

A photograph of a mushroom with a bright red cap and white spots, growing on a bed of dry, brown grass. The mushroom is the central focus of the image. The text 'Anticonvulsant Drugs' is overlaid in the center of the image in a bold, yellow font.

Anticonvulsant Drugs

A red mushroom with white spots is the central focus of the image, resting on a bed of dry, brown grass. The mushroom has a bright red cap with several white, irregular spots scattered across its surface. The background is a dense layer of dry grass, creating a textured, natural setting. The overall lighting is somewhat dim, giving the scene a slightly somber or mysterious atmosphere.

**by the end of this lecture you
should be able to**

- **formulate a treatment plan for an animal with intermittent or continuous convulsions**

What would you do?



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

epilepsy

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



causes

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

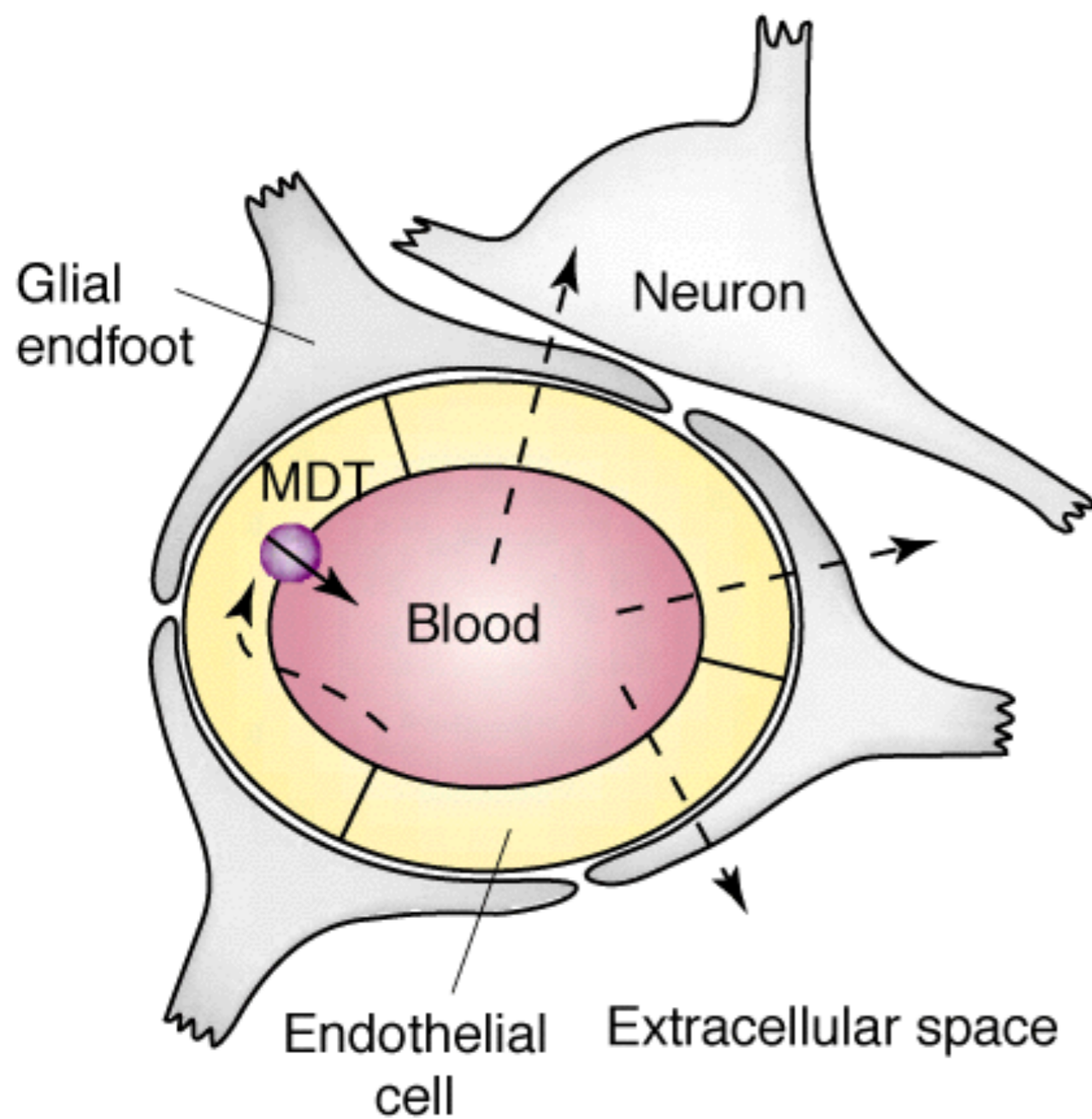
A photograph of a red mushroom with white spots on its cap, growing on a bed of pine needles. The mushroom is the central focus, with its stem visible. The background is a dense layer of dry, brown pine needles.

