MMed and DCH Lectures

Epilepsy in children

August 2, 2021

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Epilepsy in children

1. Definition
2. Epidemiology in low-middle income countries
3. Terminology, classification, types of seizures
4. Comorbidities
5. Causes of epilepsy
6. Epilepsy syndromes
7. Anti-epileptic drugs (AED)
8. Management needs

Definition of epilepsy

- At least 2 unprovoked seizures occurring more than 24 hours apart (i.e. separated by *at least* 24 hours)

- "*Unprovoked*" = NOT fever, meningitis, malaria, trauma, etc (although children with these conditions can *develop* epilepsy).

- Seizures involve the same muscle groups repetitively contracting, and are not suppressible by tactile pressure.

Febrile convulsions and epilepsy

- 3-7% of all children have one febrile convulsion up to 7 years of age
  - 24% have a family history of febrile seizures, and 4% have a family history of epilepsy
  - 20% complex febrile convulsion (longer than 10 minutes, not generalized)
  - 35% go on to have further febrile seizures
  - Benign, have a normal cognitive outcome
  - If prolonged – intranasal midazolam / rectal diazepam

Epidemiology – prevalence and incidence

- 10 per 1000 in low income countries (1%), but higher **prevalence rates** reported in rural areas.
- **Prevalence** estimates *in children* in low income countries range widely, from 3.6 - 44 per 1000 in children). This means that in some communities up to 4%, or one in 25 children will have epilepsy.
- Estimated **incidence** (new cases per year, overall adults and children) is 82 per 100,000 in low income countries.

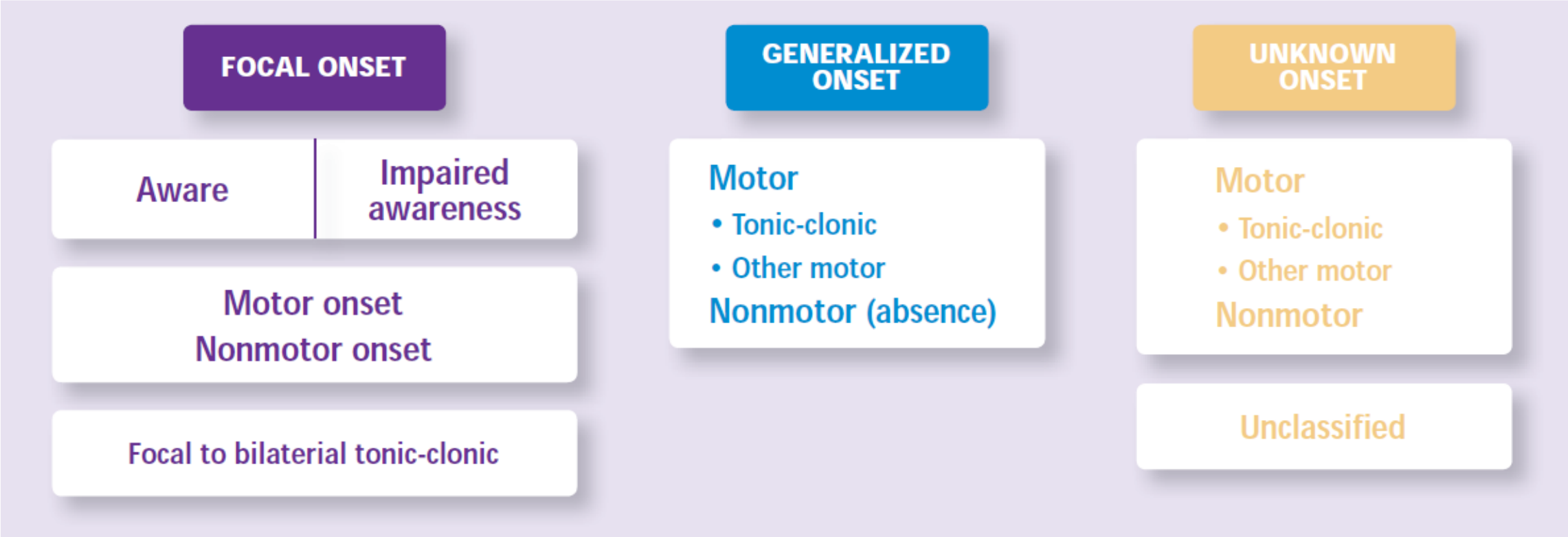
Terminology

- **Focal seizures:** when there are focal symptoms and signs, even if a person progresses to bilateral motor manifestations. Originate within neuronal networks limited to one hemisphere.

