

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

Anticonvulsant Drugs

epilepsy

- **affects 0.5% dogs & cats**
- **usually tonic – clonic seizures**
- **absence seizures not seen**

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 background is a dense field of dry, yellowish-brown grass.

causes

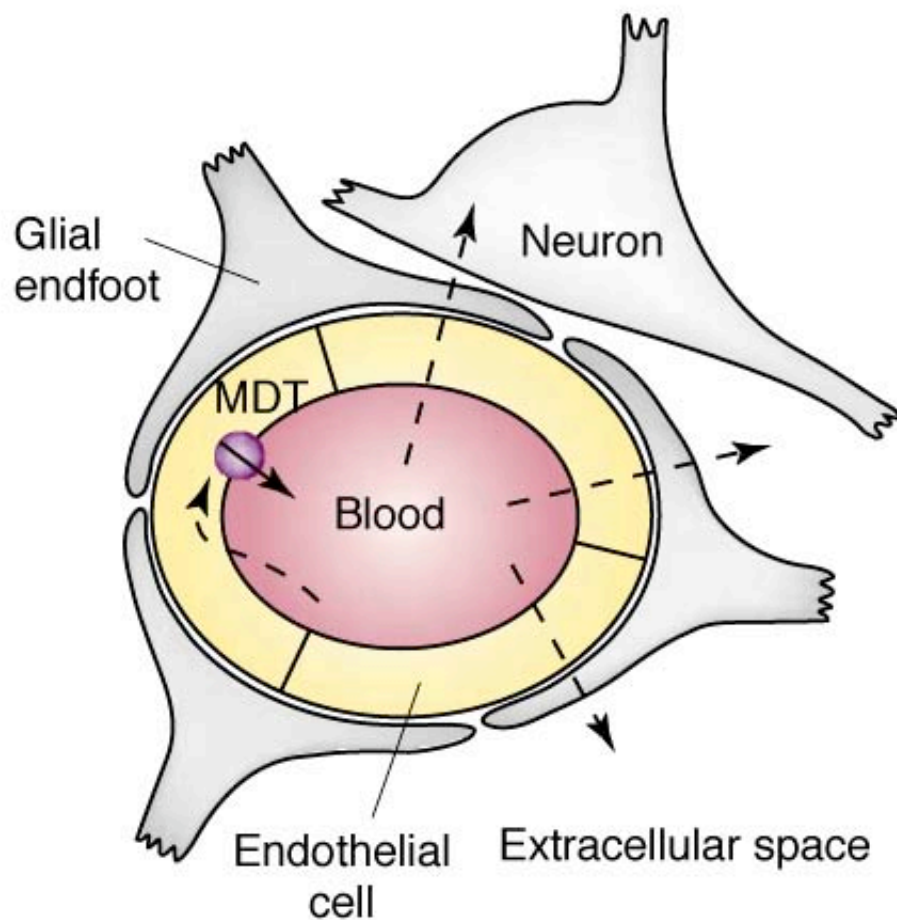
- **primary**
 - idiopathic
- **secondary**
 - distemper
 - head injury
 - encephalitis
 - tumours
- **reactive**
 - hyperthermia
 - poisoning

drugs

- effective in about 33%
- some control in 33%
- ineffective in the rest

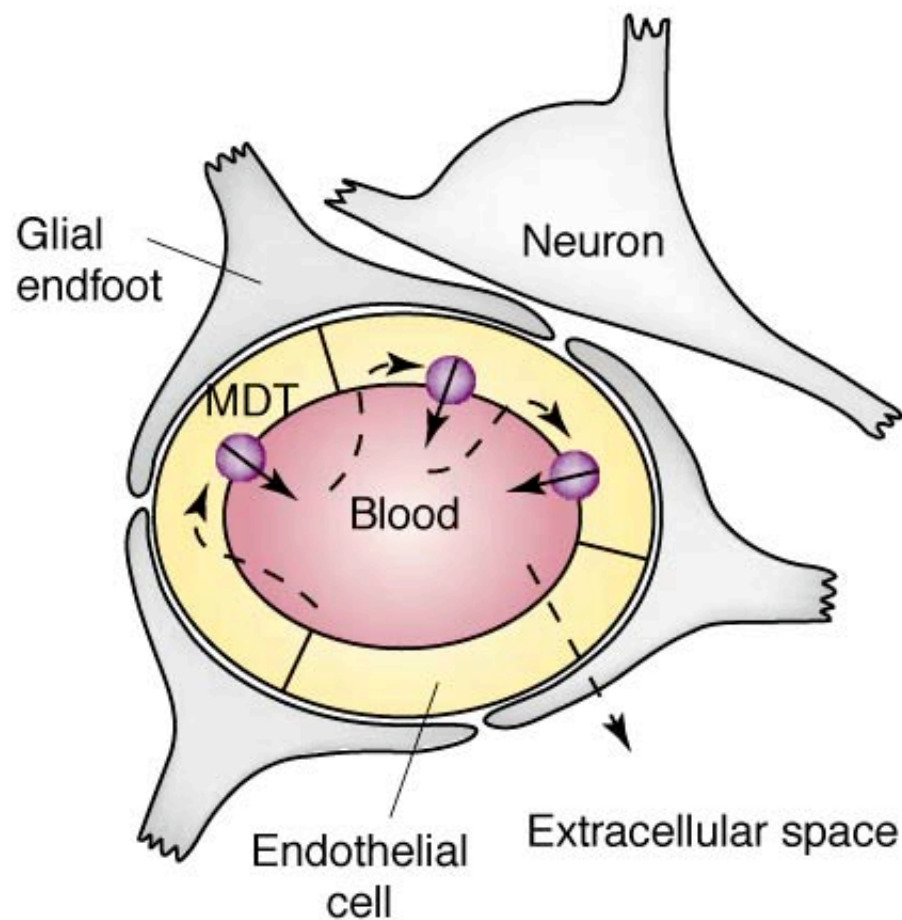
(a)

