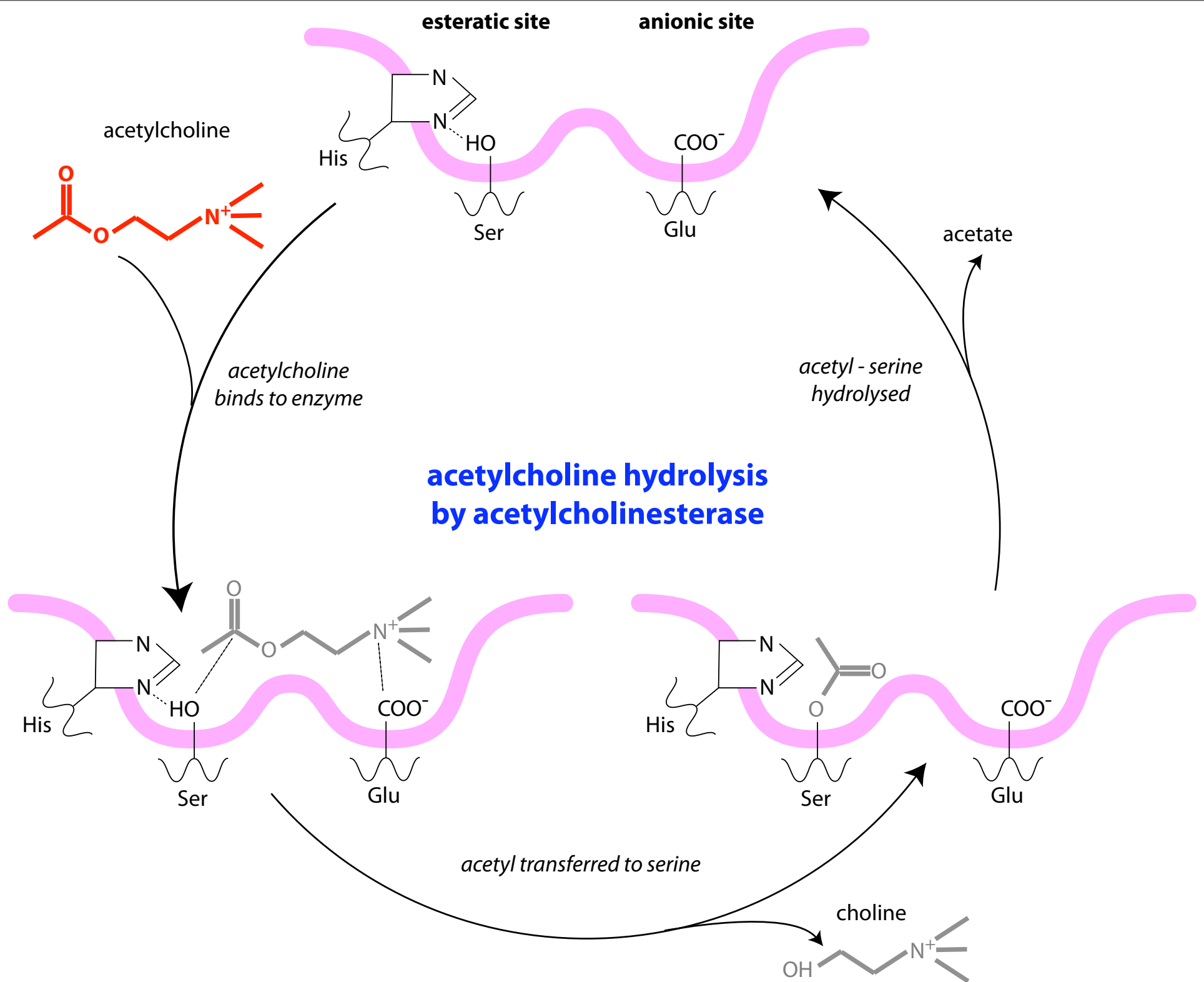
- **acetylcholinesterase**
  - **cholinergic synapses**
- **butyrylcholinesterase**
  - **plasma and other tissues**
  - **breaks down many esters**



**acetylcholinesterase**







# anticholinesterases

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

- edrophonium
- neostigmine
- physostigmine
- organophosphates
- carbamates



# anticholinesterases

A red mushroom with white spots, likely a fly agaric (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.

- **block breakdown of ACh**
- **enhance cholinergic transmission**
- **produce signs of parasympathetic overactivity**