drugs

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

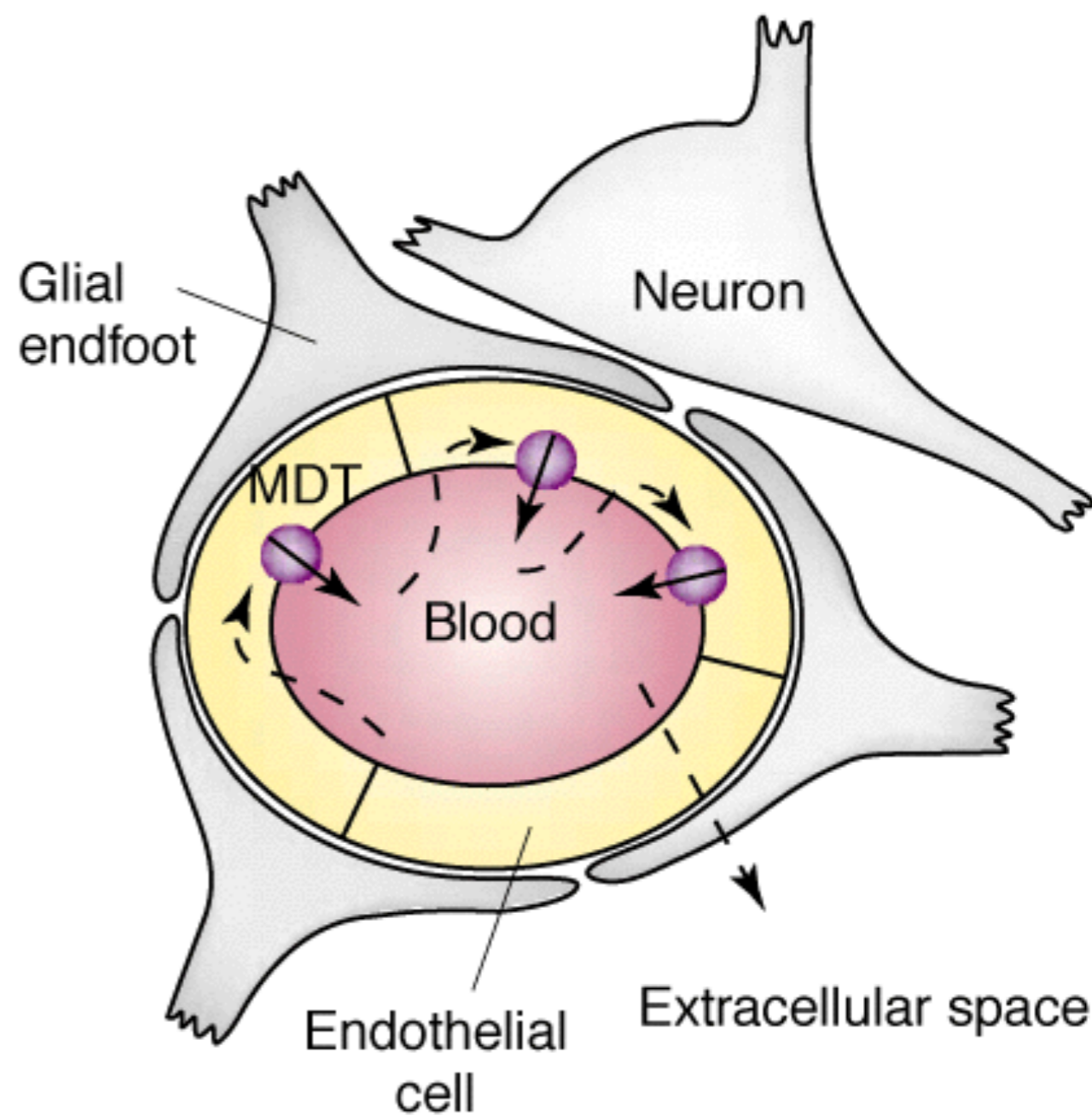
(a)