Normal expression of multidrug transporters



(b)

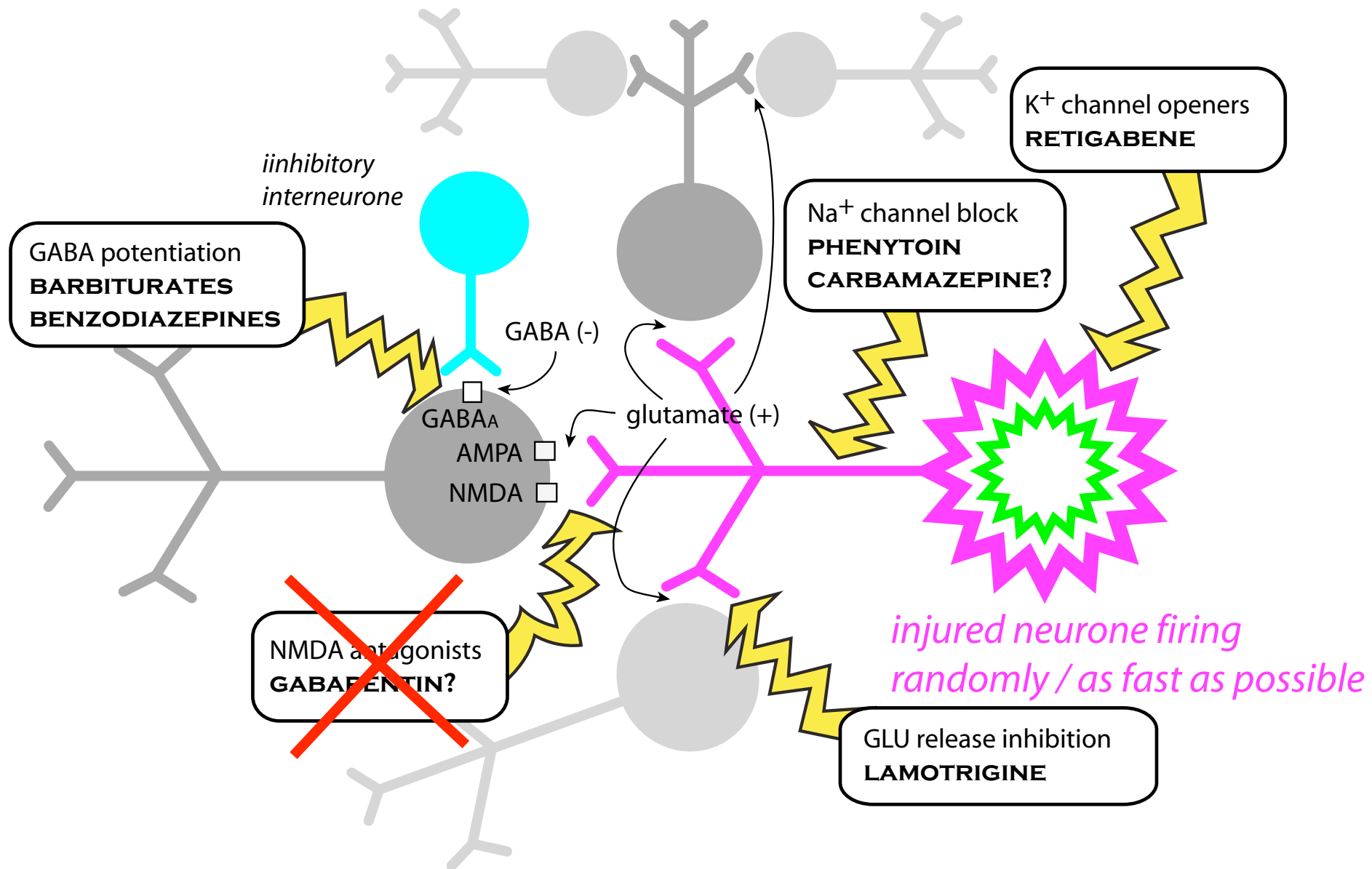
Overexpression of multidrug transporters



A red mushroom with white spots, resembling 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-yellow grass. The word "drugs" is written in yellow text over the top of the mushroom cap.

drugs

- given for life
 - side effects
 - cost
 - effects of other illness / procedures
- suppress signs rather than cure disease



BARBITURATES

OTHER INJECTION ANAESTHETICS?