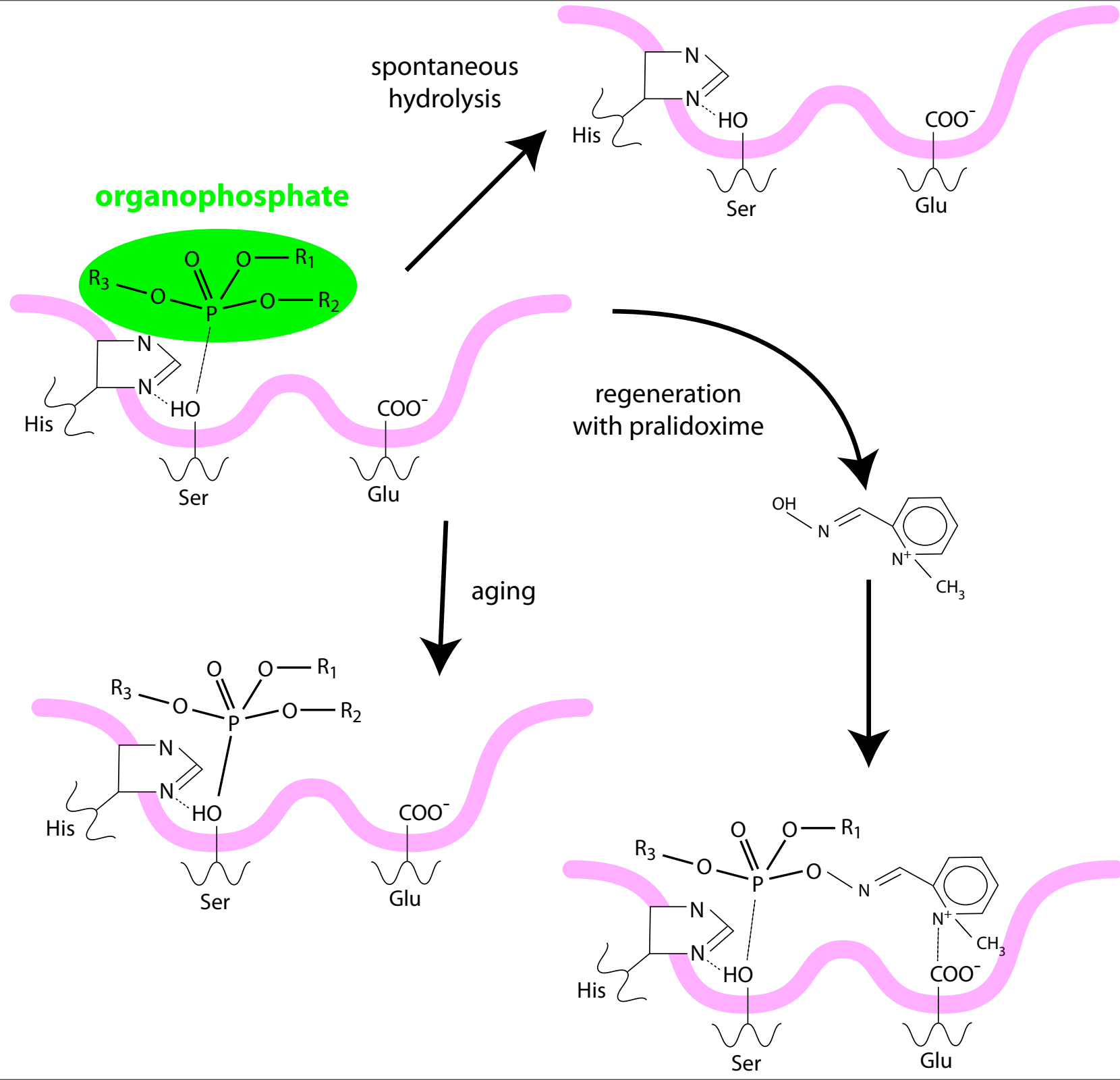


# organophosphates

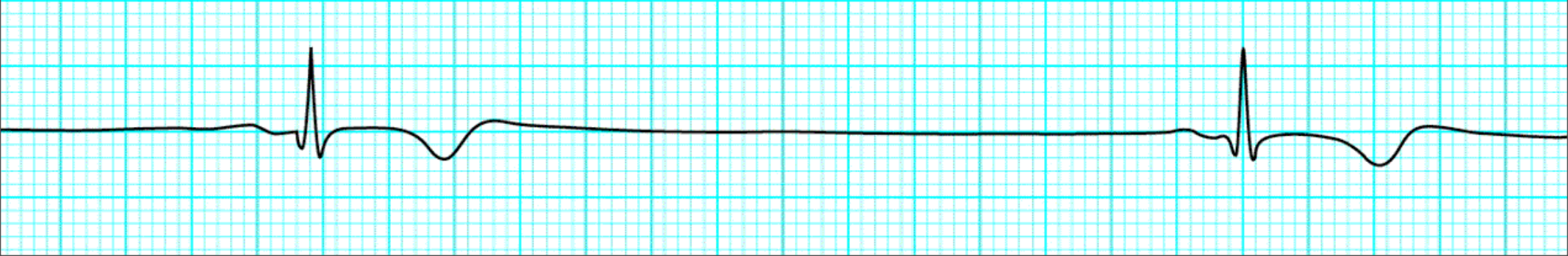
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- insecticides
  - not used much on animals now
  - still used on plants
- (nerve gases)





**What would you do?**





**What would you do?**



# cholinergic transmission

- **acetylcholine is released at postganglionic nerve endings to act at muscarinic receptors**
- **there are several subtypes of muscarinic receptors**
- **atropine is widely used as a non-specific muscarinic antagonist**
- **muscarinic agonists are not widely used because of side effects**
- **all autonomic system drugs have widespread side effects**