Normal expression of multidrug transporters



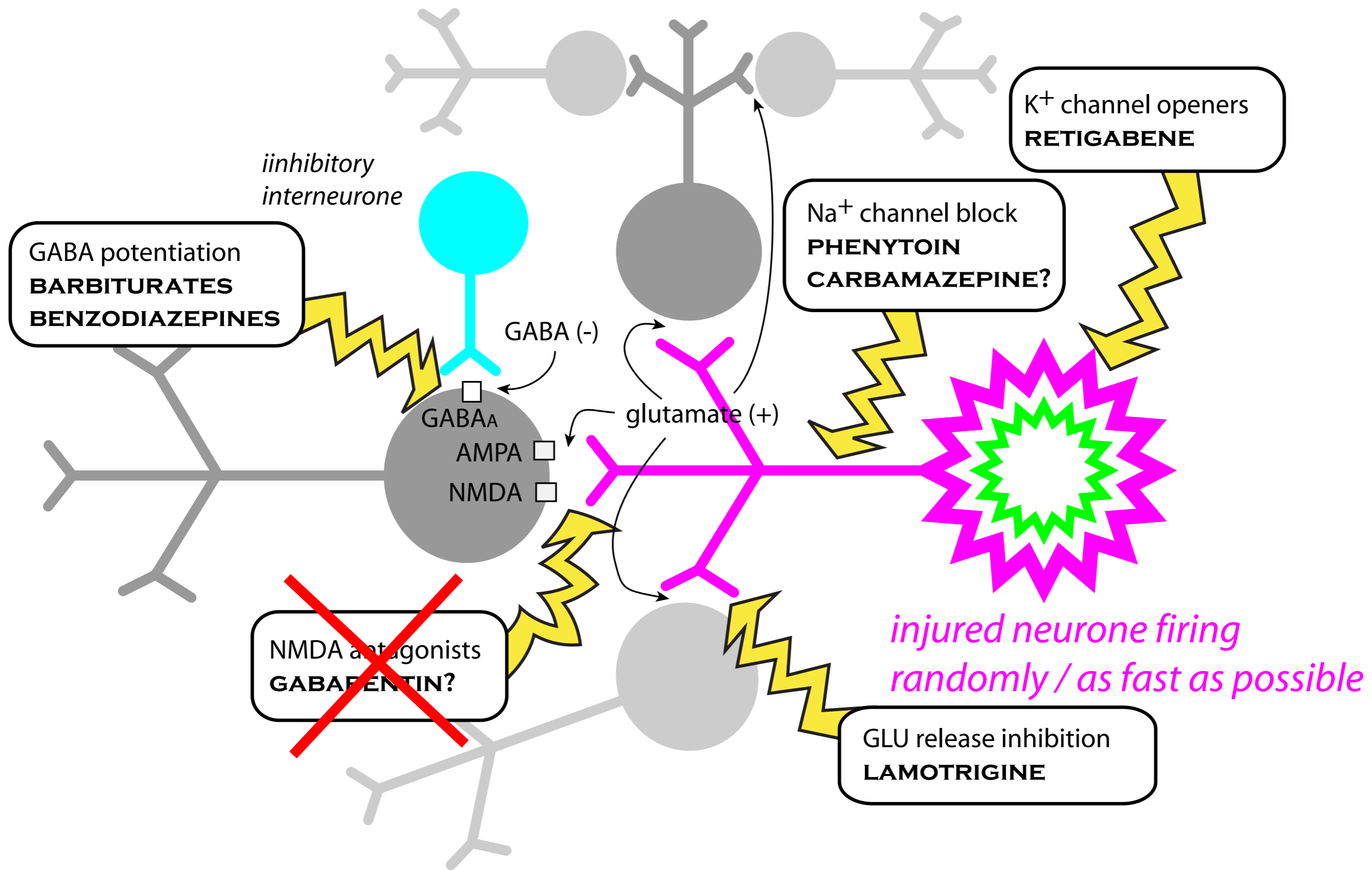
(b)

Overexpression of multidrug transporters



drugs

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



GABA potentiation
BARBITURATES
BENZODIAZEPINES

K⁺ channel openers
RETIGABENE

Na⁺ channel block
PHENYTOIN
CARBAMAZEPINE?

~~NMDA antagonists
GABAFENTIN?~~

GLU release inhibition
LAMOTRIGINE

*injured neurone firing
randomly / as fast as possible*

*inhibitory
interneurone*

GABA (-)

glutamate (+)

GABA_A
AMPA
NMDA

BARBITURATES

OTHER INJECTION ANAESTHETICS?