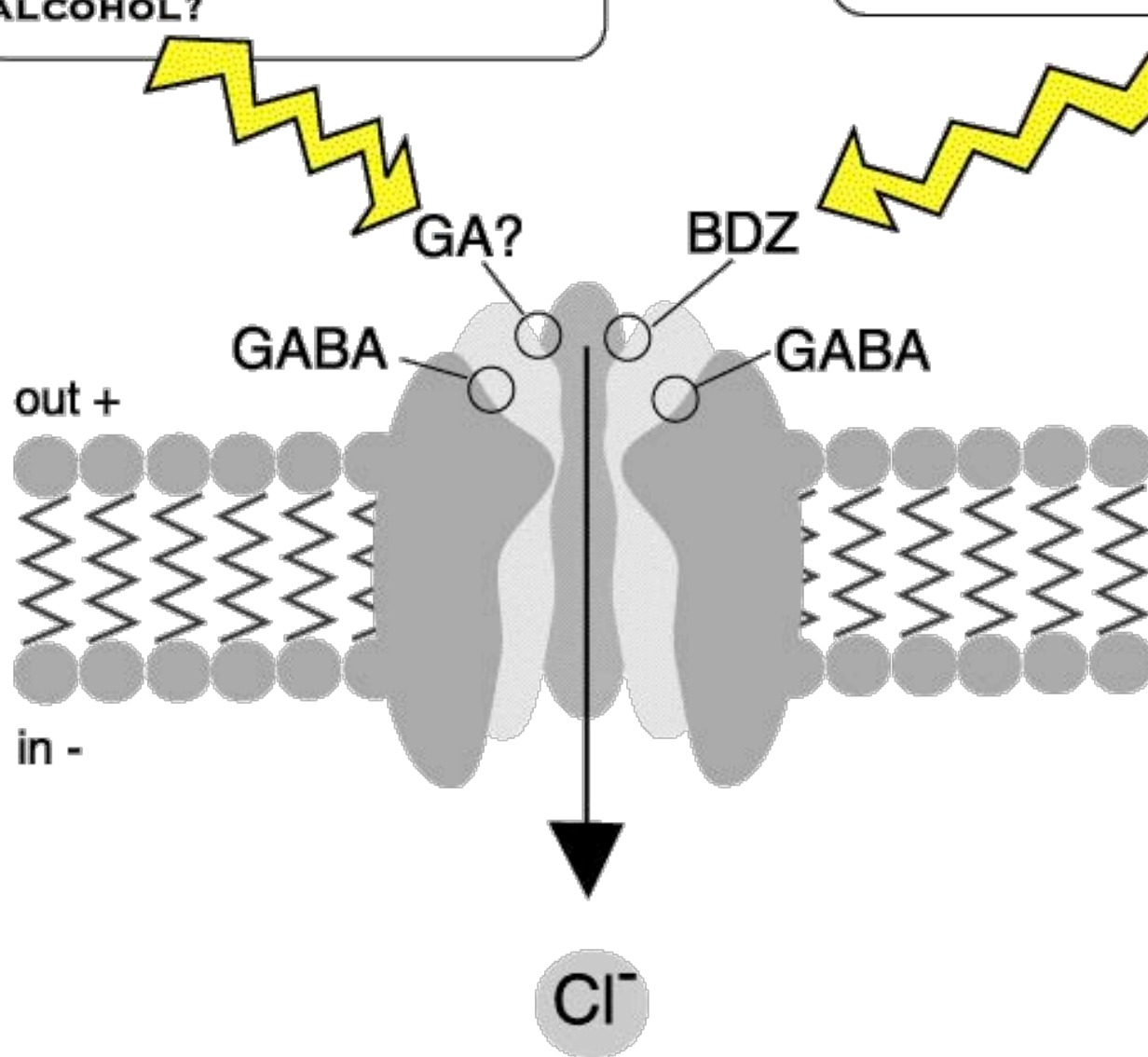
INHALATION ANAESTHETICS?

