

Antiepileptics

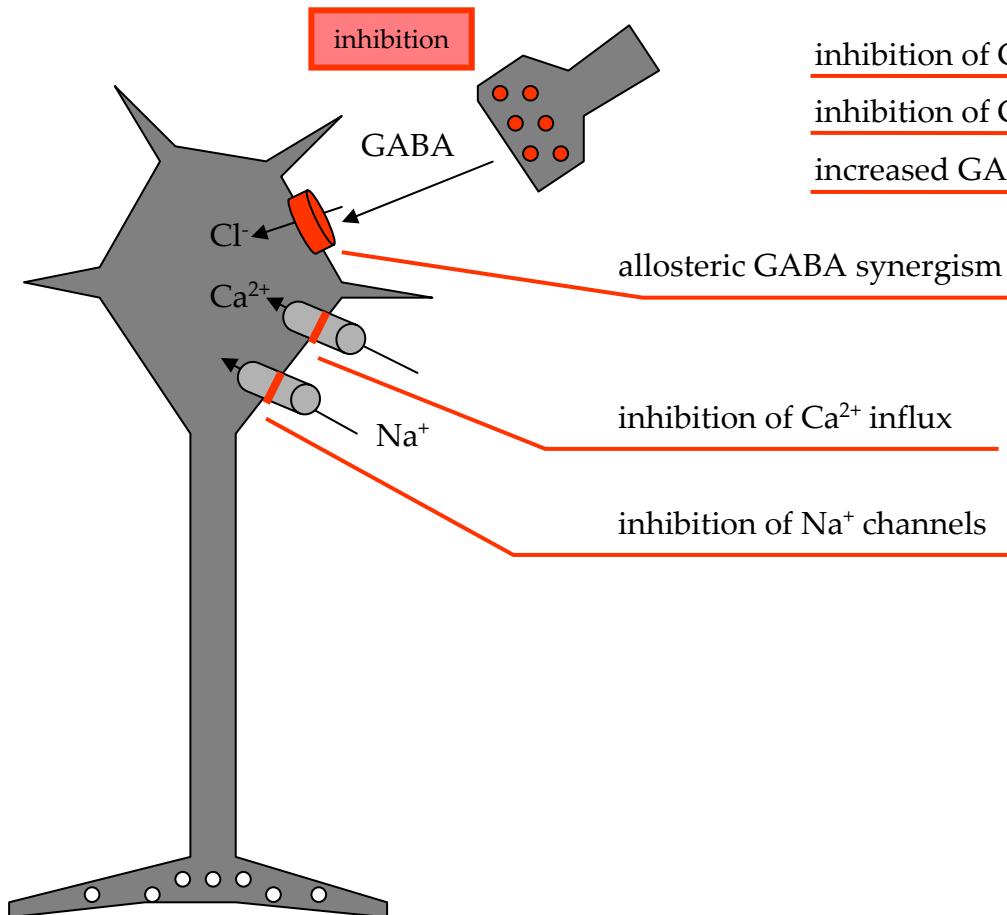
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Epilepsy



inhibition of GABA uptake

tiagabine

inhibition of GABA breakdown

vigabatrin

increased GABA release

gabapentin

allosteric GABA synergism

benzodiazepines
phenobarbital

inhibition of Ca^{2+} influx

ethosuximide

inhibition of Na^+ channels

carbamazepine
valproate
phenytoin
lamotrigine

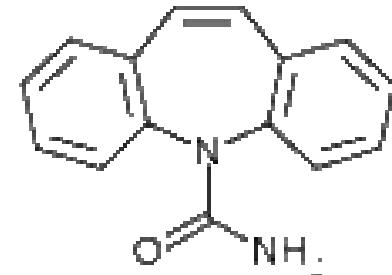
- Generalised
 - e.g. grand mal
 - loss of consciousness
 - absences
 - tonic-clonic seizures
- Partial
 - Jacksonian epilepsy
 - complex seizures

- General considerations
 - long-term treatment
 - therapeutic index
 - gradual dose titration
 - individual approach
 - monotherapy preferred
 - gradual withdrawal
 - TDM

- Interactions
 - enzyme inducers
 - competition
 - plasma protein binding
- Mechanism
 - use-dependent inhibition of channels

First choice antiepileptics

- **Carbamazepine (Tegretol®)**
 - kinetics and dynamics
 - metabolised to epoxide
 - CYP inducer – half-life from 20 to 8
 - Na^+ channel inhibitor
 - indications
 - grand mal
 - partial seizures
 - neuropathic pain
 - side effects
 - sedation, vertigo, bone marrow suppression



First choice antiepileptics

- **Valproate** (Orlept®, Epilim®)