- **Generalised seizures:** arise within or rapidly engage bilaterally distributed neuronal networks.

- The practical reason to distinguish focal from generalised seizures is that some drugs are more effective against each seizure type

Classification of epilepsy



Epilepsy, a public health imperative. WHO 2019

Causes of epilepsy

- “Idiopathic” – polygenetic, monogenetic

- Infection or post-infection: CNS tuberculous, neurocysticercosis, post meningitis cerebral infarction
- Post-hypoxic ischaemic brain injury, such as perinatal asphyxia
- Stroke (vascular), such as venous sinus thrombosis, or arterial stroke from cyanotic congenital heart disease
- Post trauma
- Brain tumour
- Cortical malformations, such as genetic cerebral dysplasia
- Inborn errors of metabolism, such as hyperammonaemia

Patterns of epilepsy

- Benign Rolandic
- Childhood absence
- Juvenile myoclonic
- Infantile spasms

Benign Rolandic epilepsy

- 15% of childhood epilepsy
- Onset 3-10 years
- Most have very few seizures and most become seizure-free by the age of 16.
- **Focal seizures**, **usually at night**, begin with a tingling feeling in the mouth, grunting noises and dribbling. Speech can be temporarily affected and may → GTC seizure.
- AEDs can be helpful to control seizures, although not always used.

Childhood absence epilepsy

- 12% of children with epilepsy
- Onset 4-10 years
- Absence seizures frequently and very brief, lasting only a few seconds. Often not noticed.
- During a seizure a child becomes unconscious. They may look blank or stare and their eyelids flutter. They may not respond to what is happening around them or be aware of what they are doing.
- Respond well to medication.
- 90% of children with CAE grow out of seizures by the age 12
- Sometimes may be associated with other types of seizure.

Juvenile myoclonic epilepsy

- Onset 12-18 years: 3 types of seizures
  - Myoclonic seizures (brief muscle jerks) in the upper body
  - Tonic-clonic
  - Absence
- Often shortly after the child wakes up
- Become less severe in adult life
- Medication successful
- Triggers: tiredness, stress, alcohol, flashing or flickering lights

Infantile spasms (West syndrome)

- Onset in 1st year of life
- Previous brain injury before the age of 6 months
- Brief spasms or jerks which happen in ‘clusters’
- Spasms can affect the whole body or just the arms and legs. Each cluster can include between 10 – 100 individual spasms
- AEDs and steroids
- 25% of children have spasms that do not respond well to medication
- Many children develop problems with learning or behavior
- Some may go on to develop Lennox-Gastaut syndrome.

Anti-epileptic drugs

- Focal seizures
  - **Carbamazepine, phenytoin, phenobarbitone**, levetiracetam
- Generalised seizures
  - **Valproic acid** (sodium valproate) most effective in generalised epilepsy
  - **Phenobarbitone and levetiracetam** effective against most types of generalised seizures

Anti-epileptic drugs

- Mechanism of action
- Type of seizures they mostly treat
- Effects on liver enzymes

Mechanisms of action

Sodium channel blockade: inhibits the generation of rapid action potentials	**Calcium channels:** block inward calcium flow into cells	**GABA enhancing:** GABA inhibitory neurotransmitter	**Glutamate inhibitor** Glutamate is excitatory neurotransmitter	**Carbonic anhydrase** inhibition	**Other / unknown**
Phenytoin	Ethosuximide	Phenobarbitone	Topiramate	Acetazolamide (Diamox)	Levetiracetam
Carbamazepine	Gabapentin	Benzodiazepines	Felbamate		
Lacosamide		Vigabatrin			
Oxycarbazine					
		Sodium valproate			
Zonisamide		Gabapentin			

Phenobarbitone

- GABA enhancement +
- For generalized seizures (sodium valproate better)
  - Side effects:
  - Sedation, difficulty concentration, mood changes, depression, hyperactivity in children
  - Reduced bone density (interaction with phenytoin)
    - (Think of conditions where there is bone demineralization - osteopenia)
- For focal seizures (carbamazepine better)
- Inducer of cytochrome p-450 enzymes (more metabolism of drugs cleared by p450 enzymes)

Phenytoin

- Sodium channel inhibitor
- For focal or generalised seizures (but other agents are better)
- Side effects:
  - Gum hypertrophy, rash, folic acid depletion
  - Decreased bone density (p450 breaks down vitamin D→ vitamin D deficiency), compounded if also on phenobarbitone
  - Neurotoxic: confusion, slurred speech, double vision, ataxia, neuropathy
- Inducer of cytochrome p-450 enzymes