ALCOHOL?

agonist **DIAZEPAM**

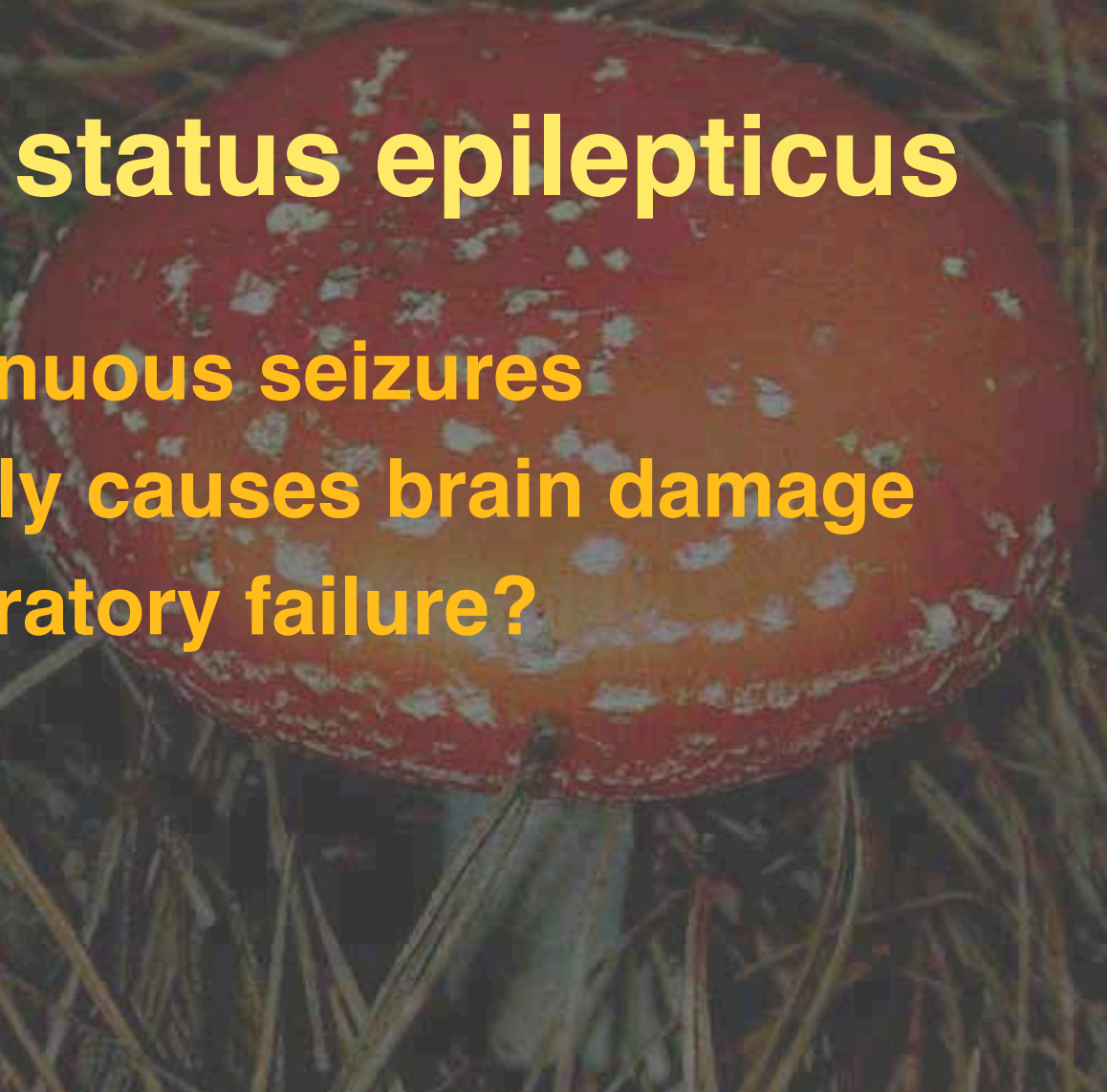
antagonist **FLUMAZENIL**

inverse agonist **βCARBOLINE**



status epilepticus

- continuous seizures
- rapidly causes brain damage
- respiratory failure?