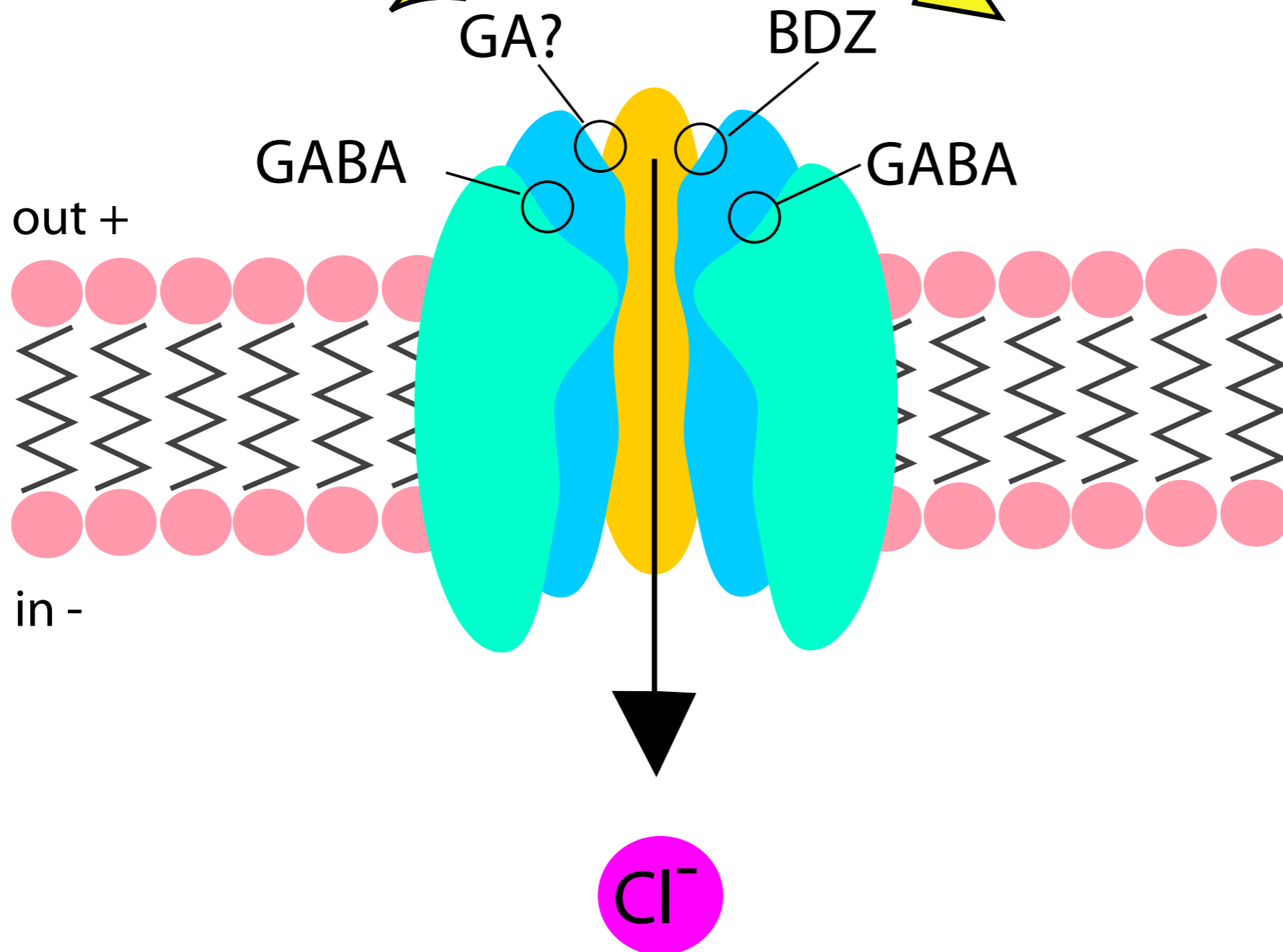
INHALATION ANAESTHETICS?

ALCOHOL?

agonist **DIAZEPAM**

antagonist **FLUMAZENIL**

inverse agonist **βCARBOLINE**



status epilepticus

- **continuous seizures**
- **rapidly causes brain damage**
 - **excitotoxicity**
- **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

A large, red, spotted mushroom with a white stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots and a thick, white, textured stem. The background is a dense field of dry, brown grass.

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

phenobarbitone

A large, red, spotted mushroom with a thick stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots. The stem is thick and appears to have a white, fuzzy texture. The background is a dense field of dry, yellowish-brown grass.

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

side effects

- **sedation ± 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**

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

A large, red, spotted mushroom with a white stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots and a thick, white, textured stem. The background is a dense field of dry, yellowish-brown grass.

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

- 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
 - an alternative to euthanasia
- **phenobarbitone & phenytoin**
 - not usually any more effective
- **phenobarbitone & gabapentin ?**
 - no data in dogs

A large, red, spotted mushroom with a white stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots and a thick, white, slightly textured stem. The background is a dense field of dry, yellowish-brown grass.

drugs to avoid

- **acepromazine**
- **butyrophenones**

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

A large, red mushroom with white spots is the central focus of the image. It is growing on a bed of dry, brown grass. The background is a soft-focus field of similar grass. The overall lighting is somewhat dim, giving the scene a natural, slightly somber feel.

- **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

A large, bright red mushroom with white spots, growing in a field of dry grass. The mushroom is the central focus of the image, with its cap showing a gradient from red to orange and yellow. The background is a dense field of dry, brown grass.

- **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**