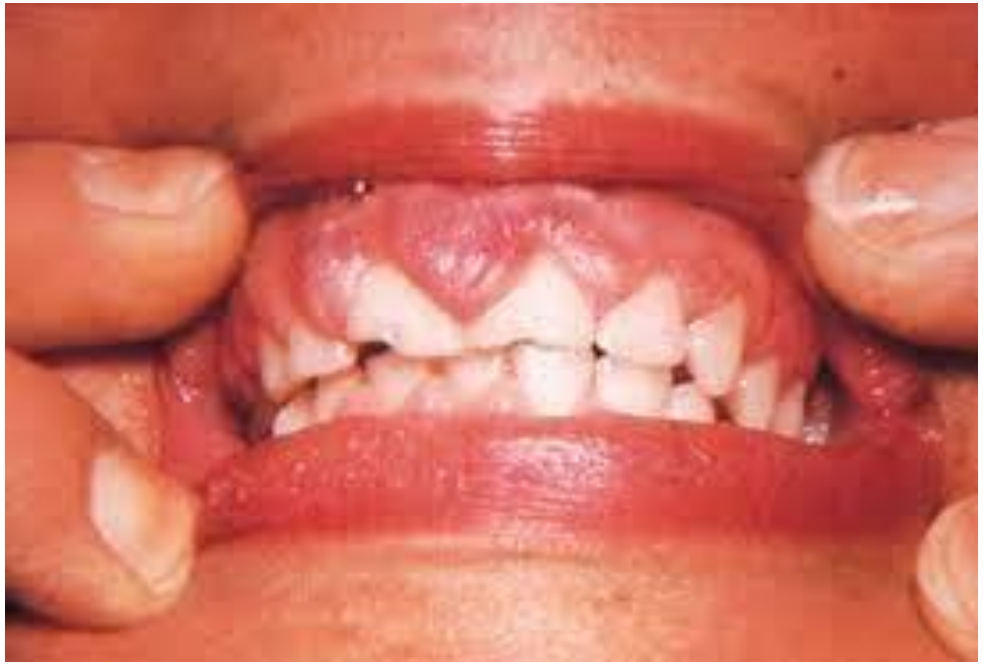
Carbamazepine

- Sodium channel inhibitor
- Very effective against focal seizures
- Nausea, vomiting, diarrhoea, hyponatremia, rash, pruritus, and fluid retention, ataxia with high doses
- Leukopenia (12%), aplastic anaemia (rare)
- Stevens Johnson Syndrome
- Inducer of cytochrome p-450 enzymes

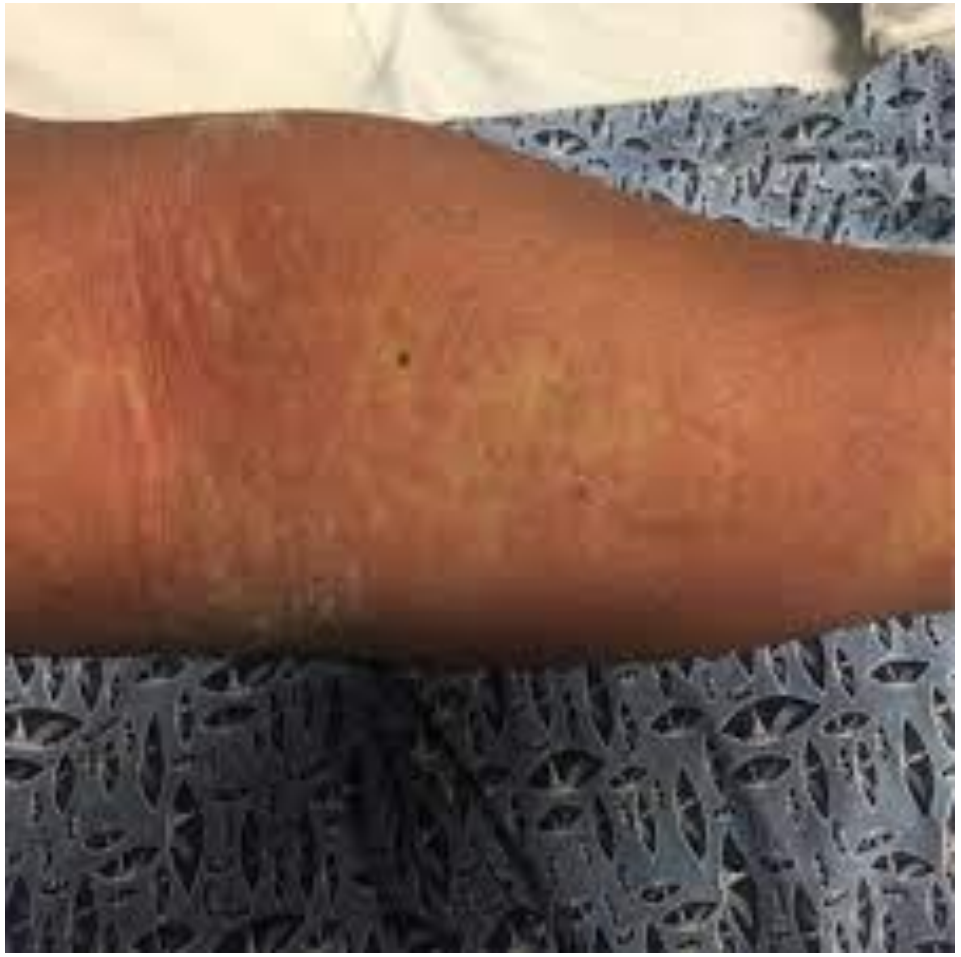
Sodium valproate = Valproic acid (Epeilim)