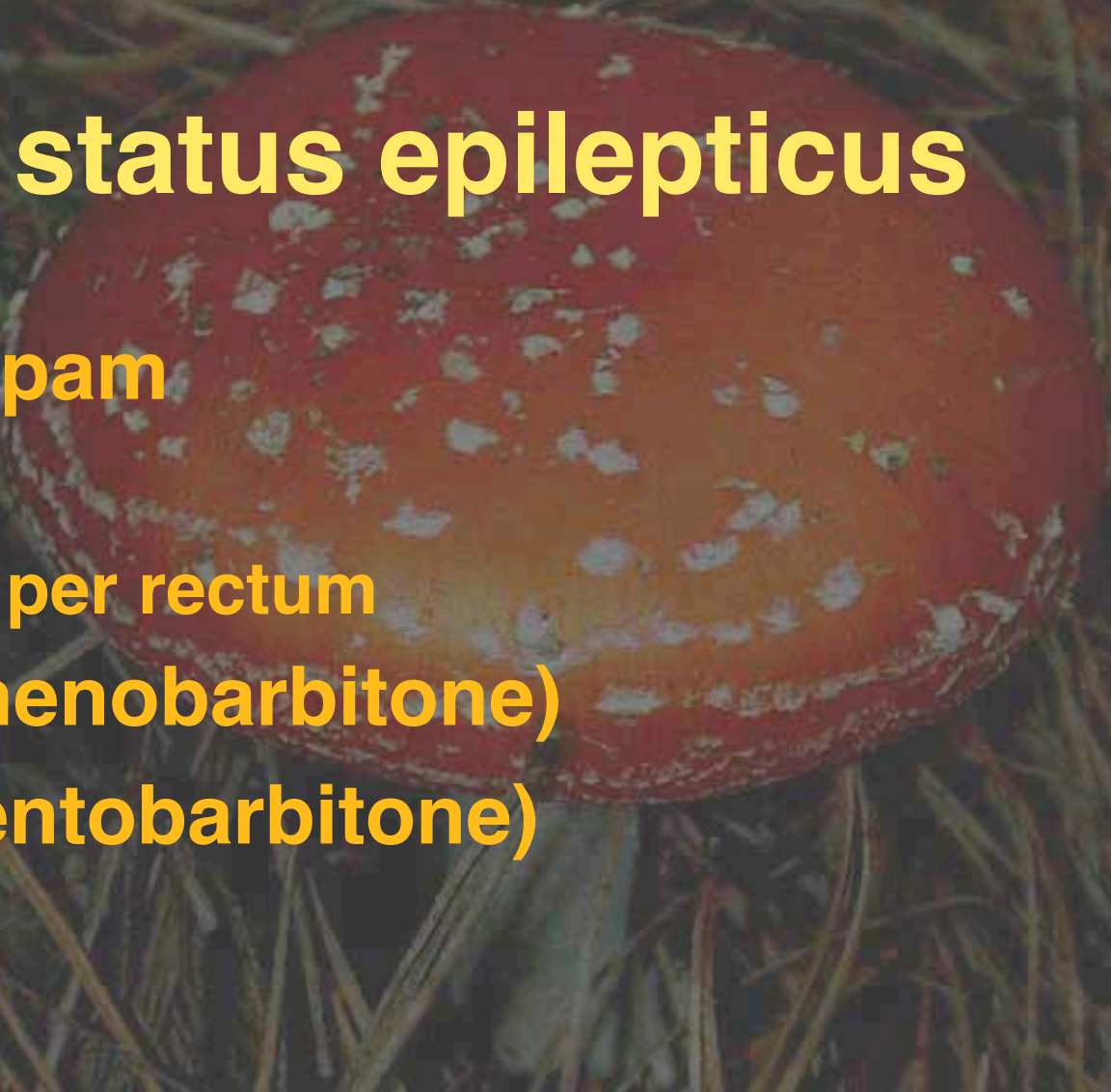
status epilepticus

- **priorities**
 - stop seizures
 - treat cause
 - prevent further brain damage?



status epilepticus

- diazepam
 - iv
 - im, per rectum
- (iv phenobarbitone)
- (iv pentobarbitone)



prevention

- **phenobarbitone**
- **primidone**
- **phenytoin**
- **valproate**
- **bromide**



phenobarbitone

A red mushroom with white spots, resembling 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 a dense field of similar grass, creating a textured, natural setting.