- kinetics and dynamics

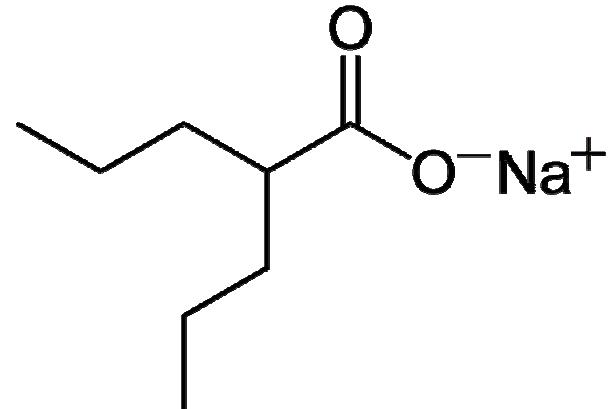
- 95% protein binding
 - half-life 8-15 hours
 - Na^+ channel inhibitor (and Ca^{2+})

- indications

- wide spectrum
 - including absences
 - mood stabiliser

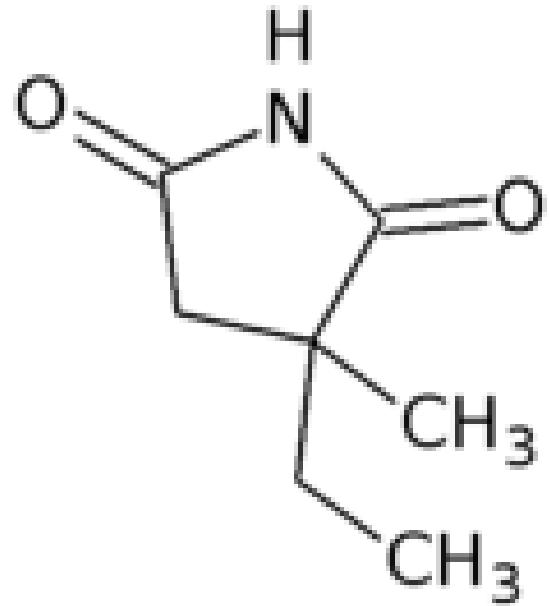
- side effects

- tremor, liver toxicity, hair loss, teratogenic



First choice antiepileptics

- Ethosuximide (Zarontin®, Emeside®)
 - kinetics and dynamics
 - T-channel blocker ???
 - half-life 20 hours
 - indications
 - absences
 - side effects
 - ataxia, bone marrow suppression



First choice antiepileptics

- Clonazepam (Rivotril®)
 - kinetics and dynamics
 - benzodiazepine (GABA_A)
 - half-life 18-50 hours
 - indications
 - absences
 - epilepsy in children
 - side effects
 - ataxia, bone marrow suppression



Reserve antiepileptics

Reserve antiepileptics

- **Phenytoin (Epanutin®)**
 - kinetics and dynamics
 - related to barbiturates
 - complicated kinetics
 - powerful inducer
 - protein binding
 - indications
 - wide spectrum
 - antiarrhythmic
 - side effects
 - sedation, psychotic symptoms, lupus, gingival hyperplasia

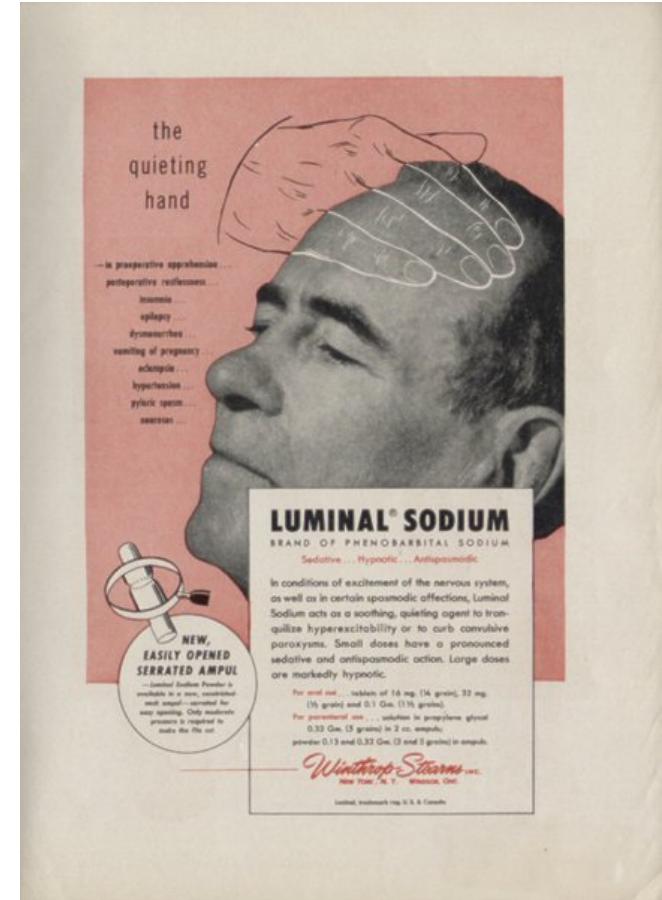


Gum hyperplasia



Reserve antiepileptics

- Phenobarbital (Luminal®)
 - kinetics and dynamics
 - powerful inducer
 - low protein binding
 - indications
 - oldest one still used
 - WHO essential drug list
 - side effects
 - sedation



