

EPILEPSY

Epilepsy: new advances

Moshe SL, et al Lancet 2015; 385:884-98

- **What is the operational definition of epilepsy?**
(a) At least 2 unprovoked seizures occurring more than 24 hours apart (i.e. separated by *at least* 24 hours), (b) one unprovoked seizure and the probability of more seizures occurring over the next 10 years, and (c) diagnosis of an epilepsy syndrome. Febrile convulsions are not epilepsy.

- **In some new classifications of epilepsy, “focal” seizures has been replaced by “partial” seizures, but what are the differences between focal and generalised seizures?**
Focal seizures occur when there are focal symptoms and signs, even if a person has bilateral motor manifestations. Focal seizures 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 (see below)

- **Which commonly available antiepileptic drugs are more effective against focal or partial seizures, and which are more effective against generalised seizures?**

Focal seizures – **Carbamazepine, phenytoin, phenobarbitone, levetiracetam**

Generalised seizures – **Valproic acid** (sodium valproate) is the most effective AED in generalised epilepsy; phenobarbitone and levetiracetam are effective against most types of generalised seizures.

- **List 6 causes of structural or metabolic epilepsy**
 - Infection or post-infection: Tuberculoma, neurocysticercosis, post meningitis ischaemia or infarction
 - Post-hypoxic ischaemic brain injury, such as perinatal asphyxia
 - Stroke, such as venous sinus thrombosis, or arterial stroke from cyanotic congenital heart disease
 - Trauma or post-trauma
 - Brain tumour
 - Cortical malformations, such as genetic cerebral dysplasia
 - Inborn errors of metabolism, such as hyperammonaemia
- **What is the estimated prevalence of epilepsy in low-income countries?**
10 per 1000 in low income countries (1%), but higher prevalence rates reported in rural areas. 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.
The estimated **incidence** (new cases per year, overall adults and children) is 82 per

100,000 in low income countries.

- **Is there an increased risk of mortality in young people with epilepsy, and to what extent?**

Yes, the mortality rate among people with epilepsy in high income countries is 2-5 times higher than the general population, but is increased to an even larger extent (up to 37 times) in low-income countries, especially in children and young people. Some forms of childhood epilepsy are not generally associated with an increased risk of death, including childhood absence epilepsy (but children still need to be protected against environmental risks such as fire and drowning).

- **What is SUDEP? In which children with epilepsy is SUDEP more likely? What can health care workers and families to reduce the risk of SUDEP?**

SUDEP is sudden unexpected death in epilepsy, often during sleep. There is a 16-24 times greater risk of sudden death in children and young people with epilepsy, compared with the very low risk of sudden death in the general population. The most important risk factor for SUDEP is poorly controlled generalised epilepsy. SUDEP mostly occurs in children *who are not in remission*, and in those with a known cause of epilepsy (such as the structural causes mentioned above). The mechanisms of SUDEP is uncertain, but may relate to cardiac or respiratory dysfunction related to an unwitnessed generalised tonic-clonic seizure (GTCS) during sleep or at other times. The risk of SUDEP is decreased by good control of epilepsy, so if children have poorly controlled seizures, they should have an review of their treatment, ensure it is correct for their age and weight, consider increasing the doses if the maximum has not been reached, consider a change in therapy, or addition of a new anti-epileptic drug (AED).

- **What are the other causes of death in young people with epilepsy? What can be done to reduce these deaths?**

Drowning, burns, status epilepticus. Parents need to be informed of the need for close supervision of children with epilepsy in baths, showers, when swimming, near waterways, avoid being close to fires or other environmental risks. Parents also need an **action plan**, so that in the event of seizures they know what to do, how to safely position the child, what extra drugs to administer at home, when to take their child to hospital or health clinic. And parents need to know if their child is having increased numbers of seizures, and have a clinical and medication review by their doctor, so that the risks of SUDEP and other complications can be minimised.

- **How can smart-phones help in the diagnosis of epilepsy?**

The diagnosis of epilepsy is a clinical one, it doesn't rely on EEG, so if parents take a video of their child during an episode it can help distinguish a true seizure from other conditions which they not be a seizure.

- **What percentage of children with epilepsy achieve seizure freedom with medical treatment?**

About 70% of patients achieve seizure freedom with appropriate medical treatment, and

most of these children respond to the initially prescribed drug.

- **Valproic acid (or sodium valproate, or Epilim) is now increasingly used for certain types of epilepsy. Which type of epilepsy responds best to sodium valproate? What are some of the toxicities of sodium valproate, and how can they be monitored?**

Sodium valproate is the best drug for generalised epilepsy, and is also effective against some forms of focal epilepsy. Sodium valproate may cause hepatic toxicity (1%) and pancreatitis (<0.1%), but routine monitoring LFTs does not usually help to predict which children will develop these complications. If a child on sodium valproate has vomiting or develops jaundice or poor conscious state, it is possible it is a side effect of the drug. Sodium valproate is teratogenic, so should not be given to adolescent girls or women of child-bearing age. It is an enzyme inhibitor, and inhibits the metabolic inactivation of zidovudine (AZT), which may prolong the plasma half-life of AZT and thus prolong the duration of the drug's effects in the body. However sodium valproate has been used safely and effectively in adults with HIV on HAART who also have epilepsy.

Epilepsy care challenges in developing countries

Kvalsund MP, et al. Current Opinion in Neurology 2012; 25:179-186

- **Name 5 infectious pathogens that are associated with development of epilepsy.**

Bacterial meningitis – H. influenzae, S. pneumoniae, N. meningitidis

E.coli or Group B streptococcus (neonatal meningitis)

Viral encephalitis (e.g. Japanese encephalitis virus, enterovirus, parechovirus)

Malaria

Neurocysticercosis

Tuberculosis granuloma

HIV

Dengue

- **Which commonly used antiepileptic drugs interact with anti-retroviral agents, and what is the mechanism?**

Phenytoin (an enzyme inducer) reduces lopinavir/ritonavir (a protease inhibitor) by 50%
Avoid enzyme-inducing agents (phenytoin, phenobarbitone, carbamazepine) in children on protease inhibitors.

Valproic acid (enzyme inhibitor) increases zidovudine (AZT), so children with epilepsy and HIV who are on sodium valproate may require a dose reduction in AZT to maintain unchanged serum AZT concentrations.

Integrated care for childhood epilepsy

Bali A, et al. Arch Dis Child 2016; 101: 1057-1062

- **Besides seizure freedom, what are the other important goals of treating children with epilepsy?**

Seizure freedom is an important goal, but is just one important outcome alongside others such as improved school attendance, educational attainment, freedom from AED complications, improved self-esteem and knowledge of epilepsy by the child and family.

- **What are the components of a model to improve epilepsy care? How could such principles be applied in PNG?**

Children with epilepsy need:

- An individualised care plan, which outlines the type of epilepsy the child has, the seizure frequency, other comorbidities, the AED treatment the child receives, an action plan for the parents and health workers when the child has a seizure, and contact people.
- A doctor or other health worker who knows the child and the family well, and is able to follow the child long-term.
- A parents' diary, which documents the frequency and duration of seizures, days when school was missed, days when medications were missed (and reasons why), and any other notes the parents want to write, so that upon clinic review this information does not need to be recalled.
- An epilepsy register, so that data on the proportion of children with successful treatment (i.e. remission or low seizure frequency), and complications, including SUDEP or episodes of status epilepticus can be summarised.
- Paediatric nurses trained in epilepsy
- Improved communication between families, the child, the medical and nursing team, and the school that the child attends
- Education for the child, peer-to-peer education can be most effective for school aged children and adolescents.