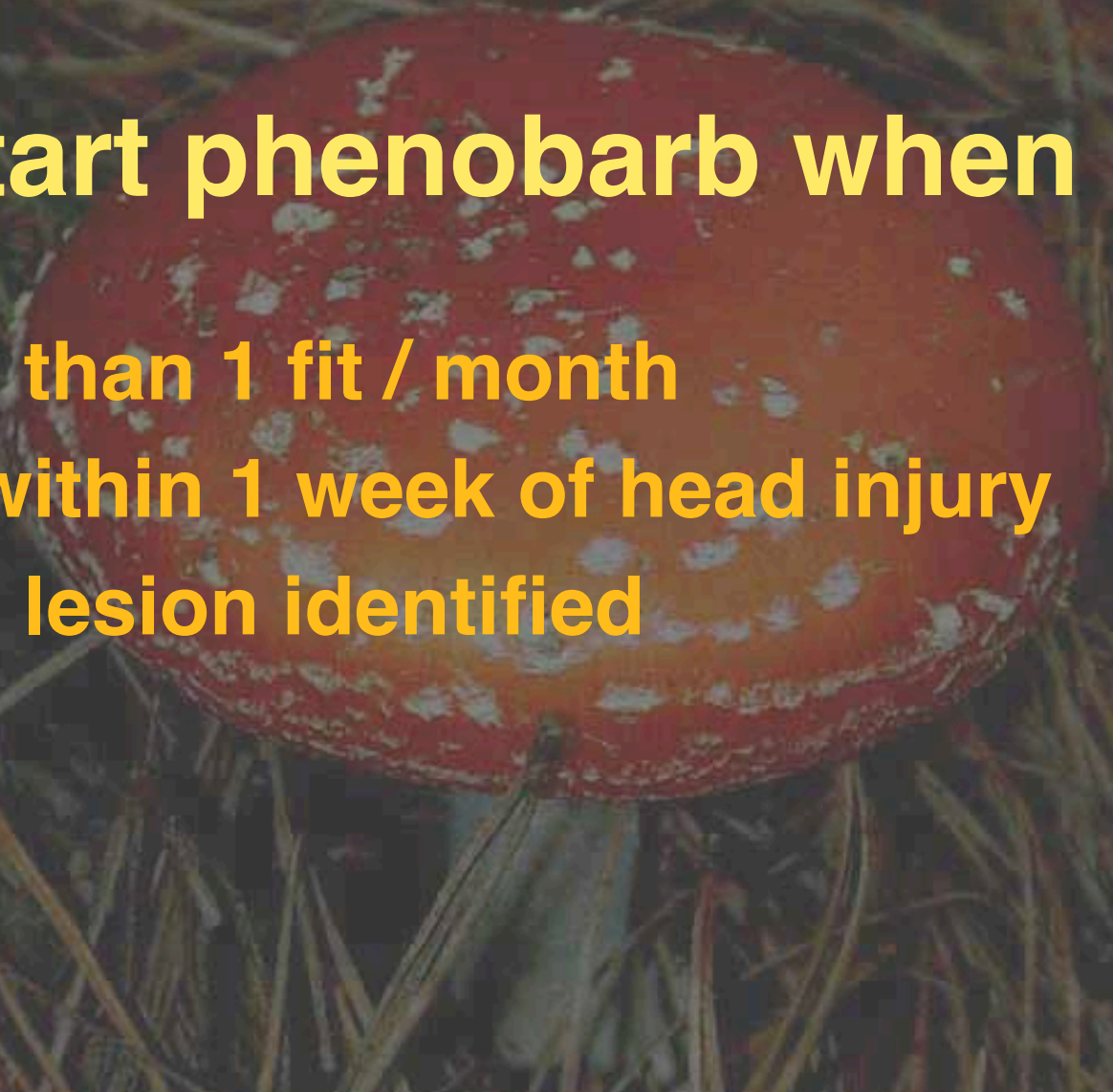
- **works reliably**
- **suitable half life**
- **cheap**
- **more anticonvulsant than other barbiturates**

side effects

- **sedation \pm ataxia**
- **cytochrome P450 induction**
 - initial half life in dog about 100 h
 - half life after induction about 24 h
- **polyuria / polydipsia**
- **raised liver enzymes**
- **very rarely liver failure**

start phenobarb when

- **more than 1 fit / month**
- **a fit within 1 week of head injury**
- **brain lesion identified**



A 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 bright red cap with numerous white, irregular spots. The stem is thick and appears to be a pale, almost white color. The background is a dense field of dry grass, creating a textured, natural setting. The overall lighting is soft, and the colors are somewhat muted, giving it a slightly somber or clinical feel.