- GABA enhancement
- Best drug for **generalised epilepsy**, also effective against some forms of focal epilepsy.
- Hepatic toxicity (1%) and pancreatitis (<0.1%)
- Teratogenic, do not give adolescent girls
- Liver enzyme *inhibitor*:
  - increases drugs that are metabolised by cytochrome p450: zidovudine (AZT), children with epilepsy and HIV who are on valproic acid need a dose reduction in AZT to maintain unchanged serum AZT concentrations

Side effects from anticonvulsant drugs



Gum hypertrophy from phenytoin
(can also occur with other AEDs:
phenobarbitone, sodium valproate)



Drug eruption rash from carbamazepine
(can also occur with other AEDs)

Cytochrome p450 and drug interactions

Inducers

- Carbamazepine
- Phenytoin
- Phenobarbitone
- Rifampicin

Levels of other drugs that are metabolised by the liver will go down: a decrease in the effect of the other medicine

Inhibitors

- Sodium valproate
- Isoniazid

Levels of other drugs that are metabolised by the liver will go up: risk is toxicity

Effectiveness of treatment

- 70% of patients achieve seizure freedom with appropriate medical treatment, and most of these children respond to the initially prescribed drug
- 30% resistant to treatment
  - If resistant to one AED, increase to maximum dose as long as no side effects
  - If still resistant: start a second AED with a *different mechanism of action* and different side effect profile
  - If the addition of the 2nd AED causes the seizures to cease, *slowly withdraw* the 1st drug

Risk of mortality

- Mortality rate among people with epilepsy in high income countries is 2-5 times higher than the general population
- Mortality is increased to a larger extent (up to 37 times) in low-income countries, especially in children and young people
- Some children with epilepsy do NOT have an increased risk of death (e.g. absence seizures, benign Rolandic epilepsy)
- Children still need to be protected against environmental risks: fire, drowning, falls

SUDEP = sudden unexpected death in epilepsy

- Often during sleep. 16-24 times greater risk of sudden death in children and young people with epilepsy.
- Risk factor for SUDEP
  - Poorly controlled generalised epilepsy
  - SUDEP mostly occurs in children *who are not in remission*
  - Those with a known cause of epilepsy (e.g. structural causes, e.g. either a congenital or acquired brain injury)