Reserve antiepileptics

- **Vigabatrin (Sabril®)**
 - kinetics and dynamics
 - inhibitor of GABA aminotransferase
 - half-life 2-4 hours
 - indications
 - severe forms of epilepsy
 - side effects
 - sedation, visual field reduction

Reserve antiepileptics

- Lamotrigin (Lamictal®)
 - kinetics and dynamics
 - sodium channel inhibitor
 - glutamate release inhibition
 - indications
 - Lennox-Gastaut syndrome
 - combinations
 - side effects
 - skin adverse effects,



Reserve antiepileptics

- Levetiracetam (Keppra®)
 - kinetics and dynamics
 - NMDA?
 - indications
 - can be now used in monotherapy
 - side effects
 - ataxia, skin adverse effects

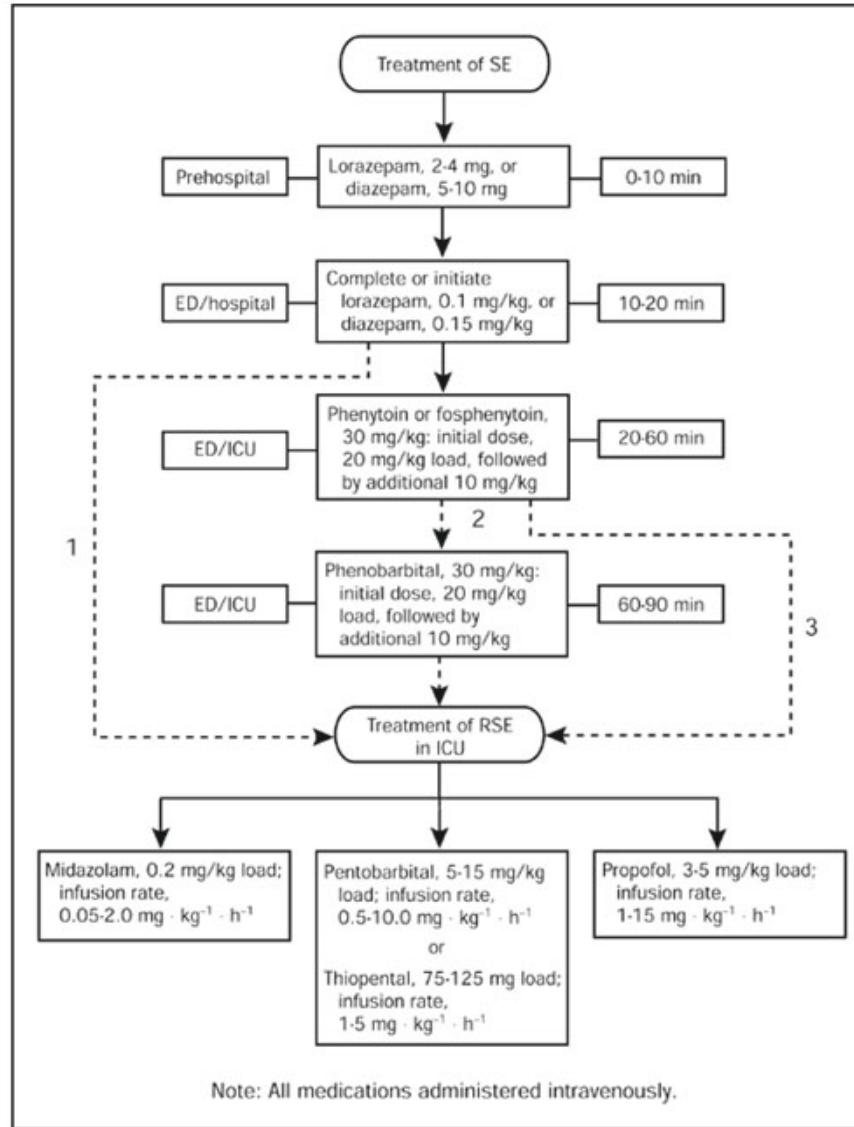


Status epilepticus

- **Diazepam** (Valium®, Apaurin®)
 - 0,15-0,25 mg/kg
 - i.v., i.m., p.r., i.p.
 - risk of respiratory depression
- **Lorazepam** (Ativan®)
 - fast, safer
- **Paraldehyde** (Paral®)
 - does not cause resp. suppression
 - 30 % eliminated via lungs



Status epilepticus



Thank you for you attention

thank you for your attention

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thank you for your attention

An apology

that was a very bad joke