primidone

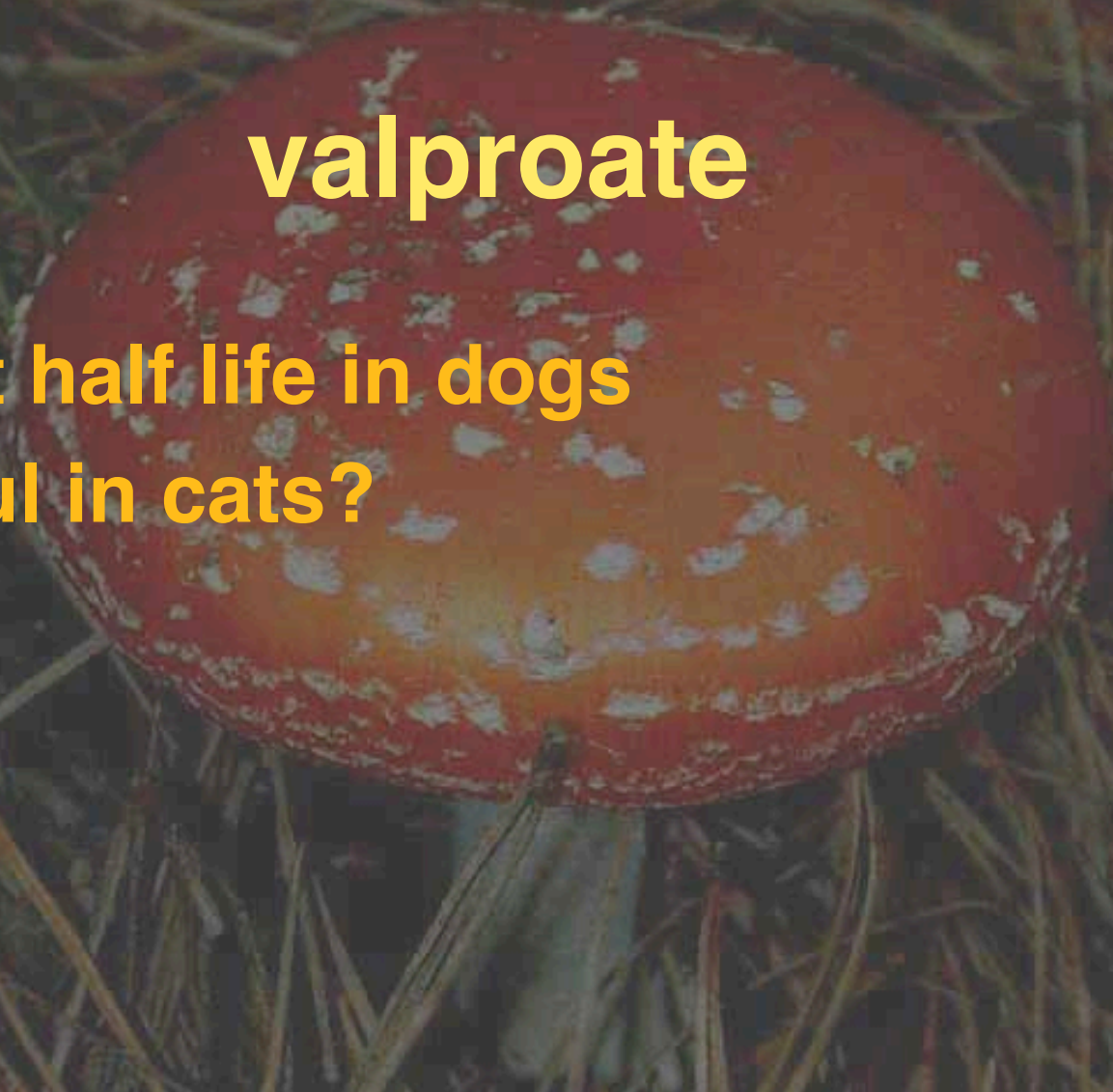
- **metabolised to phenobarbitone**
- **more likely to cause liver damage**
- **more expensive**

phenytoin

- does not work reliably
- zero order kinetics at high doses
- short half life
- induces P450
- liver damage
- (teratogenic)
- newer analogues better (not in NZ)
 - fosphenytoin

valproate

- short half life in dogs
- useful in cats?



new drugs

- gabapentin
 - unknown mechanism – Na⁺ channel blocker??
- lamotrigine
 - sodium channel blocker
- vigabatrin
 - GABA transaminase inhibitor
- felbamate ?
 - not available in NZ

useless drugs

A red mushroom with white spots, resembling 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-yellow grass. The text 'useless drugs' is overlaid on the top half of the image in a bold, yellow font.

- carbamazepine
- ethosuxamide
- benzodiazepines
 - except possibly in cats

half lives

	dog	cat	man
phenobarbitone	42 - 100 (24 - 30)	34 - 43	70 - 100
primidone	9 - 12		6 - 12
phenytoin	2 - 4	24 - 108	15 - 24
carbamazepine	1		24 - 48
valproate	1.5 - 3	8.5	8 - 15
ethosuxamide	17		16 - 70
diazepam	2 - 5	2	24 - 72
clonazepam	1 - 5		24 - 36
felbamate	12		23
bromide	25 - 46 days!		11 days

bromide

- **toxic and obsolete**
 - subjective unpleasant side effects
 - very long half life
- **cheap**
- **a drug of very last resort**

combinations

- **phenobarbitone & bromide**
 - worth trying if phenobarb alone does not work
- **phenobarbitone & phenytoin**
 - not usually any more effective
- **phenobarbitone & gabapentin ?**
 - no data in dogs

drugs to avoid

- acepromazine
- butyrophenones



A red mushroom with white spots growing in grass. The mushroom has a bright red cap with numerous white, irregular spots. It is growing in a field of dry, brown grass. The background is slightly blurred, focusing attention on the mushroom.