Epilepsy in Papua New Guinea: a longitudinal cohort study

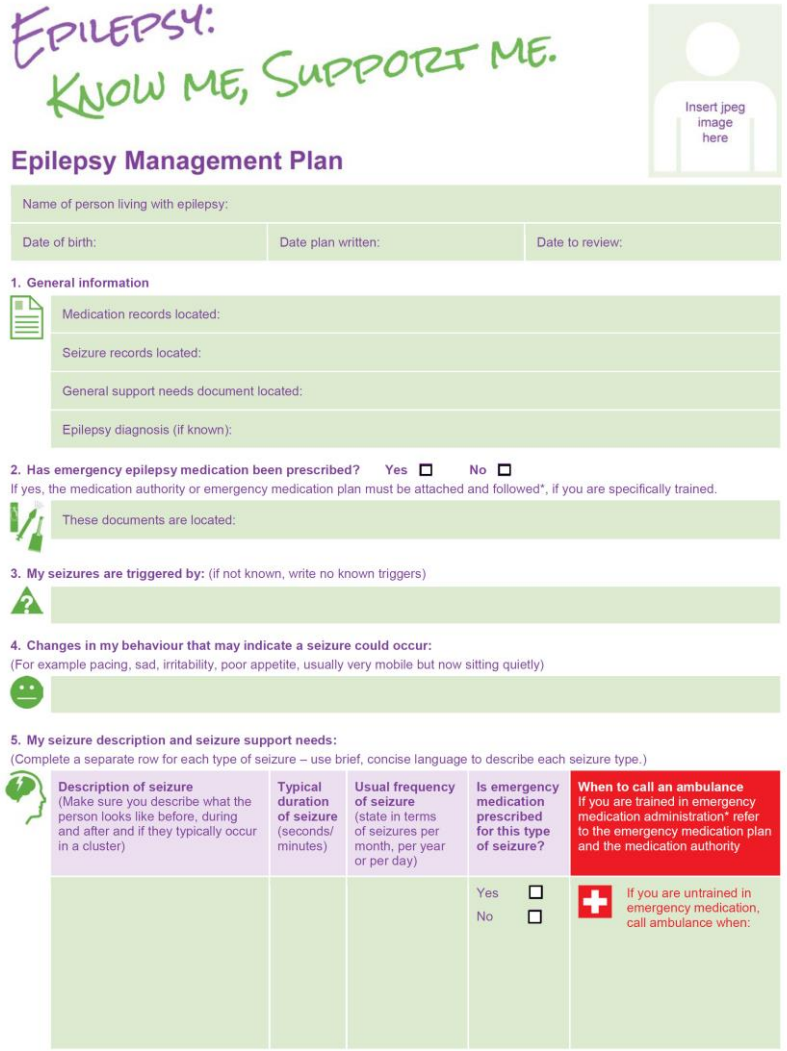
Casparia Mond,[1] Trevor Duke,[2,3] John Vince[4]

Mond C, *et al*. *Arch Dis Child* 2019;**0**:1–6. doi:10.1136/archdischild-2019-317217

- 47 children with epilepsy followed for 18 months
- 55% developmental disability
- Only 26% attended school
- Injuries, burns common
- Most on phenobarbitone monotherapy
- Many improved with better treatment, education, monitoring

Individualised management plan

- Type of epilepsy
- Seizure frequency
- Other comorbidities
- AED treatment
- Contact people
- What parents and health workers should do when the child has a seizure:
  - How to safely position the child
  - What extra drugs to administer at home
  - When to take their child to hospital or health clinic
  - When to have a clinical and medication review by their doctor



Epilepsy:
Know me, Support me.

Insert jpeg image here

Epilepsy Management Plan

Name of person living with epilepsy:

Date of birth: | Date plan written: | Date to review:

1. General information

Medication records located:

Seizure records located:

General support needs document located:

Epilepsy diagnosis (if known):

2. Has emergency epilepsy medication been prescribed? Yes ☐ No ☐

If yes, the medication authority or emergency medication plan must be attached and followed*, if you are specifically trained.

These documents are located:

3. My seizures are triggered by: (if not known, write no known triggers)

4. Changes in my behaviour that may indicate a seizure could occur:

(For example pacing, sad, irritability, poor appetite, usually very mobile but now sitting quietly)

5. My seizure description and seizure support needs:

(Complete a separate row for each type of seizure – use brief, concise language to describe each seizure type.)

Description of seizure (Make sure you describe what the person looks like before, during and after and if they typically occur in a cluster)	**Typical duration of seizure** (seconds/ minutes)	**Usual frequency of seizure** (state in terms of seizures per month, per year or per day)	**Is emergency medication prescribed for this type of seizure?**	**When to call an ambulance** If you are trained in emergency medication administration* refer to the emergency medication plan and the medication authority
			Yes ☐ No ☐	If you are untrained in emergency medication, call ambulance when:

Goals of care

- Seizure freedom
- Education about physical safety (water, fire, bicycles, trees)
- Improved school attendance, educational attainment
- Freedom from AED complications
  - Oral hygiene (chlorhexidine mouth wash, brush teeth)
  - Vitamin D supplements
  - Folic acid supplements
- Improved self-esteem
- Knowledge of epilepsy by the child and family.

Reducing stigma

- 70% of children can be seizure free with treatment, and live happy productive lives
- Not contagious
- Not “mad” or “possessed” by evil spirits
- Children with epilepsy do not need to be hidden away

- Community education – starts with immediate family, wider family, schools…