if drugs fail

- **check owner compliance**
- **plasma levels**
 - **check every 6 – 12 months**
- **increase dose**
- **try combinations**
 - **bromide**
 - **gabapentin**
- **avoid precipitating factors**

interactions with other drugs

- **protein binding**
- **faster metabolism**
- **potentiation of sedatives /
anaesthetics**



stopping anticonvulsants

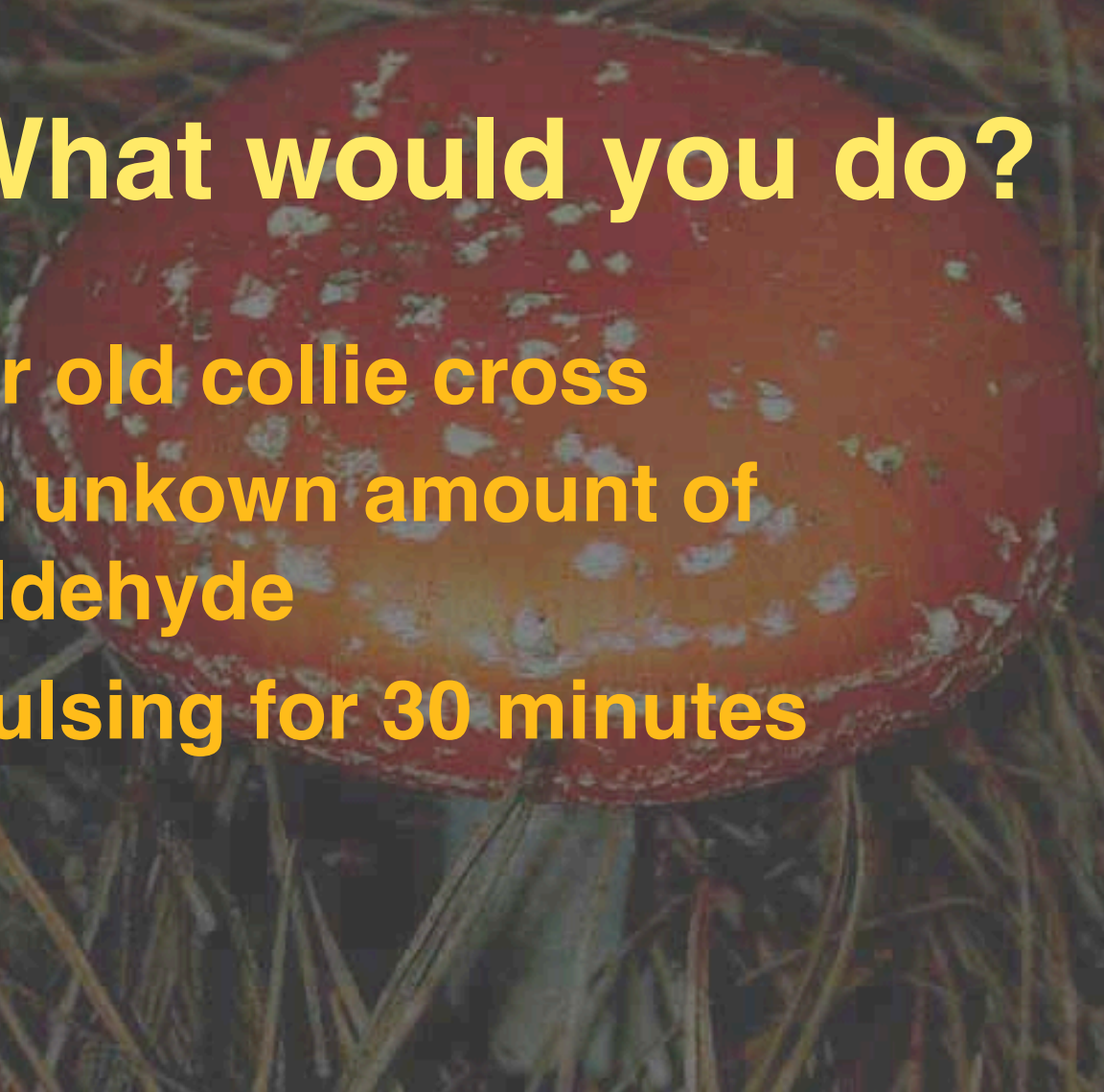
- no fits for 1 year
 - gradually reduce phenobarb
 - 2 weeks between dose changes
 - stop when plasma conc falls to ineffective levels
- start again if more than 3 fits / year

the future?

- **P glycoprotein inhibitors?**
- **high fat diets?**
 - ketones prevent fits
- **nerve stimulation?**
 - vagus / implanted brain electrodes
- **K⁺ channels?**
- **surgery???**

What would you do?

- 3 year old collie cross
- eaten unknown amount of metaldehyde
- convulsing for 30 minutes



priorities?



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priorities

- **ABC**
- **control seizures**
- **assess**
- **decontaminate**
- **longer term control**

anticonvulsants

- anticonvulsants control seizures: they do not cure epilepsy
- phenobarbitone works best for prevention of fits in most cases but induces cytochrome P450
- diazepam is used for status epilepticus
- anticonvulsants potentiate anaesthetics & sedatives